# 1,4-Dioxane (1,4-Diethyleneoxide)

123-91-1

## Hazard Summary

1,4-Dioxane is used as a solvent. Acute (short-term) inhalation exposure to high levels of 1,4-dioxane has caused vertigo, drowsiness, headache, anorexia and irritation of the eyes, nose, throat, and lungs in humans. It may also irritate the skin. Damage to the liver and kidneys has been observed in rats chronically (long-term) exposed in their drinking water. In three epidemiologic studies on workers exposed to 1,4-dioxane, the observed number of cancer cases did not differ from the expected cancer deaths. Tumors have been observed in orally exposed animals. EPA has classified 1,4-dioxane as a Group B2, probable human carcinogen.

Please Note: The main source of information for this fact sheet is EPA's Integrated Risk Information System (IRIS) (7), which contains information on the carcinogenic effects of 1,4-dioxane including the unit cancer risk for oral exposure. Other secondary sources include the Hazardous Substances Data Bank (HSDB) (5), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS) (6), a database of toxic effects that are not peer reviewed.

## Uses

- 1,4-Dioxane is used as a solvent for cellulose acetate, ethyl cellulose, benzyl cellulose, resins, oils, waxes, some dyes, and other organic and inorganic compounds. (2,4)

## Sources and Potential Exposure

- Occupational exposure to 1,4-dioxane is the most likely route of exposure. (1)
- 1,4-Dioxane has been detected in both surface water and groundwater. (2)

## Assessing Personal Exposure

- No information was located regarding the measurement of personal exposure to 1,4-dioxane.

## Health Hazard Information

Acute Effects:

- Acute inhalation exposure to high levels of 1,4-dioxane has caused vertigo and irritation of the eyes, nose, throat, and lungs in humans. It may also irritate the skin. (3,4)
- Some symptoms of poisoning include the irritation of the upper respiratory passages, coughing, irritation of eyes, drowsiness, vertigo, headache, anorexia, stomach pains, nausea, vomiting, coma, and death; these symptoms were observed in workers, but length of exposure was unknown. (5)
- In a fatal case of acute 1,4-dioxane poisoning by inhalation, hepatic and renal lesions, and demyelination and edema of the brain were observed in the individual. (2)
- Convulsions, collapse, and effects to the kidneys and liver were observed in rabbits injected with 1,4-dioxane. (2)
- Acute animal tests in rats, mice, rabbits, and guinea pigs, have demonstrated 1,4-dioxane to have moderate acute toxicity by inhalation or dermal exposure, and low to moderate acute toxicity by ingestion. (6)

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Chronic Effects (Noncancer):

- Damage to the liver and kidneys has been observed in rats chronically exposed in their drinking water. (2,11)
- EPA has not established a Reference Concentration (RfC) or a Reference Dose (RfD) for 1,4-dioxane. (7)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic reference exposure level of 3 milligrams per cubic meter ($mg/m^3$) based on no effects on the liver, kidney, or blood in rats. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct esimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (11)

Reproductive/Developmental Effects:

- No information is available on the reproductive and developmental effects of 1,4-dioxane in humans. (2)
- No evidence of gross, skeletal, or visceral malformations was found in the offspring of rats exposed via gavage (experimentally placing the chemical in the stomach). Embryotoxicity was observed only at the highest dose. (3)

Cancer Risk:

