This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organisation, or the World Health Organization.

Concise International Chemical Assessment Document 1

1,2-DICHLOROETHANE

First draft prepared by Ms K. Hughes and Ms M.E. Meek,
Environmental Health Directorate,
Health Canada

Please note that the layout and pagination of this pdf file are not identical to the printed CICAD

Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

World Health Organization
Geneva, 1998
The **International Programme on Chemical Safety (IPCS)**, established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organisation (ILO), and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The **Inter-Organization Programme for the Sound Management of Chemicals (IOMC)** was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

WHO Library Cataloguing in Publication Data

1,2-Dichloroethane.

(Concise international chemical assessment document ; 1)

4.Environmental exposure  I.International Programme for Chemical Safety  II.Series

ISBN 92 4 153001 4  (NLM Classification: QV 633)
ISSN 1020-6167

The World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full. Applications and enquiries should be addressed to the Office of Publications, World Health Organization, Geneva, Switzerland, which will be glad to provide the latest information on any changes made to the text, plans for new editions, and reprints and translations already available.

©World Health Organization 1998

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. All rights reserved.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city, or area of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers’ products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The Federal Ministry for the Environment, Nature Conservation and Nuclear Safety, Germany, provided financial support for the printing of this publication.

Printed by Wissenschaftliche Verlagsgesellschaft mbH, D-70009 Stuttgart 10
<table>
<thead>
<tr>
<th>TABLE OF CONTENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOREWORD</strong></td>
</tr>
<tr>
<td><strong>1. EXECUTIVE SUMMARY</strong></td>
</tr>
<tr>
<td><strong>2. IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES</strong></td>
</tr>
<tr>
<td><strong>3. ANALYTICAL METHODS</strong></td>
</tr>
<tr>
<td><strong>4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE</strong></td>
</tr>
<tr>
<td><strong>5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION</strong></td>
</tr>
<tr>
<td><strong>6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE</strong></td>
</tr>
<tr>
<td>6.1 Environmental levels</td>
</tr>
<tr>
<td>6.2 Human exposure</td>
</tr>
<tr>
<td><strong>7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS</strong></td>
</tr>
<tr>
<td><strong>8. EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS</strong></td>
</tr>
<tr>
<td>8.1 Single exposure</td>
</tr>
<tr>
<td>8.2 Irritation and sensitization</td>
</tr>
<tr>
<td>8.3 Short-term exposure</td>
</tr>
<tr>
<td>8.4 Long-term exposure</td>
</tr>
<tr>
<td>8.4.1 Subchronic exposure</td>
</tr>
<tr>
<td>8.4.2 Chronic exposure and carcinogenicity</td>
</tr>
<tr>
<td>8.5 Genotoxicity and related end-points</td>
</tr>
<tr>
<td>8.6 Reproductive and developmental toxicity</td>
</tr>
<tr>
<td>8.7 Immunological and neurological effects</td>
</tr>
<tr>
<td><strong>9. EFFECTS ON HUMANS</strong></td>
</tr>
<tr>
<td>9.1 Case reports</td>
</tr>
<tr>
<td>9.2 Epidemiological studies</td>
</tr>
<tr>
<td><strong>10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD</strong></td>
</tr>
<tr>
<td>10.1 Aquatic environment</td>
</tr>
<tr>
<td>10.2 Terrestrial environment</td>
</tr>
<tr>
<td><strong>11. EFFECTS EVALUATION</strong></td>
</tr>
<tr>
<td>11.1 Evaluation of health effects</td>
</tr>
<tr>
<td>11.1.1 Hazard identification and dose–response assessment</td>
</tr>
<tr>
<td>11.1.2 Criteria for setting guidance values for 1,2-dichloroethane</td>
</tr>
<tr>
<td>11.1.3 Sample risk characterization</td>
</tr>
<tr>
<td>11.2 Evaluation of environmental effects</td>
</tr>
<tr>
<td><strong>12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES</strong></td>
</tr>
</tbody>
</table>
FOREWORD

Concise International Chemical Assessment Documents (CICADs) are the latest in a family of publications from the International Programme on Chemical Safety (IPCS) — a cooperative programme of the World Health Organization (WHO), the International Labour Organisation (ILO), and the United Nations Environment Programme (UNEP). CICADs join the Environmental Health Criteria documents (EHCs) as authoritative documents on the risk assessment of chemicals.

CICADs are concise documents that provide summaries of the relevant scientific information concerning the potential effects of chemicals upon human health and/or the environment. They are based on selected national or regional evaluation documents or on existing EHCs. Before acceptance for publication as CICADs by IPCS, these documents have undergone extensive peer review by internationally selected experts to ensure their completeness, accuracy in the way in which the original data are represented, and the validity of the conclusions drawn.

The primary objective of CICADs is characterization of hazard and dose–response from exposure to a chemical. CICADs are not a summary of all available data on a particular chemical; rather, they include only that information considered critical for characterization of the risk posed by the chemical. The critical studies are, however, presented in sufficient detail to support the conclusions drawn. For additional information, the reader should consult the identified source documents upon which the CICAD has been based.

Risks to human health and the environment will vary considerably depending upon the type and extent of exposure. Responsible authorities are strongly encouraged to characterize risk on the basis of locally measured or predicted exposure scenarios. To assist the reader, examples of exposure estimation and risk characterization are provided in CICADs, whenever possible. These examples cannot be considered as representing all possible exposure situations, but are provided as guidance only. The reader is referred to EHC 170\(^1\) for advice on the derivation of health-based guidance values.

While every effort is made to ensure that CICADs represent the current status of knowledge, new information is being developed constantly. Unless otherwise stated, CICADs are based on a search of the scientific literature to the date shown in the executive summary. In the event that a reader becomes aware of new information that would change the conclusions drawn in a CICAD, the reader is requested to contact the IPCS to inform it of the new information.

Procedures

The flow chart shows the procedures followed to produce a CICAD. These procedures are designed to take advantage of the expertise that exists around the world — expertise that is required to produce the high-quality evaluations of toxicological, exposure, and other data that are necessary for assessing risks to human health and/or the environment.

The first draft is based on an existing national, regional, or international review. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The first draft undergoes primary review by IPCS and one or more experienced authors of criteria documents to ensure that it meets the specified criteria for CICADs.

The second stage involves international peer review by scientists known for their particular expertise and by scientists selected from an international roster compiled by IPCS through recommendations from IPCS national Contact Points and from IPCS Participating Institutions. Adequate time is allowed for the selected experts to undertake a thorough review. Authors are required to take reviewers’ comments into account and revise their draft, if necessary. The resulting second draft is submitted to a Final Review Board together with the reviewers’ comments.

The CICAD Final Review Board has several important functions:

- to ensure that each CICAD has been subjected to an appropriate and thorough peer review;
- to verify that the peer reviewers’ comments have been addressed appropriately;
- to provide guidance to those responsible for the preparation of CICADs on how to resolve any remaining issues if, in the opinion of the Board, the author has not adequately addressed all comments of the reviewers; and
- to approve CICADs as international assessments.

Concise International Chemical Assessment Document 1

CICAD PREPARATION FLOW CHART

1. SELECTION OF PRIORITY CHEMICAL
2. SELECTION OF HIGH QUALITY NATIONAL/REGIONAL ASSESSMENT DOCUMENT(S)
3. FIRST DRAFT PREPARED
4. PRIMARY REVIEW AT PRODUCER LEVEL
   (1-2 OTHER DOCUMENT PRODUCERS)
5. REVIEW BY IPCS CONTACT POINTS
6. REVIEW OF COMMENTS (PRODUCER/RO), PREPARATION OF SECOND DRAFT
7. FINAL REVIEW BOARD
8. FINAL DRAFT
9. EDITING
10. APPROVAL BY DIRECTOR, IPCS
11. PUBLICATION

1 Revision as necessary.
2 Taking into account the comments from reviewers.
3 The second draft of documents is submitted to the Final Review Board together with the reviewers’ comments (6-10 CICADs are usually reviewed at the Final Review Board). In the case of pesticides the role of the Final Review Board is fulfilled by a joint meeting on pesticides.
4 Includes any revisions requested by the Final Review Board.
Board members serve in their personal capacity, not as representatives of any organization, government, or industry. They are selected because of their expertise in human and environmental toxicology or because of their experience in the regulation of chemicals. Boards are chosen according to the range of expertise required for a meeting and the need for balanced geographic representation.

Board members, authors, reviewers, consultants, and advisers who participate in the preparation of a CICAD are required to declare any real or potential conflict of interest in relation to the subjects under discussion at any stage of the process. Representatives of nongovernmental organizations may be invited to observe the proceedings of the Final Review Board. Observers may participate in Board discussions only at the invitation of the Chairperson, and they may not participate in the final decision-making process.
1. EXECUTIVE SUMMARY

This CICAD on 1,2-dichloroethane was prepared by the Environmental Health Directorate of Health Canada based on an International Programme on Chemical Safety (IPCS) Environmental Health Criteria (EHC) document (IPCS, 1995), which assesses the potential effects on human health of indirect exposure to 1,2-dichloroethane in the general environment as well as the chemical’s environmental effects. Data identified as of May 1993 (human health effects) and October 1994 (environmental effects) were considered in these reviews. Information on the nature of the peer review process and the availability of the EHC document is presented in Appendix 1. For this CICAD, the peer review process prior to consideration by the Final Review Board was covered by the peer review carried out for the EHC. This CICAD on 1,2-dichloroethane was finalized and approved for publication, through correspondence, by members of the Final Review Board, who also considered the peer review comments provided during the development of the EHC. The composition of the Final Review Board is outlined in Appendix 2. The International Chemical Safety Card (ICSC 0250) produced by the IPCS (1993) has also been reproduced in this document.

1,2-Dichloroethane (CAS no. 107-06-2) is a volatile, synthetic hydrocarbon that is used principally in the synthesis of vinyl chloride monomer and other chlorinated solvents. It has also been used as a leaded gasoline additive and a fumigant, although its use as a gasoline additive is declining. The majority of environmental releases are to ambient air, where it is moderately persistent. However, it is not expected to contribute to ozone depletion. 1,2-Dichloroethane has a low potential for bioaccumulation; inhalation in air is likely the primary source of human exposure.

