

## 1,1-Dichloroethane; CASRN 75-34-3

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

### STATUS OF DATA FOR 1,1-Dichloroethane

**File First On-Line 10/01/1990**

| Category (section)                      | Assessment Available? | Last Revised |
|---|-----------------------|--------------|
| <b>Oral RfD (I.A.)</b>                  | not evaluated         |              |
| <b>Inhalation RfC (I.B.)</b>            | not evaluated         |              |
| <b>Carcinogenicity Assessment (II.)</b> | yes                   | 10/01/1990   |

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — 1,1-Dichloroethane

CASRN — 75-34-3

Not available at this time.

---

### I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — 1,1-Dichloroethane

CASRN — 75-34-3

Not available at this time.

---

## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — 1,1-Dichloroethane

CASRN — 75-34-3

Last Revised — 10/01/1990

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

### **II.A. Evidence for Human Carcinogenicity**

#### **II.A.1. Weight-of-Evidence Characterization**

Classification — C; possible human carcinogen

Basis — Based on no human data and limited evidence of carcinogenicity in two animal species (rats and mice) as shown by an increased incidence of mammary gland adenocarcinomas and hemangiosarcomas in female rats and an increased incidence of hepatocellular carcinomas and benign uterine polyps in mice.

#### **II.A.2. Human Carcinogenicity Data**

None

### II.A.3. Animal Carcinogenicity Data

Limited. An NCI bioassay (1978a) provides limited evidence of the carcinogenicity of 1,1-dichloroethane in Osborne-Mendel rats and B6C3F1 mice. This is based on significant dose-related increases in the incidence of hemangiosarcomas at various sites and mammary carcinomas in female rats and statistically significant increases in the incidence of liver carcinoma in male mice and benign uterine polyps in female mice. The study is limited by high mortality in many groups; the low survival rates precluded the appearance of possible late-developing tumors and decreased the statistical power of this bioassay.

Technical grade 1,1-dichloroethane in corn oil was administered by gavage 5 days/week for 78 weeks to groups of 50 Osborne-Mendel rats/sex/dose. All surviving animals were necropsied following a 33-week observation period. Due to toxicity, dosing was not continuous (3 weeks on then 1 week off), making the TWAs for 5 days/week 382 and 764 mg/kg/day for low- and high-dose males and 475 and 950 mg/kg/day for low- and high-dose females, respectively. Both a vehicle and an untreated (not intubated) control group (20 rats/sex/group) were included in the study. A high incidence of pneumonia (approximately 80%) in all 4 groups of each sex was considered to be the cause for the low survival at termination of the study. Survival at 111 weeks was 30, 5, 4, and 8% in the untreated control, the vehicle control, the low-dose, and the high-dose male rat groups, respectively. Survival at termination for the female rat groups was 40, 20, 16, and 18% for the untreated control, vehicle control, low- and high-dose groups, respectively. In female rats there was a statistically significant positive dose-related trend in incidence of hemangiosarcomas (0/19 for matched vehicle controls, 0/50 for the low-dose group, and 4/50 for the high-dose group). The incidence of mammary gland adenocarcinomas (1/20 for the untreated group, 0/19 for the vehicle control group, 1/50 for low-dose, and 5/50 for high-dose groups) showed a statistically significant dose-related positive trend in those female rats surviving at least 52 weeks; tumor incidence was 0/16, 1/28 and 5/31 for vehicle control, low- and high-dose groups, respectively. (Tumor incidence at termination for the untreated control females surviving at least 52 weeks was not reported.) This bioassay was conducted before the life table tests were implemented, so results adjusted for mortality are not available. No mammary gland adenomas or hemangiosarcomas were observed in the dosed-male rats.

In the same NCI (1978a) study, groups of 50 B6C3F1 mice/sex/group were administered technical grade 1,1-dichloroethane in corn oil by gavage 5 days/week for 70 weeks. As in the rat study, the dosage pattern was 3 weeks on and 1 week off; the surviving animals were necropsied 13 weeks after the termination of dosing. The TWAs for 5 days/week for the low- and high-dose groups were 1442 and 2885 mg/kg/day for male and 1665 and 3331 mg/kg/day for female mice. Control groups, identical to those in the rat study and consisting of 20 mice/sex/group were also used. Survival at termination was 80, 80, 80, and 50% for the untreated control group, the vehicle control group, the low-, and high-dose females, respectively. In male mice survival was

35, 55, 62, and 32% in the untreated control group, the vehicle control group, the low-, and high-dose groups, respectively. An increased incidence of hepatocellular carcinoma in male mice was not statistically significant by either pair-wise or trend test (2/17 in the untreated control group, 1/19 in the vehicle control group, 8/49 in the low-dose and 8/47 in the high-dose groups). The incidence of hepatocellular carcinoma in male mice surviving at least 52 weeks was 1/19, 6/72, 8/48, and 8/32 in the matched vehicle control group, a pooled vehicle control group consisting of mice from this and identical controls from other concurrent experiments, and the low-, and high-dose groups, respectively; this positive trend was statistically significant. In female mice, liver carcinomas were reported in only the vehicle control (1/19) and the low-dose groups (1/47): no liver tumors were seen in the untreated controls or in the high-dose group. A statistically significant increase in benign uterine endometrial stromal polyps (4/46) was observed in high-dose females; these were not observed in any other group. A preliminary report of the NCI (1978a) study was published by Weisburger (1977).