Little information is available on the effects of 1,2-dichloroethane in humans. The few identified epidemiological investigations on its potential carcinogenicity are inconclusive.

1,2-Dichloroethane is moderately acutely toxic in experimental animals. Limited information on non-neoplastic effects presented in short-term, subchronic, and chronic studies indicates that the liver and kidneys are the principal target organs; lowest reported effect levels for ingestion and inhalation were 49–82 mg/kg body weight per day (increases in liver weight in rats exposed for 13 weeks) and 202 mg/m³ (effects on liver and kidney function in rats exposed for 12 months), respectively. Based on the results of a limited number of studies, there is no evidence that 1,2-dichloroethane is teratogenic in experimental animals or that it induces reproductive or developmental effects at levels of exposure lower than those that cause other systemic effects.

Exposure to 1,2-dichloroethane by gavage for 78 weeks induced a significant increase in the incidence of tumours at several sites (including haemangiosarcomas and tumours of the stomach, mammary gland, liver, lung, and endometrium) in both rats and mice. Although there were no significant increases in tumour incidence in rats or mice exposed via inhalation, repeated dermal or intraperitoneal application of 1,2-dichloroethane resulted in an increase in lung tumours in mice. 1,2-Dichloroethane has been consistently genotoxic in numerous in vitro assays in prokaryotes, fungi, and mammalian (including human) cells. Similarly, results were consistently positive for genotoxic activity (as well as binding to DNA) in in vivo studies in rats, mice, and insects.

The lowest reported IC₅₀s and EC₅₀s for various end-points in aquatic organisms were 25 and 105 mg/litre, respectively. The lowest reported LC₅₀ value for Daphnia was 220 mg/litre, whereas effects on reproduction occurred at 20.7 mg/litre. The most sensitive freshwater vertebrate tested was the northwestern salamander (Ambystoma gracile), in which reduced larval survival was observed at 2.5 mg/litre. Only limited data are available on the effects of 1,2-dichloroethane on terrestrial species.

Based on available data, 1,2-dichloroethane is considered to be a probable human carcinogen, and therefore exposure should be reduced to the extent possible. The carcinogenic potency (expressed as the dose associated with a 5% increase in tumour incidence), derived on the basis of studies in which animals were exposed by gavage, was calculated to be 6.2–34 mg/kg body weight per day. Guidance values for air (the principal source of human exposure) of 3.6–20 µg/m³ or 0.36–2.0 µg/m³, calculated on the basis of a margin 5000- or 50 000-fold less than the estimated carcinogenic potency, have been derived; however, it should be noted that risks are overestimated on this basis, as available data indicate that 1,2-dichloroethane is less potent when inhaled. (Corresponding values for ingestion are 1.2–6.8 µg/kg body weight per day or 0.12–0.68 µg/kg body weight per day.) These values correspond to those considered by some agencies to represent “essentially negligible” risk (i.e. 10⁻³ to 10⁻⁶ for a genotoxic carcinogen). Based on a sample estimate, indirect exposure in the general environment is up to approximately 300 times less than these values.
2. IDENTIFY AND PHYSICAL/CHEMICAL PROPERTIES

1,2-Dichloroethane (CAS no. 107-06-2; ethylene dichloride, dichlоро-1,2-ethane; see structural diagram below) is a synthetic chemical that is a colourless liquid at room temperature. It is also highly volatile, with a vapour pressure of 8.5 kPa (at 20°C), and soluble in water, with a solubility of 8690 mg/litre (at 20°C). The log octanol/water partition coefficient of 1,2-dichloroethane is 1.76. Additional physical/chemical properties are presented in the International Chemical Safety Card, reproduced in this document.

3. ANALYTICAL METHODS

Analysis for 1,2-dichloroethane in environmental media is usually by gas chromatography, in combination with electron capture detection, flame ionization detection, or mass spectrometry. Detection limits range from 0.016 to >4 \( \mu \text{g/m}^3 \) for air, from 0.001 to 4.7 \( \mu \text{g/litre} \) for water, and from 6 to 10 \( \mu \text{g/kg} \) for various foodstuffs (ATSDR, 1992).

4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

There are no known natural sources of 1,2-dichloroethane. The principal use for 1,2-dichloroethane is in the synthesis of vinyl chloride monomer and, to a lesser extent, in the manufacture of various chlorinated solvents. It is also incorporated into antiknock gasoline additives (although this use is declining with the phase-out of leaded gasoline in some countries) and has been used as a fumigant. Total annual production of 1,2-dichloroethane in Canada (1990) and the USA (1991) is about 922 and 6318 kt, respectively (CPL, 1991; Chemical Marketing Reporter, 1992).

5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

The majority of 1,2-dichloroethane released to the environment is in emissions to air. 1,2-Dichloroethane is moderately persistent in air; its estimated atmospheric lifetime is between 43 and 111 days. Small amounts of 1,2-dichloroethane are transported to the stratosphere, where photolysis may produce chlorine radicals, which may in turn react with ozone (Spence & Hanst, 1978; Callaghan et al., 1979). Some 1,2-dichloroethane may be released in industrial effluents to the aquatic environment, from where it is removed rapidly by volatilization (Dilling et al., 1975). 1,2-Dichloroethane may also leach to groundwater near industrial waste sites. It is not expected to bioconcentrate in aquatic or terrestrial species.

6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

6.1 Environmental levels

Data considered to be most representative of current levels of 1,2-dichloroethane in environmental media are summarized in Table 1. Mean concentrations of 1,2-dichloroethane in surveys of ambient air in non-source-dominated areas in cities are 0.07–0.28 \( \mu \text{g/m}^3 \) in Canada, <0.004–3.8 \( \mu \text{g/m}^3 \) in Japan, and 1.2 \( \mu \text{g/m}^3 \) in the United Kingdom and the Netherlands. Earlier surveys in the USA reported mean levels of 0.33–6.05 \( \mu \text{g/m}^3 \); however, peak levels near chemical manufacturing plants have ranged as high as 736 \( \mu \text{g/m}^3 \) (US EPA, 1985). Mean levels in residential indoor air are reported to be <0.1 \( \mu \text{g/m}^3 \) in Canada, 0.1–0.5 \( \mu \text{g/m}^3 \) in the USA, and 3.4 \( \mu \text{g/m}^3 \) in the Netherlands.

In drinking-water, mean 1,2-dichloroethane concentrations are generally less than 0.5 \( \mu \text{g/litre} \), based on the results of surveys in Canada, the USA, Japan, and Spain. Although there are few recent data, 1,2-dichloroethane has only very rarely been detected in surface water at concentrations greater than 10 \( \mu \text{g/litre} \).

1,2-Dichloroethane has only rarely been detected in foodstuffs in extensive surveys in Canada and the USA. Also, as 1,2-dichloroethane has low potential for bioaccumulation, food is unlikely to be a major source of exposure.
Table 1: Levels of 1,2-dichloroethane in environmental media.

<table>
<thead>
<tr>
<th>Medium</th>
<th>Location</th>
<th>Year</th>
<th>Concentrations</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient air</td>
<td>Canada</td>
<td>1988–1990</td>
<td>0.07–0.28 : g/m$^3$ (means)</td>
<td>T. Dann, unpublished data, 1992</td>
</tr>
<tr>
<td>Ambient air</td>
<td>Japan</td>
<td>1992</td>
<td>&lt;0.004–3.8 : g/m$^3$ (means)</td>
<td>Environment Agency Japan, 1993</td>
</tr>
<tr>
<td>Ambient air</td>
<td>UK</td>
<td>1982, 1983</td>
<td>1.2 : g/m$^3$ (mean)</td>
<td>Clark et al., 1984a,b</td>
</tr>
<tr>
<td>Ambient air</td>
<td>Netherlands</td>
<td>1980</td>
<td>1.2 : g/m$^3$ (mean)</td>
<td>Guicherit &amp; Schulting, 1985</td>
</tr>
<tr>
<td>Ambient air</td>
<td>USA</td>
<td>1980–1982</td>
<td>0.33–6.05 : g/m$^3$ (means)</td>
<td>Singh et al., 1980, 1981, 1982</td>
</tr>
<tr>
<td>Indoor air (residential)</td>
<td>Canada</td>
<td>1991</td>
<td>&lt;0.1 : g/m$^3$ (mean)</td>
<td>Fellin et al., 1992</td>
</tr>
<tr>
<td>Indoor air (residential)</td>
<td>USA</td>
<td>1984–1985</td>
<td>0.1–0.5 : g/m$^3$ (means)</td>
<td>US EPA, 1992</td>
</tr>
<tr>
<td>Indoor air (residential)</td>
<td>Netherlands</td>
<td>1984–1985</td>
<td>3.4 : g/m$^3$ (mean)</td>
<td>Kliest et al., 1989</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>Canada</td>
<td>1988–1991</td>
<td>&lt;0.05–0.139 : g/litre (mean)</td>
<td>P. Lachmaniuk, personal communication, 1991</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>USA</td>
<td>1990</td>
<td>0.2 : g/litre (mean)</td>
<td>Ecobichon &amp; Allen, 1990</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>USA</td>
<td>Early 1980s</td>
<td>ND – 19 : g/litre</td>
<td>Letkiewicz et al., 1982</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>Japan</td>
<td>1976</td>
<td>&lt;0.5–0.9 : g/litre</td>
<td>Fujii, 1977</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>Spain</td>
<td>1987</td>
<td>2–22 : g/litre</td>
<td>Freiria-Gandara et al., 1992</td>
</tr>
<tr>
<td>Surface water</td>
<td>Canada</td>
<td>1981–1985</td>
<td>&lt;0.08 : g/litre</td>
<td>Kaiser et al., 1985; Comba &amp; Kiser, 1985; Kiser &amp; Comba, 1986; Lum &amp; Kiser, 1986</td>
</tr>
<tr>
<td>Surface water</td>
<td>Japan</td>
<td>1992</td>
<td>0.01–3.4 : g/litre</td>
<td>Environment Agency Japan, 1993</td>
</tr>
<tr>
<td>Food (34 groups)</td>
<td>Canada</td>
<td>1991</td>
<td>&lt;50 : g/kg (solids); &lt;1 : g/litre (liquids)</td>
<td>Enviro-Test Laboratories, 1991</td>
</tr>
<tr>
<td>Food (19 items)</td>
<td>USA</td>
<td>Not specified</td>
<td>ND – 0.31 : g/kg</td>
<td>Heikes, 1987, 1990</td>
</tr>
<tr>
<td>Food (231 items)</td>
<td>USA</td>
<td>Not specified</td>
<td>ND – 8.2 : g/kg</td>
<td>Heikes, 1987</td>
</tr>
</tbody>
</table>

Detection limit not reported.

6.2 Human exposure

An example of estimated indirect exposure in the general environment is presented here. Exposure of the general population to 1,2-dichloroethane in environmental media may be estimated based on concentrations determined in various media and reference values for body weight and consumption patterns. Owing to the availability of relevant data, exposure has been estimated based primarily on data from North America. However, countries are encouraged to estimate total exposure on the basis of national data, possibly in a manner similar to that outlined here.

Based on a daily inhalation volume for adults of 22 m$^3$, a mean body weight for males and females of 64 kg, the assumption that 4 of 24 hours are spent outdoors (IPCS, 1994), and the range of mean levels of 1,2-dichloroethane in ambient air of 0.07–0.28 : g/m$^3$ in a survey of cities across Canada, the mean intake of 1,2-dichloroethane from ambient air for the general population is estimated to range from 0.004 to 0.02 : g/kg body weight per day. The mean intake of 1,2-dichloroethane in indoor air, based on the assumption that 20 of 24 hours are spent indoors (IPCS, 1994) and the range of concentrations in indoor or “personal” air in Canada and the USA of <0.1–0.5 : g/m$^3$, is estimated to range from <0.03 to 0.1 : g/kg body weight per day. Based on a daily volume of water consumption for adults of 1.4 litres, a mean body weight of 64 kg (IPCS, 1994), and the mean levels of 1,2-dichloroethane in provincial surveys in Canada of <0.05–0.139 : g/litre, the mean intake from drinking-water is estimated to range from <0.001 to 0.003 : g/kg body weight per day. Intake of 1,2-dichloroethane in food is likely to be negligible, as it has not been detected in extensive surveys and as it has low potential for bioaccumulation. Therefore, the principal source of exposure of the general population to 1,2-dichloroethane is indoor and outdoor air, with only minor amounts being contributed by drinking-water.

Few data on occupational exposure to 1,2-dichloroethane were identified. In North America, workers are exposed to 1,2-dichloroethane principally in the manufacture of other chemical substances; in such situations, the principal route of exposure is most likely inhalation and, possibly, dermal contact.
7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

1,2-Dichloroethane is readily absorbed following inhalation, ingestion, and dermal exposure and is rapidly and widely distributed throughout the body. Relative distribution of radioactivity (presumably as metabolites) was similar in rats administered a single oral dose of 150 mg/kg body weight and those exposed by inhalation to 150 ppm (600 mg/m$^3$) for 6 hours (Reitz et al., 1982). 1,2-Dichloroethane is rapidly and extensively metabolized in rats and mice, with principally sulfur-containing metabolites being eliminated in the urine in a dose-dependent manner. Metabolism appears to be saturated or limited in rats at levels of exposure resulting in concentrations in blood of 5–10 g/ml (Reitz et al., 1982). Levels of DNA alkylation were higher following exposure to a bolus dose of 150 mg/kg body weight by gavage compared with inhalation of 150 ppm (600 mg/m$^3$) over a 6-hour period (Reitz et al., 1982).

Available data suggest that 1,2-dichloroethane is metabolized via two principal pathways. The first involves a saturable microsomal oxidation mediated by cytochrome P-450 to 2-chloroacetaldehyde and 2-chloroethanol, followed by conjugation with glutathione. The second pathway entails direct conjugation with glutathione to form S-(2-chloroethyl)-glutathione, which may be non-enzymatically converted to a glutathione episulfonium ion; this ion can form adducts with proteins, DNA, or RNA. Although DNA damage has been induced by the P-450 pathway in vitro (Banerjee et al., 1980; Guengerich et al., 1980; Lin et al., 1985), several lines of evidence indicate that the glutathione conjugation pathway is probably of greater significance than the P-450 pathway as the major route for DNA damage (Guengerich et al., 1980; Rannug, 1980; Sundheimer et al., 1982; Inskeep et al., 1986; Koga et al., 1986; Simula et al., 1993).

8. EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS

8.1 Single exposure

1,2-Dichloroethane is moderately acutely toxic in experimental animals. For example, LC$_{50}$s for rats exposed by inhalation for 6 or 7.25 hours ranged from 4000 mg/m$^3$ (Spencer et al., 1951) to 6600 mg/m$^3$ (Bonnet et al., 1980), whereas oral LD$_{50}$s for rats, mice, dogs, and rabbits ranged from 413 to 2500 mg/kg body weight (Barsoum & Saad, 1934; McCollister et al., 1956; Smyth, 1969; Larionov and Kokarovtseva, 1976; Munson et al., 1982; NIOSH, 1994a).

8.2 Irritation and sensitization

Application of 1,2-dichloroethane to the skin of experimental animals has resulted in microscopic changes and moderate oedema (Duprat et al., 1976; Kronevi et al., 1981; Jakobson et al., 1982). Similarly, histological changes and mild irritation in the eye have been observed in animals following direct application (Kuwabara et al., 1968; Duprat et al., 1976). No information on the sensitization potential of this substance was identified.

8.3 Short-term exposure

Few data were identified on the toxicity of 1,2-dichloroethane following short-term exposure. Degeneration and necrosis of the liver and kidneys, accompanied by congestion and haemorrhage of the lungs and adrenal glands, were observed in small groups of rats, rabbits, guinea-pigs, dogs, and pigs exposed to 1,2-dichloroethane by inhalation at 6000 mg/m$^3$, 7 hours/day, for 6 days (Heppel et al., 1945). No effects on body or organ weights, histology, or clinical chemistry were noted in rats administered oral doses of up to 150 mg/kg body weight per day for 2 weeks (van Esch et al., 1977; Reitz et al., 1982).

8.4 Long-term exposure

8.4.1 Subchronic exposure

The results of subchronic studies in several species of experimental animals indicate that the liver and kidneys are the target organs of 1,2-dichloroethane exposure; however, most of these studies were inadequate to serve as a basis for establishing reliable no-observed-effect levels or lowest-observed-effect levels, generally because of the inadequate documentation and the limited range of end-points examined in small groups of animals. In a series of early limited studies, morphological changes in the liver were observed in several species following subchronic exposure (7 hours/day) to airborne concentrations as low as 800 mg/m$^3$ (Heppel et al., 1946; Spencer et al., 1951; Hofmann et al., 1971). Increases in relative liver weight have been observed in rats following subchronic oral administration of doses of 49–82 mg/kg body weight per day and above for 13 weeks (van Esch et al., 1977; NTP, 1991).
8.4.2 Chronic exposure and carcinogenicity

Little information was presented on non-neoplastic effects in available chronic studies. Changes in serum parameters indicative of liver and kidney toxicity were observed in groups of 8–10 male or female Sprague-Dawley rats exposed to airborne concentrations as low as 202 mg/m³ for 12 months, although histopathological examinations were not conducted in this study (Spreadco et al., 1980).

The carcinogenicity of 1,2-dichloroethane has been investigated in a few limited bioassays in experimental animals (limits include short duration of exposure and high mortality). In an inhalation study, no significant increase in the incidence of any type of tumour was reported in groups of 90 male or female Sprague-Dawley rats exposed to concentrations of 1,2-dichloroethane up to 150 ppm (607 mg/m³), 7 hours/day, 5 days/week, for 78 weeks and observed until spontaneous death (Maltoni et al., 1980). However, mortality was high in this study, although it was not related to concentration, and incidence rates were not adjusted for differential mortality among groups. There was a non-significant increase in the incidence of mammary gland adenomas and fibroadenomas in female Sprague-Dawley rats (n = 50) exposed to 1,2-dichloroethane at 50 ppm (200 mg/m³), 7 hours/day, 5 days/week, for 2 years in an assay in which no other compound-related toxicity was observed (Cheever et al., 1990). No increase in the incidence of any type of tumour was observed in groups of 90 male or female Swiss mice exposed to concentrations of 1,2-dichloroethane up to 150 ppm (607 mg/m³), 7 hours/day, 5 days/week, for 78 weeks and observed until spontaneous death (Maltoni et al., 1980).

In contrast, there has been convincing evidence of increases in tumour incidence in two species following ingestion. There were significant increases in the incidence of tumours at several sites in Osborne-Mendel rats (n = 50 of each sex in exposed groups; n = 20 matched controls; n = 60 pooled controls) administered time-weighted-average doses of 47 or 195 mg/kg body weight per day (males) and 149 or 299 mg/kg body weight per day (females) in corn oil by gavage, 5 days/week, for 78 weeks, followed by 13 weeks of observation. The incidence of hepatocellular carcinomas was significantly increased in exposed males (4/59, 1/19, 6/47, and 12/48 in pooled vehicle controls, matched vehicle controls, low-dose group, and high-dose group, respectively), although the authors noted that the increase in the incidence of this tumour could not be convincingly attributed to the test chemical, owing to the high variability of hepatocellular neoplasms among historical controls. The incidence of alveolar/bronchiolar adenomas was significantly increased in males in the high-dose group (0/59, 0/19, 1/47, and 15/48) and in both groups of exposed females (2/60, 1/20, 7/50, and 15/48); one female in the high-dose group had an alveolar/bronchiolar carcinoma. The incidence of mammary gland adenocarcinomas was significantly increased in females at both doses (0/60, 0/20, 9/50, and 7/48). The incidence of endometrial stromal polyp or endometrial stromal sarcoma (combined) in females was significantly elevated at both doses (0/60, 0/20, 5/49, and 5/47). There was a dose-related increase in mortality in females, but not in males; in addition, body weight was decreased in females receiving the higher dose (NCI, 1978).