#### **II.A.4. Supporting Data for Carcinogenicity**

To determine if 1,1-dichloroethane in drinking water could act as a tumor promoter or a complete carcinogen, Klaunig et al. (1986) exposed groups of 35 male B6C3F1 mice to 1,1-dichloroethane in drinking water at 0, 835, or 2500 mg/L for up to 52 weeks following a 4-week treatment with either drinking water containing 10 mg/L diethyl nitrosamine (DNA-initiated groups) or with deionized water (noninitiated groups). The investigators estimated that the approximate weekly dose of 1,1-dichloroethane was 3.8 mg/g/week (corresponding to 543 mg/kg/day) for the groups exposed to 2500 mg/L. Upon sacrifice at the end of either 24 weeks (10 mice/group) or 52 weeks (25 mice/group) of promotion, all tissues were examined for gross pathologic lesions and histologic sections of the liver, kidneys and lungs were examined. Neither the initiated nor the noninitiated 1,1-dichloroethane-treated groups showed a significant increase in the incidence of liver or lung tumors compared with initiated or noninitiated controls, respectively. The authors concluded that 1,1-dichloroethane was not carcinogenic to mice and did not act as a tumor promoter following initiation with DNA. These conclusions may not be entirely justified, since the duration of the study may have been inadequate for the development of tumors in noninitiated 1,1-dichloroethane-treated animals. In addition, the incidence of liver tumors in DNA-initiated controls was 70% at 24 weeks and 100% at 52 weeks, and the number of tumors/mouse in DNA-initiated controls at these times was 3.00 and 29.30, respectively. Hence, an increase in tumors or decrease in latency in 1,1-dichloroethane-treated DNA-initiated animals would have to be marked in order to be detectable.

Milman et al. (1988) and Story et al. (1986) investigated the chlorinated ethanes and ethylenes to detect their potential tumor initiating or promoting effects in a liver foci assay in Osborne-Mendel rats. In this assay, 1,1-dichloroethane did not give positive results for initiation (with phenobarbital as promoter), or as a complete carcinogen when administered in the absence of

initiation or promotion. Positive results for were seen for promotion with DENA as initiator. The assumption that the liver foci seen in this type of assay are precancerous has not been validated.

When tested by plate incorporation in a desiccator (because of volatility) in the presence and absence of metabolic activation systems, 1,1- dichloroethane was reported to be mutagenic for *Salmonella typhimurium* TA1535, TA98, and TA100, but not to TA1537 (Riccio et al., 1983; Mitoma et al., 1984). Negative results were reported for 1,1-dichloroethane in a cell transformation assay with BALB/c-3T3 cells, tested in the absence of an exogenous metabolic activation system in a sealed glass incubation chamber (Tu et al., 1985; Arthur D. Little, Inc., 1983). When tested in a similar manner in a DNA repair assay with hepatocyte primary cultures from rats or mice, 1,1-dichloroethane produced positive results (Williams, 1977). The results obtained in these three assays were also summarized in a joint publication (Milman et al., 1988).

Positive results were obtained in a viral transformation assay in which 1,1-dichloroethane was incubated with cultured Syrian Hamster embryo cells in a sealed glass chamber prior to addition of adenovirus SA7 (Hatch et al., 1983).

Lattanzi et al. (1988) determined that 1,1-dichloroethane, like 1,2- dichloroethane, binds covalently to DNA, forming DNA adducts. The Covalent Binding Index (CBI) of both 1,1-dichloroethane and 1,2-dichloroethane classifies them as weak initiators.

Chronic bioassays performed by NCI (1978b) on the isomer 1,2-dichloroethane resulted in many of the same tumor types as seen in the bioassays of 1,1-dichloroethane. Significant increases in the incidences of forestomach squamous cell carcinomas and hemangiosarcomas were observed in male rats and an increased incidence of mammary adenocarcinomas was observed in both female rats and mice. In addition, alveolar and bronchiolar adenomas were reported in male and female mice; endometrial stromal polyps and sarcomas in female mice; and hepatocellular carcinomas in male mice.

Based on these findings, as well as the appearance of lung papillomas in mice after topical treatment, 1,2-dichloroethane was classified as a group B2 chemical, a probable human carcinogen (U.S. EPA, 1990). Because of similarities in structure and target organs, the carcinogenic evidence for 1,2-dichloroethane is considered to be supportive of the classification of 1,1-dichloroethane in group C, a possible human carcinogen.

## **II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure**

None.

---

## **II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure**

None.

---

## **II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)**

### **II.D.1. EPA Documentation**

Source Document — U.S. EPA, 1985, 1986, 1990

The 1984 Health Effects Assessment for 1,1-Dichloroethane has received Office of Health and Environmental Assessment review.