In a similar bioassay, B6C3F1 mice (n = 50 of each sex in exposed groups; n = 20 matched controls; n = 60 pooled controls) were administered time-weighted-average doses of 97 or 195 mg/kg body weight per day (males) and 149 or 299 mg/kg body weight per day (females) in corn oil by gavage, 5 days/week, for 78 weeks. Concomitant exposure to disulfiram in the diet resulted in an increased incidence of hepatocellular carcinoma in rats, compared with rats administered either compound alone or...
untreated controls (Cheever et al., 1990). No potential to initiate or promote tumour development was evident in three bioassays (van Duuren et al., 1979; Klaunig et al., 1986; Story et al., 1986; Milman et al., 1988), although the extent of histopathological examination was limited in these studies.

8.5 Genotoxicity and related end-points

1,2-Dichloroethane has been consistently demonstrated to be genotoxic in numerous in vitro (Table 2) and in vivo (Table 3) assays for a wide range of end-points. It has been mutagenic in Salmonella typhimurium, especially in the presence of an exogenous activation system, and induces unscheduled DNA synthesis, induces gene mutation, and forms adducts with DNA in mammalian cells in vitro. It binds to DNA in all reported in vivo studies in rats and mice. 1,2-Dichloroethane has also induced somatic cell and sex-linked recessive lethal mutations in Drosophila melanogaster.

Available data on genotoxicity are consistent with the hypothesis that the glutathione pathway of conjugation (i.e. production of the glutathione episulfonium ion) is probably of greater significance than the P-450 pathway as the major route for DNA damage (Guengerich et al., 1980; Rannug, 1980; Sundheimer et al., 1982; Inskeep et al., 1986; Koga et al., 1986; Simula et al., 1993); mutation frequency in human cell lines has been correlated with variations in levels of glutathione-S-transferase activities (Crespi et al., 1985).

8.6 Reproductive and developmental toxicity

Based on the results of a limited number of studies, there is no evidence that 1,2-dichloroethane is teratogenic in experimental animals and little convincing evidence that it induces reproductive or developmental effects at doses below those that cause other systemic effects (Alumot et al., 1976; Vozovaya, 1977; Kavlock et al., 1979; Rao et al., 1980; Lane et al., 1982).

8.7 Immunological and neurological effects

Immunological effects, including reduced resistance to streptococcal challenge, decreased pulmonary bactericidal activity in mice, and altered levels of antibody production in rabbits, have been observed following acute or subchronic exposure to 1,2-dichloroethane at 20 and 10 mg/m³ and above, respectively (Shmuter, 1977; Sherwood et al., 1987), whereas there were no effects in rats exposed to up to 800 mg/m³ for several days (Sherwood et al., 1987).

Effects on antibody levels and reversible effects on cell-mediated responses were also noted in mice exposed to 1,2-dichloroethane in drinking-water at concentrations equivalent to doses of 3 mg/kg body weight per day and above for 14 or 90 days (Munson et al., 1982).

Data on the neurological effects of 1,2-dichloroethane have not been identified.

9. EFFECTS ON HUMANS

9.1 Case reports

Acute incidental exposure to 1,2-dichloroethane by inhalation or ingestion has resulted in a variety of effects in humans, including effects on the central nervous system, liver, kidney, lung, and cardiovascular system (e.g. Hinkel, 1965; Suveev & Babichenko, 1969; Dorndorf et al., 1975; Andriukin, 1979; Nouchi et al., 1984). Based on limited available data in humans, the lethal oral dose of 1,2-dichloroethane has been estimated to be between 20 and 50 ml.

9.2 Epidemiological studies

The potential carcinogenicity of 1,2-dichloroethane in exposed human populations has not been extensively investigated. Mortality due to pancreatic cancer was significantly increased (standardized mortality ratio [SMR] = 492, based on eight cases) in a group of 278 workers at a chemical production plant who had been principally exposed to 1,2-dichloroethane in combination with other chemicals. Mortality due to this cause increased with duration of exposure. In addition, although the number of cases was small (i.e. four) and the association with duration of exposure was less consistent, mortality due to leukaemia was also increased in these workers (Benson & Teta, 1993).

No association between occupational exposure to 1,2-dichloroethane and brain cancer was noted in a small case–control study (Austin & Schnatter, 1983). Although the incidence of colon and rectal cancer increased with concentration of 1,2-dichloroethane in drinking-water in an inherently limited ecological study, concomitant exposure to other substances may have contributed to the observed effects (Isacson et al., 1985).
Table 2: Genotoxicity of 1,2-dichloroethane in vitro (modified from ATSDR, 1992).

<table>
<thead>
<tr>
<th>Result</th>
<th>With activation</th>
<th>Without activation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROKARYOTIC SYSTEMS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmonella typhimurium</td>
<td>Gene mutation</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>NT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>S. typhimurium/spot test</td>
<td>Gene mutation</td>
<td>NT</td>
<td>(+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(+)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td>S. typhimurium/Ara test (standard)</td>
<td>Gene mutation</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>S. typhimurium/Ara test (liquid)</td>
<td>Gene mutation</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Streptomyces coelicolor</td>
<td>Gene mutation</td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td>Escherichia coli K12/343/113</td>
<td>Gene mutation</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>E. coli Pol II</td>
<td>Gene mutation</td>
<td>NT</td>
<td>(+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>E. coli Pol A</td>
<td>DNA damage</td>
<td>NT</td>
<td>(+)</td>
</tr>
<tr>
<td>Bacillus subtilis/rec assay</td>
<td>DNA damage</td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td>EUKARYOTIC ORGANISMS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— FUNGI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspergillus nidulans</td>
<td>Gene mutation</td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td>A. nidulans</td>
<td>Mitotic segregation aberrations</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>A. nidulans</td>
<td>Aneuploidy induction</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Saccharomyces cerevisiae</td>
<td>Mitotic recombination</td>
<td>NT</td>
<td>(+)</td>
</tr>
<tr>
<td>— ANIMAL SYSTEMS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamster CHO/HGPRT</td>
<td>Gene mutation</td>
<td>+</td>
<td>(+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>(+)</td>
</tr>
<tr>
<td>Rat hepatocytes</td>
<td>Unscheduled DNA synthesis</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Mouse hepatocytes</td>
<td>Unscheduled DNA synthesis</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Mouse liver DNA</td>
<td>DNA binding</td>
<td>+</td>
<td>NT</td>
</tr>
<tr>
<td>Calf thymus DNA</td>
<td>DNA binding</td>
<td>+</td>
<td>NT</td>
</tr>
<tr>
<td>Salmon sperm DNA</td>
<td>DND binding</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Mouse BALB/c-3T3</td>
<td>Cell transformation</td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td>Mouse C3H10T1/2</td>
<td>Cell transformation</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Syrian hamster embryo cells</td>
<td>Cell transformation</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>— HUMAN CELLS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human lymphoblasts A9-H-1</td>
<td>Gene mutation</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Human lymphoblasts TH6</td>
<td>Gene mutation</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Human embryo epithelial-like EUE cells</td>
<td>Gene mutation</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Human peripheral lymphocytes</td>
<td>Unscheduled DNA synthesis</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>

NT = not tested  
– = negative result  
+ = positive result  
(+)= weakly positive or marginal result

* Increase in cells expressing GSTA1-1.

b Transformed cells induced tumours in nude mice.
<table>
<thead>
<tr>
<th>Species (test system)</th>
<th>End-point</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAMMALIAN ASSAYS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>Dominant lethal mutations</td>
<td>–</td>
<td>Lane et al., 1982</td>
</tr>
<tr>
<td>Mouse/spot test</td>
<td>Gene mutation</td>
<td>(+)</td>
<td>Gocke et al., 1983</td>
</tr>
<tr>
<td>Mouse bone marrow</td>
<td>Sister chromatid exchange</td>
<td>+</td>
<td>Gir &amp; Que Hee, 1988</td>
</tr>
<tr>
<td>Mouse bone marrow</td>
<td>Micronuclei</td>
<td>–</td>
<td>King et al., 1979; Jenssen &amp; Ramal, 1980</td>
</tr>
<tr>
<td>Mouse peripheral erythrocytes</td>
<td>Micronuclei</td>
<td>–</td>
<td>Armstrong &amp; Galloway, 1993</td>
</tr>
<tr>
<td>Mouse liver, kidney, lung, and stomach</td>
<td>DNA binding</td>
<td>+</td>
<td>Prod et al., 1986</td>
</tr>
<tr>
<td>Mouse liver, kidney, lung, and stomach</td>
<td>DNA binding</td>
<td>+</td>
<td>Arfellini et al., 1984</td>
</tr>
<tr>
<td>Mouse forestomach and kidney</td>
<td>DNA binding</td>
<td>+</td>
<td>Hellman &amp; Brandt, 1986</td>
</tr>
<tr>
<td>Mouse liver</td>
<td>DNA binding</td>
<td>+</td>
<td>Barerjee, 1988</td>
</tr>
<tr>
<td>Rat liver, kidney, spleen, lung, forestomach, and stomach</td>
<td>DNA binding</td>
<td>+</td>
<td>Reitz et al., 1982</td>
</tr>
<tr>
<td>Rat liver, kidney, lung, and stomach</td>
<td>DNA binding</td>
<td>+</td>
<td>Arfellini et al., 1984</td>
</tr>
<tr>
<td>Rat liver, kidney, lung, and stomach</td>
<td>DNA binding</td>
<td>+</td>
<td>Prod et al., 1986</td>
</tr>
<tr>
<td>Rat liver and kidney</td>
<td>DNA binding</td>
<td>+</td>
<td>Inskeep et al., 1986</td>
</tr>
<tr>
<td>Rat liver and lung</td>
<td>DNA binding</td>
<td>+</td>
<td>Baarsch et al., 1991</td>
</tr>
<tr>
<td>Rat liver</td>
<td>DNA binding</td>
<td>+</td>
<td>Barerjee, 1988</td>
</tr>
<tr>
<td>Rat liver</td>
<td>DNA binding</td>
<td>+</td>
<td>Cheever et al., 1990</td>
</tr>
<tr>
<td>Mouse liver</td>
<td>DNA damage</td>
<td>+</td>
<td>Storer &amp; Conolly, 1983, 1985; Storer et al., 1984</td>
</tr>
<tr>
<td>Mouse liver</td>
<td>DNA damage</td>
<td>+</td>
<td>Taningher et al., 1991</td>
</tr>
<tr>
<td><strong>INSECT ASSAYS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Drosophila melanogaster</em> somatic mutation</td>
<td>Gene mutation</td>
<td>+</td>
<td>Nylander et al., 1978</td>
</tr>
<tr>
<td><em>D. melanogaster</em> somatic mutation</td>
<td>Gene mutation</td>
<td>+</td>
<td>Romert et al., 1990</td>
</tr>
<tr>
<td><em>D. melanogaster</em> somatic mutation</td>
<td>Gene mutation</td>
<td>+</td>
<td>Kramers et al., 1991</td>
</tr>
<tr>
<td><em>D. melanogaster</em> recessive lethal</td>
<td>Gene mutation</td>
<td>(+)</td>
<td>Baltiering et al., 1993</td>
</tr>
<tr>
<td><em>D. melanogaster</em> vermilion locus</td>
<td>Gene mutation</td>
<td>+</td>
<td>Baltiering et al., 1993</td>
</tr>
<tr>
<td><em>D. melanogaster</em> sex-linked recessive</td>
<td>Gene mutation</td>
<td>+</td>
<td>King et al., 1979</td>
</tr>
<tr>
<td><em>D. melanogaster</em> sex-linked recessive</td>
<td>Gene mutation</td>
<td>+</td>
<td>Kramers et al., 1991</td>
</tr>
<tr>
<td><em>D. melanogaster</em></td>
<td>Chromosomal loss/gain</td>
<td>+/+</td>
<td>Valencia et al., 1984</td>
</tr>
<tr>
<td><strong>HOST-MEDIATED ASSAYS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em> K12/343/113 mouse host-mediated assay</td>
<td>Gene mutation</td>
<td>–</td>
<td>King et al., 1979</td>
</tr>
</tbody>
</table>

= negative result  + = positive result  (+) = weakly positive or marginal result

10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

10.1 Aquatic environment

The effects of exposure to 1,2-dichloroethane on a number of aquatic organisms in the laboratory and field have also been investigated. In bacteria, the lowest reported IC<sub>50</sub> for inhibition of gas production and ammonia consumption were 25 and 29 mg/litre in methanogens and *Nitrosomonas*, respectively (Blum & Speece, 1991). The most sensitive freshwater alga studied was *Microcystis aeruginosa*, in which an EC<sub>50</sub> for inhibition of cell multiplication of 105 mg/litre was observed (Bringmann & Kühn, 1978); in the only identified study in marine algae, an EC<sub>50</sub> for carbon uptake of 340 mg/litre was reported in *Phaeodactylym tricornutum* (Pearson & McConnell, 1975). Toxicity thresholds (cell multiplication inhibition) were above 800 mg/litre for three species of aquatic protozoa (Bringmann & Kühn, 1980).

The lowest reported LC<sub>50</sub> value for *Daphnia* was 220 mg/litre (Leblanc, 1980), whereas the lowest EC<sub>50</sub> (for 10% immobilization) was 150 mg/litre (Freitag et al., 1994). Effects on reproductive success and growth were observed in *Daphnia* at 20.7 and 71.7 mg/litre, respectively. There were no effects on these end-points at 10.6 and 41.6 mg/litre, respectively (Richter et al., 1983).
Based on available data, the most sensitive freshwater vertebrate species appears to be the northwestern salamander, in which 9-day larval survival (4 days post-hatch) was reduced at 2.5 mg/litre (Black et al., 1982).

10.2 Terrestrial environment

Identified data on the toxicity of 1,2-dichloroethane to terrestrial organisms are inadequate to permit assessment.

11. EFFECTS EVALUATION

11.1 Evaluation of health effects

11.1.1 Hazard identification and dose–response assessment

Based on limited available data in humans, the lethal oral dose of 1,2-dichloroethane has been estimated to be between 20 and 50 ml. 1,2-Dichloroethane is moderately acutely toxic by inhalation, based on the results of studies in experimental animals. Skin and eye irritation may also be induced by 1,2-dichloroethane.

Owing to the limitations of the available studies in humans, it is necessary to rely on available experimental data in animal species as a basis for derivation of no-effect levels or quantitative estimates of carcinogenic potency. However, in most of the identified short-term and subchronic studies, only a limited range of endpoints was examined and documentation was incomplete. Similarly, little information on non-neoplastic effects was presented in the long-term carcinogenicity bioassays. Lowest reported effect levels were 49–82 mg/kg body weight per day for 13 weeks (increases in liver weight in rats) for ingestion (NTP, 1991) and 202 mg/m³ (effects on liver and kidney function in rats exposed for 12 months) for inhalation (Spreafico et al., 1980). Based on limited data, there is no evidence that 1,2-dichloroethane is teratogenic in experimental animals or that it induces reproductive or developmental effects at doses below those that cause other systemic effects.

Based on the limited evidence of carcinogenicity in workers exposed principally to 1,2-dichloroethane in the most reliable epidemiological study conducted to date (Benson & Teta, 1993), the induction of both rare and common tumours in rats and mice exposed by ingestion (NCI, 1978) and supporting evidence in other limited bioassays, the production of a reactive intermediate that alkylates DNA in vivo, and positive results in a range of in vitro assays for genotoxicity, 1,2-dichloroethane is considered to be a probable human carcinogen.

The carcinogenic potency of 1,2-dichloroethane has been calculated based on the increased incidence of squamous cell carcinomas of the stomach, haemangiosarcomas, fibromas of the subcutaneous tissue, and adenocarcinomas or fibroadenomas (combined) of the mammary gland in Osborne-Mendel rats exposed orally by gavage, as well as the increased incidence of alveolar/bronchiolar adenomas, hepatocellular carcinomas, mammary gland adenocarcinomas, and endometrial stromal polyps or sarcomas (combined) in similarly exposed B6C3F₁ mice; data from both the matched (same study) and pooled (concurrent studies) vehicle controls were incorporated. It should be noted, however, that mortality was higher at the high dose in female mice and rats of both sexes than in other dose groups in this study. Therefore, these high-dose groups were not included in the derivation of quantitative estimates of carcinogenic potency.

Based on multistage modelling of these data, amortized for continuous exposure for a standard duration of 104 weeks and corrected for the expected rate of increase in tumour formation in rodents in a standard bioassay of 104 weeks, the doses associated with a 5% increase in tumour incidence (TD₅₀) range from 6.2 to 34 mg/kg body weight per day. Incorporation of a scaling factor for the differences in body surface area between rodents and humans was not considered appropriate, as it is likely that the carcinogenicity of 1,2-dichloroethane is due to a metabolite, rather than to the parent compound.

11.1.2 Criteria for setting guidance values for 1,2-dichloroethane

As available data indicate that 1,2-dichloroethane is a genotoxic carcinogen, exposure should be reduced to the extent possible. The following guidance is provided as a possible basis for derivation of limits of exposure and judgement of the quality of environmental media by relevant authorities, based on the potential carcinogenicity of 1,2-dichloroethane in humans. Based on available data, air is believed to be the principal source of exposure in the general environment (see section 6.2) and, therefore, is the principal medium addressed here. Available data are considered inadequate to serve as a basis for development of tolerable intakes for non-neoplastic effects.
Although it is desirable to reduce exposure to genotoxic carcinogens to the extent possible, a value, for example, 5000 or 50,000 times less than the TD_{0.05}s might be considered appropriate as a guidance value. This margin (5000–50,000) affords protection similar to that associated with the range for low-dose risk estimates generally considered by various agencies to be “essentially negligible” (i.e. 10^{-5} to 10^{-6}). This corresponds to a range of airborne concentrations of 3.6–20 \text{ g/m³} or 0.36–2.0 \text{ g/m³}. (Corresponding values for ingestion are 1.2–6.8 \text{ g/kg body weight per day} or 0.12–0.68 \text{ g/kg body weight per day}.)

It should be noted, however, that the risk of exposure in air is most likely overestimated, as the TD_{0.05}s were based on a study in which the experimental animals were administered bolus doses of 1,2-dichloroethane by gavage, whereas exposure in the general population is likely to be mostly via inhalation. Based on available data, the carcinogenic potency of 1,2-dichloroethane appears to be less following inhalation than following ingestion of bolus doses, most likely because of inter-route variations in toxicokinetics.

### 11.1.3 Sample risk characterization

Non-neoplastic effects in animals have been observed only at concentrations more than 700,000 times greater than those in the principal medium of exposure (air) in the general environment, based on the sample estimation of exposure presented in section 6.2 for indirect exposure in the general environment. Identified data are inadequate to allow an estimation of exposure to 1,2-dichloroethane in the occupational environment.

Although, wherever possible, exposure to genotoxic carcinogens should be reduced to the extent possible, indirect population exposure in the general environment, based on the sample estimate presented in section 6.2, is up to approximately 300 times less than a guidance value that might be considered appropriate on the basis of available dose–response data for carcinogenicity (i.e. 3.6–20 \text{ g/m³} or 0.36–2.0 \text{ g/m³}, the TD_{0.05}s divided by 5000 or 50,000). Identified data are inadequate to estimate exposure to 1,2-dichloroethane in the occupational environment.

### 11.2 Evaluation of environmental effects

Because 1,2-dichloroethane is released principally in emissions from industrial sources and because of its high volatility, the atmosphere is the predominant environmental sink for 1,2-dichloroethane. It is moderately persistent in air. Stratospheric photolysis may produce chlorine radicals, which may in turn react with ozone. However, the ozone depleting potential is low (0.001 relative to CFC-11), and the compound is not listed in the Montreal Protocol on Substances that Deplete the Ozone Layer.