### **II.D.2. EPA Review (Carcinogenicity Assessment)**

Agency Work Group Review — 12/07/1989

Verification Date — 12/07/1989

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for 1,1-Dichloroethane conducted in September 2002 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or (202)566-1676.

### **II.D.3. EPA Contacts (Carcinogenicity Assessment)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

---

## **VI. Bibliography**

Substance Name — 1,1-Dichloroethane

CASRN — 75-34-3

### **VI.A. Oral RfD References**

None

---

### **VI.B. Inhalation RfD References**

None

---

### **VI.C. Carcinogenicity Assessment References**

Arthur D. Little, Inc. 1983. Cell transformation assays of 11 chlorinated hydrocarbon analogs. Microfiche No. OTS0509392, Document No. 40-8324457.

Hatch, G.G., P.D. Mamay, M.L. Ayer, B.C. Casto and S. Nesnow. 1983. Chemical enhancement of viral transformation in Syrian hamster embryo cells by gaseous and volatile chlorinated methanes and ethanes. *Cancer Res.* 43(5): 1945-1950.

Klaunig, J.E., R.J. Ruch and M.A. Pereira. 1986. Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. *Environ. Health Perspect.* 69: 89-95.

Lattanzi, G., A. Colacci, S. Grilli, et al. 1988. Binding of hexachloroethane to biological macromolecules from rat and mouse organs. *J. Toxicol. Environ. Health.* 24: 403-411.

Milman, H.A., D.L. Story, E.S. Riccio, et al. 1988. Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. *Ann. NY Acad. Sci.* 534: 521-530.

Mitoma, C., C.A. Tyson and E.S. Riccio. 1984. Investigations of the species sensitivities and mechanism of carcinogenicity of halogenated hydrocarbons. Microfiche No. OTS0509408, Document No. 40-8424225.

NCI (National Cancer Institute). 1978a. Bioassay of 1,1-dichloroethane for possible carcinogenicity. CAS No. 78-34-3. NCI/NTP Technical Report No. 066. DHEW Publ. No. (NIH) 78-1316, Washington, DC.

NCI (National Cancer Institute). 1978b. Bioassay of 1,2-Dichloroethane for Possible Carcinogenicity. NCI Carcinogenesis Technical Report Series No. 55. DHEW Publ. No. (NIH) 78-1361, Washington, DC.

Riccio, E., A. Griffin, K. Mortelmans and H.A. Milman. 1983. A comparative mutagenicity study of volatile halogenated hydrocarbons using different metabolic activation systems. *Environ. Mutagen.* 5: 472. (Abstract)

Story, D.L., E.F. Meierhenry, C.A. Tyson and H.A. Milman. 1986. Differences in rat liver enzyme-altered foci produced by chlorinated aliphatics and phenobarbital. *Toxicol. Ind. Health.* 2(4): 351-362.

Tu, A.S., T.A. Murray, K.M. Hatch, A. Sivak and H.A. Milman. 1985. In vitro transformation of BALB/c-3T3 cells by chlorinated ethanes and ethylenes. *Cancer Lett.* 28(1): 85-92.

U.S. EPA. 1985. Health and Environmental Effects Profile for Dichloroethanes. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1986. Guidelines for Carcinogen Risk Assessment. *Federal Register.* 51(185): 33992-34003.

U.S. EPA. 1990. Integrated Risk Information System (IRIS). Online. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

Weisburger, E.K. 1977. Carcinogenicity studies on halogenated hydrocarbons. *Environ. Health Perspect.* 21: 7-16.



Williams, E.M. 1977. Detection of chemical carcinogens by unscheduled DNA synthesis in rat liver primary cell cultures. *Cancer Res.* 37(6): 1845-1851.

---

## VII. Revision History

Substance Name — 1,1-Dichloroethane

CASRN — 75-34-3

| Date       | Section | Description  |
|------------|---------|--|
| 10/01/1990 | II.     | Carcinogen assessment on-line                                      |
| 12/03/2002 | II.D.2. | Screening-Level Literature Review Findings message has been added. |

---

## VIII. Synonyms

Substance Name — 1,1-Dichloroethane

CASRN — 75-34-3

Last Revised — 10/01/1990

- 75-34-3
- AETHYLIDENCHLORID [GERMAN]
- CHLORINATED HYDROCHLORIC ETHER
- CHLORURE D'ETHYLIDENE [FRENCH]
- CLORURO DI ETILIDENE [ITALIAN]
- 1,1-DICHLOROETHAN [DUTCH]
- 1,1-DICHLORAETHAN [GERMAN]
- 1,1-DICHLORETHANE
- DICHLORO-1,1 ETHANE [FRENCH]
- 1,1-DICHLOROETHANE
- 1,1-DICLOROETANO [ITALIAN]
- 1,1-DICLOROETANO [SPANISH]
- ETHANE, 1,1-DICHLORO-

- ETHYLIDENE CHLORIDE
- ETHYLIDENE DICHLORIDE
- HSDB 64
- NCI-C04535
- RCRA WASTE NUMBER U076
- UN 2362