Terrestrial organisms will have the greatest potential for exposure to 1,2-dichloroethane in ambient air. However, available data on the effects of 1,2-dichloroethane are inadequate to allow the characterization of risks in terrestrial species.

Although 1,2-dichloroethane may be released to surface waters or soil through industrial processes and disposal, and although hydrolysis and microbial degradation are slow, the substance is not likely to persist in these media because of its volatility. A range of toxicity tests in aquatic species have indicated that effect levels are generally above 10 mg/litre. As concentrations in surface waters are generally several orders of magnitude less than those demonstrated to cause effects, it is likely that 1,2-dichloroethane poses negligible risk to aquatic organisms.

### 12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

The International Agency for Research on Cancer (IARC, 1979) has classified 1,2-dichloroethane in group 2B (possibly carcinogenic to humans) based on sufficient evidence of carcinogenicity in experimental animals.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has evaluated 1,2-dichloroethane on three occasions (WHO, 1971, 1980, 1992). In its last evaluation, the Committee concluded that this compound is genotoxic in both in vitro and in vivo test systems and carcinogenic in mice and rats when administered by the oral route. No acceptable daily intake (ADI) was therefore allocated. The Committee expressed the opinion that 1,2-dichloroethane should not be used in food.

In the current WHO Guidelines for drinking-water quality (WHO, 1993), the concentrations of 1,2-dichloroethane in drinking-water estimated to be associated with excess risks of 10^{-4}, 10^{-5}, and 10^{-6} are 300, 30, and 3 \text{ g/litre}, respectively, based on linear multistage modelling of the incidence of haemangiosarcomas in male rats in the NCI (1978) study.

Information on international hazard classification and labelling is included in the International Chemical Safety Card reproduced in this document.
13. HUMAN HEALTH PROTECTION AND EMERGENCY ACTION

Human health hazards, together with preventative and protective measures and first aid recommendations, are presented on the International Chemical Safety Card (ICSC 0250) reproduced in this document.

13.1 Human health hazards

1,2-Dichloroethane is highly flammable. On long-term or repeated exposure, it is considered to be a probable human carcinogen.

13.2 Advice to physicians

In case of emergency, it is important to wash skin with soap and water after removing contaminated clothing. In the event of poisoning, the treatment is symptomatic and supportive. Survival for 48 hours usually implies complete recovery, although deaths have occurred up to 5 days after exposure.

13.3 Health surveillance advice

Monitoring of both liver and kidney functions should be included in the health surveillance programme of humans exposed to 1,2-dichloroethane.

13.4 Explosion and fire hazards

13.4.1 Explosion hazards

1,2-Dichloroethane vapours of between 6 and 12% in air form an explosive mixture.

13.4.2 Fire hazards

1,2-Dichloroethane is highly flammable.

13.4.3 Prevention

Because of its low electroconductivity, 1,2-dichloroethane can generate electrostatic charges as a result of flow or agitation. Use only closed systems, ventilation, and explosion-proof electrical equipment. All equipment must be grounded.

13.5 Spillage

1,2-Dichloroethane is highly flammable. In the event of spillage, eliminate all sources of ignition in the vicinity. Because the substance is absorbed through the skin, do not touch or walk through the spilled material without proper equipment. To avoid the flammability hazard, remove wet or contaminated clothing immediately, and use non-sparking tools for clean-up. Do not let the substance enter the drains or watercourses.

The IDLH (Immediately Dangerous to Life or Health) value for this substance is very low, at 50 ppm (200 mg/m$^3$) (NIOSH, 1994b).

14. CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

Information on national regulations, guidelines, and standards is available from the International Register of Potentially Toxic Chemicals (IRPTC) legal file.

The reader should be aware that regulatory decisions about chemicals taken in a certain country can be fully understood only in the framework of the legislation of that country. The regulations and guidelines of all countries are subject to change and should always be verified with appropriate regulatory authorities before application.
### Types of Hazard/Exposure

<table>
<thead>
<tr>
<th>FIRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly flammable. Gives off irritating or toxic fumes (or gases) in a fire.</td>
</tr>
<tr>
<td>PREVENTION</td>
</tr>
<tr>
<td>NO open flames, NO sparks, and NO smoking.</td>
</tr>
<tr>
<td>FIRST AID/FIRE FIGHTING</td>
</tr>
<tr>
<td>Powder, water spray, foam, carbon dioxide.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EXPLOSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vapour/air mixtures are explosive.</td>
</tr>
<tr>
<td>PREVENTION</td>
</tr>
<tr>
<td>Closed system, ventilation, explosion-proof electrical equipment and lighting. Prevent build-up of electrostatic charges (e.g., by grounding). Do NOT use compressed air for filling, discharging, or handling.</td>
</tr>
<tr>
<td>FIRST AID/FIRE FIGHTING</td>
</tr>
<tr>
<td>In case of fire: keep drums, etc., cool by spraying with water.</td>
</tr>
</tbody>
</table>

### Exposure

#### Inhalation

- Abdominal pain. Cough.

- Prevention: Ventilation, local exhaust, or breathing protection.
- First Aid/Fire Fighting: Fresh air, rest. Half-upright position. Artificial respiration if indicated. Refer for medical attention.

#### Skin

- Redness.

- Prevention: Protective gloves.
- First Aid/Fire Fighting: Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.

#### Eyes


- Prevention: Safety goggles, face shield, or eye protection in combination with breathing protection.
- First Aid/Fire Fighting: First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.

#### Ingestion

- Abdominal cramps. Diarrhoea (further see Inhalation).

- Prevention: Do not eat, drink, or smoke during work. Wash hands before eating.
- First Aid/Fire Fighting: Give nothing to drink. Refer for medical attention.

### Spillage Disposal

Evacuate danger area! Collect leaking and spilled liquid in sealable containers as far as possible. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Do NOT wash away into sewer (extra personal protection; self-contained breathing apparatus).

### Packaging & Labelling

- F Symbol: R: 45-11-22-36/37/38
- T Symbol: S: 53-45
- UN Hazard Class: 3
- UN Subsidiary Risks: 6.1
- UN Pack Group: II

Unbreakable packaging; put breakable packaging into closed unbreakable container. Do not transport with food and feedstuffs. Marine pollutant.

### Emergency Response

Transport Emergency Card: TEC (R)-605 NFPA Code: H 2; F 3; R 0;

Fireproof. Separated from strong oxidants, food and feedstuffs and other incompatible substances (see Chemical Dangers). Cool. Dry.

Prepared in the context of cooperation between the International Programme on Chemical Safety and the European Commission © IPCS 1999

SEE IMPORTANT INFORMATION ON THE BACK.
**IMPORTANT DATA**

**Physical State; Appearance**
COLOURLESS, VISCOUS LIQUID, WITH CHARACTERISTIC ODOUR. TURNS DARK ON EXPOSURE TO AIR, MOISTURE AND LIGHT.

**Physical Dangers**
The vapour is heavier than air and may travel along the ground; distant ignition possible. As a result of flow, agitation, etc., electrostatic charges can be generated.

**Chemical Dangers**
The substance decomposes on heating and on burning producing toxic and corrosive fumes including hydrogen chloride (ICSC # 0163) and phosgene (ICSC # 0007). Reacts violently with aluminium, alkali metals, alkali amides, ammonia, bases, strong oxidants. Attacks many metals in presence of water. Attacks plastic.

**Occupational Exposure Limits**
TLV: 10 ppm; 40 mg/m³ (as TWA) (ACGIH 1994-1995).

**Routes of Exposure**
The substance can be absorbed into the body by inhalation of its vapour, through the skin and by ingestion.

**Inhalation Risk**
A harmful contamination of the air can be reached very quickly on evaporation of this substance at 20°C.

**Effects of Short-term Exposure**
The vapour irritates the eyes, the skin and the respiratory tract. Inhalation of the vapour may cause lung oedema (see Notes). The substance may cause effects on the central nervous system, kidneys, liver, resulting in impaired functions.

**Effects of Long-term or Repeated Exposure**
Repeated or prolonged contact with skin may cause dermatitis. This substance is probably carcinogenic to humans.

**PHYSICAL PROPERTIES**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boiling point</td>
<td>83.5°C</td>
</tr>
<tr>
<td>Melting point</td>
<td>-35.7°C</td>
</tr>
<tr>
<td>Relative density (water = 1)</td>
<td>1.235</td>
</tr>
<tr>
<td>Solubility in water, g/100 ml</td>
<td>0.87</td>
</tr>
<tr>
<td>Vapour pressure, kPa at 20°C</td>
<td>8.7</td>
</tr>
<tr>
<td>Relative vapour density (air = 1)</td>
<td>3.42</td>
</tr>
</tbody>
</table>

**ENVIRONMENTAL DATA**

**NOTES**
Depending on the degree of exposure, periodic medical examination is indicated. The symptoms of lung oedema often do not become manifest until a few hours have passed and they are aggravated by physical effort. Rest and medical observation are therefore essential. Immediate administration of an appropriate spray, by a doctor or a person authorized by him/her, should be considered.

**ADDITIONAL INFORMATION**

**LEGAL NOTICE**
Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible for the use which might be made of this information.

© IPCS 1999
REFERENCES


Armstrong MJ, Galloway SM (1993) Micronuclei induced in peripheral blood of E...PIM-1 transgenic mice by chronic oral treatment with 2-acetylaminofluorene or benzene but not with diethylnitrosamine or 1,2-dichloroethane. *Mutation research*, 302:61–70.


Concise International Chemical Assessment Document 1


Crespi CL, Seixas GM, Turner TR, Ryan CG, Penman BW (1985) Mutagenicity of 1,2-dichloroethane and 1,2-dibromomethane in two human lymphoblastoid cell lines. Mutation research, 142:133–140.


NIOSH (1994b) NIOSH pocket guide to chemical hazards. US Department of Health and Human Services, Public Health Service, Center for Disease Control and Prevention, National Institute for Occupational Safety and Health, June.


NTP (1991) Toxicity studies of 1,2-dichloroethane (ethylene dichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6CF, mice (drinking water and gavage studies). Research Triangle Park, NC, National Institutes of Health, National Toxicology Program (NIH Publication No. 91-3123).


Spencer HC, Rowe VK, Adams EM, McCollister DD, Irish DD (1951) Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. American Medical Association archives of Industrial hygiene and occupational medicine, 4:482–493.


APPENDIX 1 — SOURCE DOCUMENTS


Copies of the Environmental Health Criteria document on 1,2-dichloroethane, prepared by the International Programme on Chemical Safety, as well as the Health and Safety Guide (1991) and the International Chemical Safety Card (1993), may be obtained from:

International Programme on Chemical Safety
World Health Organization
Geneva, Switzerland

The first draft of the monograph, prepared by Ms K. Hughes of the Environmental Health Directorate, Health Canada, was circulated to IPCS Contact Points (approximately 150 government, industrial, academic, and independent organisations and individuals) for comment in June 1994. The second draft, revised on the basis of the comments received, was also prepared by Ms K. Hughes. Dr E. Smith and Dr P.G. Jenkuns, both members of the IPCS Central Unit, were responsible for the scientific content and technical editing, respectively.

The monograph on 1,2-dichloroethane was finalized by the Core Assessment Group (CAG) of the Joint Meeting on Pesticides (JMP), which met in Geneva from 25 October to 3 November 1994. The Core Assessment Group reviewed and revised the draft monograph and made an evaluation of the risks for human health and the environment from exposure to 1,2-dichloroethane. Participants at the Core Assessment Group meeting were:

Dr T. Bailey, Ecological Effects Branch, Environmental Fate and Effects Division, US Environmental Protection Agency, Washington, DC, USA
Dr A.L. Black, Department of Human Services and Health, Canberra, ACT, Australia
Mr D.J. Clegg, Carp, Ontario, Canada
Dr S. Dobson, Institute of Terrestrial Ecology, Monks Wood, Abbots Ripton, Huntingdon, Cambridgeshire, United Kingdom (Vice-Chairperson)
Dr P.E.T. Dougan, Her Majesty’s Inspectorate of Pollution, London, United Kingdom (EHC Joint Rapporteur)
Dr P. Fenner-Crisp, Office of Pesticide Programs, US Environmental Protection Agency, Washington, DC, USA
Dr R. Hailey, National Institute of Environmental Health Sciences, National Institutes of Health, Public Health Service, Department of Health and Human Services, Research Triangle Park, NC, USA
Ms K. Hughes, Priority Substances Section, Environmental Health Directorate, Health Canada, Ottawa, Ontario, Canada (EHC Joint Rapporteur)
Dr D. Karungu, Division of Medical Toxicology, Central Insecticides Laboratory, Government of India, Ministry of Agriculture & Cooperation, Directorate of Plant Protection, Quarantine & Storage, Faridabad, Haryana, India
Dr L. Landner, MFG, European Environmental Research Group Ltd, Stockholm, Sweden
Dr M.H. Litchfield, Melrose Consultancy, Fontwell, Arundel, West Sussex, United Kingdom
Professor M. Lotti, Institute of Occupational Medicine, University of Padua, Padua, Italy (Chairperson)
Dr D.R. Mattison, University of Pittsburgh, Graduate School of Public Health, Pittsburgh, PA, USA
Dr J. Sekizawa, Division of Information on Chemical Safety, National Institute of Health Sciences, Setagaya-ku, Tokyo, Japan
Dr P. Sinhaseni, Department of Pharmacology, Chulalongkorn University, Bangkok, Thailand
Dr S.A. Soliman, Pesticide Chemicals & Toxicology, King Saud University, Riyadh, Saudi Arabia
Dr M. Tasheva, Department of Toxicology, National Center of Hygiene, Medical Ecology and Nutrition, Sofia, Bulgaria
Mr J.R. Taylor, Pesticides Safety Directorate, Ministry of Agriculture, Fisheries and Food, York, United Kingdom
Dr H.M. Tenmink, Department of Toxicology, Wageningen Agricultural University, Wageningen, The Netherlands
Dr M.I. Witters, Department of Occupational Toxicology, THO Nutrition and Food Research Institute, AJ Zaat, The Netherlands

Procedures for the preparation of an Environmental Health Criteria document

The order of procedures that result in the publication of an EHC monograph is shown in the flow chart. A designated staff member of IPCS, responsible for the scientific quality of the document, serves as Responsible Officer (RO). The IPCS Editor is responsible for layout and language. The first draft, prepared by consultants or, more usually, staff from an IPCS Participating Institution, is based initially on data provided from the International Register of Potentially Toxic Chemicals and reference databases such as Medline and Toxline.

The draft document, when received by the RO, may require an initial review by a small panel of experts to determine its scientific quality and objectivity. Once the RO finds the document acceptable as a first draft, it is distributed, in its unedited form, to well over 150 EHC Contact Points throughout the world who are asked to comment on its completeness and accuracy and, where necessary, provide additional material. The Contact Points, usually designated by governments, may be Participating Institutions, IPCS Focal Points, or individual scientists known for their particular expertise. Generally, some four months are allowed before the comments are considered by the RO and author(s). A second draft incorporating comments received and approved by the Director, IPCS, is then distributed to Task Group members, who carry out the peer review, at least six weeks before their meeting.

The Task Group members serve as individual scientists, not as representatives of any organization, government, or industry. Their function is to evaluate the accuracy, significance, and relevance of the information in the document and to assess the health and environmental risks from exposure to the chemical. A summary and recommendations for further research and improved safety aspects are also required. The composition of the Task Group is dictated by the range of expertise required for the subject of the meeting and by the need for a balanced geographical distribution.

The three cooperating organizations of the IPCS recognize the important role played by nongovernmental organizations. Representatives from relevant national and international associations may be invited to join the Task Group as observers. While observers may provide a valuable contribution to the process, they can speak only at the invitation of the Chairperson.
Observers do not participate in the final evaluation of the chemical; this is the sole responsibility of the Task Group members. When the Task Group considers it to be appropriate, it may meet in camera.

All individuals who as authors, consultants, or advisers participate in the preparation of the EHC monograph must, in addition to serving in their personal capacity as scientists, inform the RO if at any time a conflict of interest, whether actual or potential, could be perceived in their work. They are required to sign a conflict of interest statement. Such a procedure ensures the transparency and probity of the process.

When the Task Group has completed its review and the RO is satisfied as to the scientific correctness and completeness of the document, it then goes for language editing, reference checking, and preparation of camera-ready copy. After approval by the Director, IPCS, the monograph is submitted to the WHO Office of Publications for printing. At this time, a copy of the final draft is sent to the Chairperson and Rapporteur of the Task Group to check for any errors.
APPENDIX 2 — CICAD FINAL REVIEW BOARD

Members

Dr A. Aitio, Institute of Occupational Health, Helsinki, Finland

Dr K. Bentley, Director, Environment Policy Section, Commonwealth Department of Human Services and Health, Canberra, Australia

Mr R. Cary, Toxicology and Existing Substances Regulation Unit, Health and Safety Executive, Merseyside, United Kingdom

Dr J. de Fouw, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands

Dr C. DeRosa, Director, Division of Toxicology, Agency for Toxic Substances and Disease Registry, Atlanta, GA, USA

Dr S. Dobson, Institute of Terrestrial Ecology, Monks Wood, Abbots Ripton, Huntingdon, Cambridgeshire, United Kingdom

Dr W. Farland, Director, National Center for Environmental Assessment, Office of Research and Development, US Environmental Protection Agency, Washington, DC, USA (Chairperson)

Dr T.I. Fortoul, Depto. Biologia Celular y Tisular, National University of Mexico and Environmental Health Directorate of the Health Ministry, Mexico D.F., Mexico

Dr H. Gibb, National Center for Environmental Assessment, US Environmental Protection Agency, Washington, DC, USA

Dr R.F. Hertel, Federal Institute for Health Protection of Consumers & Veterinary Medicine, Berlin, Germany

Mr J.R. Hickman, Environmental Health Directorate, Health Canada, Ottawa, Ontario, Canada

Dr T. Lakhanisky, Head, Division of Toxicology, Institute of Hygiene and Epidemiology, Brussels, Belgium (Vice-Chairperson)

Dr I. Mangelsdorf, Documentation and Assessment of Chemicals, Fraunhofer Institute for Toxicology and Aerosol Sciences, Hanover, Germany

Ms E. Meek, Head, Priority Substances Section, Environmental Health Directorate, Health Canada, Ottawa, Ontario, Canada

Dr K. Paksy, National Institute of Occupational Health, Budapest, Hungary

Mr D. Renshaw, Department of Health, London, United Kingdom

Dr J. Sekizawa, Division of Chemo-Bio Informatics, National Institute of Hygienic Sciences, Tokyo, Japan

Dr H. Sterzl-Eckert, GSF-Forschungszentrum für Umwelt und Gesundheit GmbH, Institut für Toxikologie, Oberschleißheim, Germany

Professor S. Tarkowski, Department of Environmental Health Hazards, The Nofer Institute of Occupational Medicine, Lodz, Poland

Dr M. Wallen, National Chemicals Inspectorate (KEMI), Solna, Sweden

Secretariat

Dr M. Baril, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr L. Harrison, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr M. Mercier, Director, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr P. Toft, Associate Director, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland
1,2-Dichloroethane

RÉSUMÉ D’ORIENTATION


Le 1,2-dichloréthane (CAS N° 107-06-2) est un hydrocarbure synthétique volatile utilisé principalement dans la synthèse du chlorure de vinyle monomère et d’autres solvants chlorés. Il a également été utilisé comme additif de l’essence au plomb et comme fumigant, mais son utilisation comme additif de l’essence est en déclin. La plus grande partie du 1,2-dichloréthane libéré dans l’environnement se retrouve dans l’air ambiant où sa persistance est modérée. Toutefois, il ne devrait pas contribuer à la destruction de l’ozone. Le potentiel de bioaccumulation du 1,2-dichloréthane est faible; son inhalation avec l’air est probablement la principale source d’exposition humaine.

On dispose de peu d’information sur les effets du 1,2-dichloréthane chez l’homme. Les quelques études épidémiologiques qui ont été faites sur sa cancérогénicité potentielle ne sont guère concluantes.

Le 1,2-dichloréthane présente une toxicité aiguë modérée chez les animaux d’expérience. Les quelques données que l’on trouve sur ses effets non néoplasiques dans des études de chronicité à court terme, sub-chronique ou chronique indiquent que les principaux organes cibles sont le foie et le rein; les doses les plus faibles pour lesquelles on ait signalé un effet après ingestion et inhalation sont respectivement de 49–82 mg/kg de poids corporel par jour (augmentation du poids du foie chez des rats exposés pendant 13 semaines) et 202 mg/m³ (effets sur les fonctions hépatique et rénale chez des rats exposés pendant 12 mois). D’après les résultats d’un petit nombre d’études, il n’y a pas de preuve que le 1,2-dichloréthane soit tératogène chez les animaux de laboratoire, ni qu’il induise des effets sur la reproduction ou le développement lorsque les niveaux d’exposition sont inférieurs aux niveaux qui entraînent d’autres effets systémiques.

L’exposition au 1,2-dichloréthane par gavage pendant 78 semaines a été suivie d’une augmentation significative de l’incidence des tumeurs de différents organes (notamment des hémostoycrocomes et des tumeurs de l’estomac, des glandes mammaires, du foie, des poumons et de l’endomètre), tant chez le rat que chez la souris. Il n’y a eu aucune augmentation significative de l’incidence des tumeurs chez des rats ou des souris exposés par inhalation, mais l’administration répétée par voie dermique ou intrapéritonéale a provoqué une augmentation du nombre des tumeurs des poumons chez la souris. Le 1,2-dichloréthane s’est constamment révélé génétiquement dans de nombreuses épures in vitro sur des cellules de procaryotes, de champignons et de mammifères (y compris des cellules humaines). De même, les résultats ont été constamment positifs en ce qui concerne l’activité génétiquement (ainsi que la fixation sur l’ADN) dans des études in vivo chez le rat, la souris et les insectes.

Les valeurs les plus faibles de la CI₅₀ et de la CE₀₅ qui aient été signalées pour différents effets sur des organismes aquatiques sont respectivement de 25 et 105 mg/litre. La CI₅₀, la plus faible pour les daphnies était de 220 mg/litre, des effets ayant toutefois été observés sur la reproduction à 20,7 mg/litre. Le vertébré d’eau douce le plus sensible à être une salamandre (Ambystoma gracile) chez laquelle on a constaté une réduction de la survie des larves à 2,5 mg/litre. On ne dispose que de données limitées sur la toxicité du 1,2-dichloréthane pour les espèces terrestres.

D’après les données disponibles, le 1,2-dichloréthane peut être considéré comme un cancérогène probable pour l’homme, de sorte que l’exposition doit être réduite dans toute la mesure possible. Le potentiel cancérогène (exprimé par la dose associée à une augmentation de 5 % de l’incidence des tumeurs), calculé à partir d’études de gavage, a été évalué à 6,2–34 mg/kg de poids corporel par jour. En appliquant un facteur de
sécurité de 5000 ou de 50 000 au potentiels cancérigène estimé, on arrive à une valeur guide pour l’air (principale source d’exposition humaine) de 3,6–20 : g/m$^3$ ou 0,36–2,0 : g/m$^3$; il faut cependant noter que cette méthode surestime les risques, car les données disponibles montrent que le 1,2-dichloréthane est moins actif lorsqu’il est inhalé. (Les valeurs correspondantes pour l’ingestion sont respectivement de 1,2–6,8 ou 0,12–0,68 : g/kg de poids corporel par jour.) Ces valeurs correspondent à ce que certains organismes considèrent comme un risque “pratiquement négligeable” (c’est-à-dire $10^{-5}$–$10^{-6}$ pour un cancérigène génotoxique). D’après une des estimations qui ont été faites, l’exposition indirecte dans un environnement normal est approximativement 300 fois inférieure à ces valeurs.
RESUMEN DE ORIENTACIÓN

Esta reseña de la evaluación química internacional del 1,2-dicloroetano ha sido preparada por la Dirección de Higiene del Medio de Health Canada sobre la base de un documento de la serie “Criterios de Salud Ambiental” (EHC) del Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 1995) en el que se evalúan los efectos potenciales sobre la salud humana de la exposición indirecta al 1,2-dicloroetano en el medio ambiente general, así como los efectos ambientales de dicha sustancia química. En este análisis se examinan datos obtenidos en mayo de 1993 (efectos sobre la salud humana) y octubre de 1994 (efectos ambientales). En el apéndice 1 se proporciona información sobre el proceso de revisión científica y los documentos disponibles de la serie EHC. Por lo que respecta a esta reseña de la evaluación química internacional, el proceso de revisión científica previo al examen realizado por el Comité de Revisión Final se ha cumplido mediante la revisión científica efectuada para la elaboración del documento de la serie EHC. Comunicándose por correspondencia, los miembros del Comité de Revisión Final ultimaron esta reseña de la evaluación química internacional del 1,2-dicloroetano, aprobaron su publicación y examinaron las observaciones dimanantes de la revisión científica efectuada durante la preparación del documento de la serie EHC. La composición del Comité de Revisión Final figura en el apéndice 2. En el presente documento también se reproduce la Ficha Internacional de Seguridad Química (ICSC 0250) emitida por el IPCS (1993).

El 1,2-dicloroetano (CAS n° 107-06-2) es un hidrocarburo sintético volátil que se utiliza principalmente en la síntesis del monómero cloruro de vinilo y de otros disolventes clorados. También se ha utilizado como aditivo de la gasolina con plomo y como fumigante, aunque su uso como aditivo de la gasolina se está reduciendo. La mayor parte de la liberación en el entorno se produce en el aire ambiente, donde es moderadamente persistente. Sin embargo, no parece que contribuya al agotamiento de la capa de ozono. El 1,2-dicloroetano tiene un potencial de bioacumulación bajo; la inhalación con el aire probablemente sea la principal fuente de exposición humana.

Se dispone de poca información sobre los efectos del 1,2-dicloroetano en el ser humano. Las pocas investigaciones epidemiológicas conocidas sobre su carcinogenicidad potencial no son concluyentes.

El 1,2-dicloroetano tiene una toxicidad aguda moderada en animales de experimentación. La escasa información sobre efectos no neoplásicos presentada en estudios de corta duración, subcrónicos y crónicos indica que los principales órganos afectados son el hígado y los riñones; los niveles mínimos de ingestión e inhalación con efectos comunicados fueron de 49–82 mg/kg de peso corporal por día (aumento de peso del hígado en las ratas expuestas durante 13 semanas) y 202 mg/m³ (efectos sobre la función hepática y renal en las ratas expuestas durante 12 meses), respectivamente. Los resultados de un número limitado de estudios, no aportaron indicios de que el 1,2-dicloroetano sea teratogénico en animales de experimentación o que tenga efectos sobre la reproducción o el desarrollo a niveles de exposición inferiores a los que causan otros efectos sistémicos.

La exposición al 1,2-dicloroetano administrado por sonda durante 78 semanas produjo un aumento significativo de la incidencia de tumores en distintos lugares (hemangiosarcomas y tumores en el estómago, las glándulas mamarías, el hígado, los pulmones y el endometrio) tanto en ratas como en ratones. Aunque no hubo un aumento significativo de la incidencia de tumores en las ratas y los ratones expuestos por inhalación, la aplicación cutánea o intraperitoneal repetida de 1,2-dicloroetano se ha revelado sistemáticamente genotóxica en numerosas pruebas realizadas in vitro en células de procariotas, hongos y mamíferos (incluidas células humanas). Análogamente, se han obtenido resultados invariablemente positivos indicadores de actividad genotóxica (así como enlaces con el ADN) en estudios realizados in vivo con ratas, ratones e insectos.

Las CL₅₀ y CE₅₀, más bajas notificadas en relación con diversos puntos finales en organismos acuáticos fueron de 25 y 105 mg/litro respectivamente. La CL₅₀ más baja notificada para Daphnia fue de 220 mg/litro, mientras que los efectos sobre la reproducción se produjeron con concentraciones de 20,7 mg/litro. El vertebrado de agua dulce más sensible estudiado fue la salamandra noroccidental (Ambystoma gracile), en la que se observó una reducción de la supervivencia de las larvas con niveles de 2,5 mg/litro. Se dispone sólo de datos limitados sobre los efectos del 1,2-dicloroetano en especies terrestres.

Teniendo en cuenta los datos disponibles, es probable que el 1,2-dicloroetano sea carcinógeno para el ser humano y, por lo tanto, la exposición a éste debería reducirse en la medida de lo posible. Sobre la base de estudios realizados en animales expuestos a una administración por sonda, se ha calculado que la potencia carcinogénica (expresada como la dosis asociada a un aumento del 5% en la incidencia de
tumores) oscila entre 6,2 y 34 mg/kg de peso corporal por día. Con respecto al aire (fuente principal de exposición humana), se han obtenido valores orientativos 3,6–20 g/m³ o 0,36–2,0 g/m³, calculados para un margen 5.000 a 50.000 veces inferior a la potencia carcinogénica estimada; sin embargo, hay que tener en cuenta que se han sobreestimado los riesgos, ya que los datos disponibles indican que el 1,2-dicloroetano inhalado resulta menos potente. (En cuanto a la ingesta, los valores correspondientes son de 1,2–6,8 g/m³ de peso corporal por día o 0,12–0,68 g/m³ de peso corporal por día.) Estos valores comportan lo que algunas entidades consideran como un riesgo “prácticamente insignificante” (es decir, $10^{-5} - 10^{-6}$ para un carcinógeno genotóxico). Según las estimaciones estadísticas, la exposición indirecta a través del medio ambiente general es aproximadamente 300 veces inferior a esos valores.