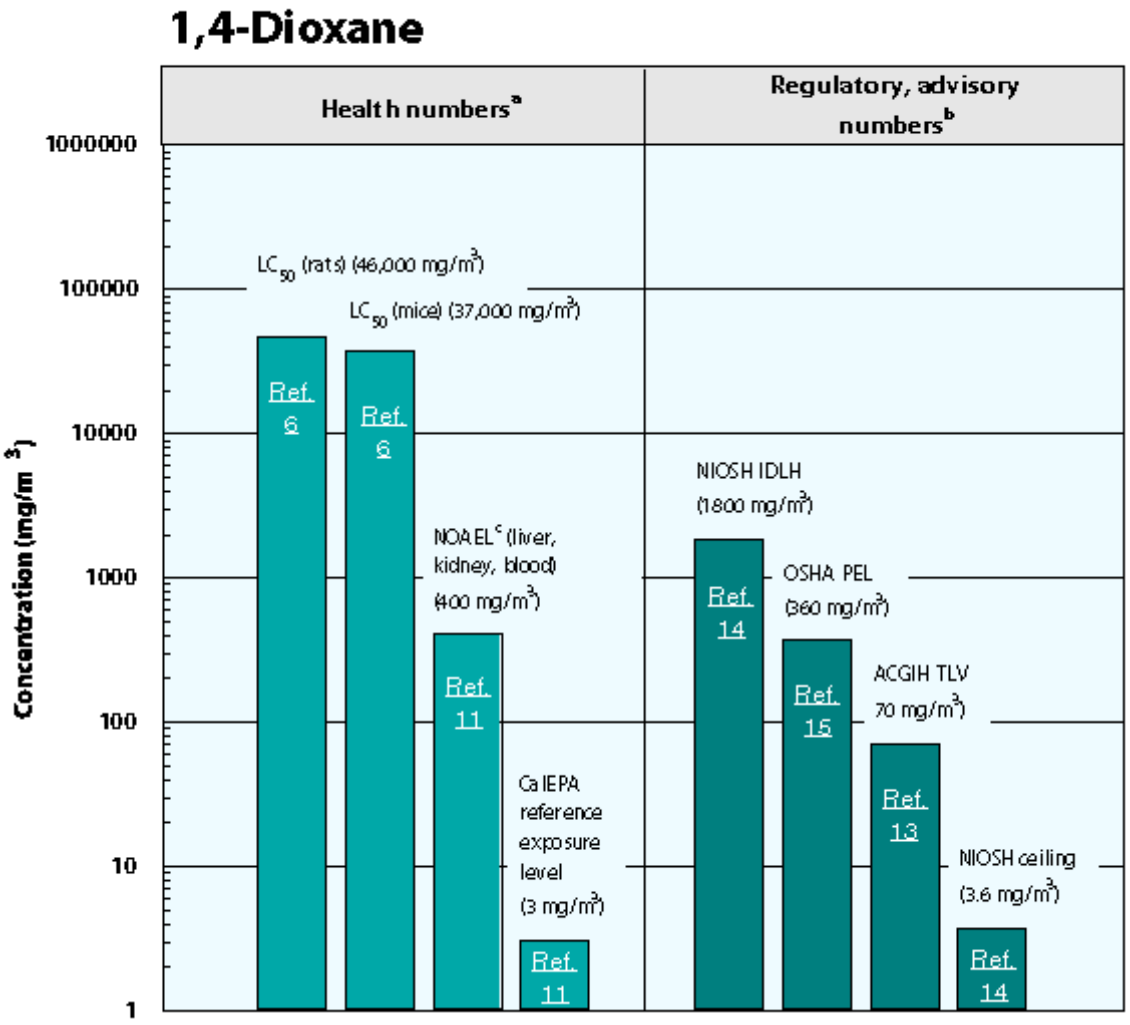
- In three epidemiologic studies on workers exposed to 1,4-dioxane, the observed number of cancer cases did not differ from the expected cancer deaths. (7)
- A study by the National Cancer Institute (NCI) of rats and mice exposed to 1,4-dioxane in their drinking water reported increased incidences of liver carcinomas and adenomas and nasal cavity squamous cell carcinomas. (9)
- Liver carcinomas and gallbladder carcinomas were observed in mice and guinea pigs, respectively. (7)
- No treatment-related lesions resulted from exposure to 1,4-dioxane vapor in rats. (7)
- EPA has classified 1,4-dioxane as a Group B2, probable human carcinogen. (7)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from drinking water containing a specified concentration of a chemical. EPA calculated an oral unit risk estimate of $3.1 \times 10^{-7}$ $(\mu g/L)^{-1}$. EPA estimates that, if an individual were to continuously drink water containing 1,4-dioxane at an average of 3.0 µg/L ($3 \times 10^{-3}$ milligrams per liter (mg/L)) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of drinking water containing this chemical. Similarly, EPA estimates that drinking water containing 30.0 µg/L ($3 \times 10^{-2}$ mg/L) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and water containing 300.0 µg/L ($3 \times 10^{-1}$ mg/L) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency factors, please see IRIS. (7)
- EPA has calculated an oral cancer slope factor of 0.011 $(mg/kg/d)^{-1}$. (7)
- The CalEPA has calculated an inhalation unit risk factor of $7.7 \times 10^{-6}$ $(\mu g/m^3)^{-1}$. (12)

# Physical Properties

- The chemical formula of 1,4-dioxane is $C_4H_8O_2$, and its molecular weight is 88.10 g/mol. (4)
- 1,4-Dioxane occurs as a colorless flammable liquid that is miscible in water. (2,4)
- 1,4-Dioxane has a faint pleasant odor, with an odor threshold of 24 parts per million (ppm). (4,10)
- The vapor pressure for 1,4-dioxane is 30 mm Hg at 20 °C. (2)
- 1,4-Dioxane is also called 1,4-diethyleneoxide.

Conversion Factors:
To convert concentrations in air (at 25 °C) from ppm to $mg/m^3$: $mg/m^3$ = (ppm) × (molecular weight of the compound)/(24.45). For 1,4-dioxane: 1 ppm = 3.6 $mg/m^3$.

## Health Data from Inhalation Exposure




ACGIH TLV --American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
$LC_{50}$ (Lethal Concentration $_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
NIOSH IDLH --National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL ceiling --NIOSH's recommended exposure limit ceiling; the concentration that should not be exceeded at any time.
NOAEL--No-observed-adverse-effect level.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
The health and regulatory values cited in this factsheet were obtained in December 1999.
[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers

are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.

[c] This NOAEL is from the critical study used as the basis for the CalEPA reference exposure level.

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References


1. M. Sittig. Handbook of Toxic and Hazardous Chemicals and Carcinogens. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.
2. U.S. Environmental Protection Agency. p-Dioxane Health Advisory. Office of Drinking Water, Washington, DC. 1987.
3. E.J. Calabrese and E.M. Kenyon. Air Toxics and Risk Assessment. Lewis Publishers, Chelsea, MI. 1991.
4. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
5. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
6. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
7. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS) on 1,4-Dioxane. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.
8. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man: Cadmium, Nickel, Some Epoxides, Miscellaneous Industrial Chemicals and General Considerations on Volatile Anaesthetics. Volume 11. World Health Organization, Lyon. 1976.
9. National Cancer Institute (NCI). Bioassay of 1,4-Dioxane for Possible Carcinogenicity. CAS No. 123-91-1. NCI Carcinogenesis Technical Report Series No. 80. NCI-CG-TR80. National Institutes of Health, Bethesda, MD. 1978.
10. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. Journal of Applied Toxicology, 3(6):272-290. 1983.
11. California Environmental Protection Agency (CalEPA). Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.
12. California Environmental Protection Agency (CalEPA). Air Toxics Hot Spots Program Risk Assessment Guidelines: Part II. Technical Support Document for Describing Available Cancer Potency Factors. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1999
13. American Conference of Governmental Industrial Hygienists (ACGIH). 1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. Cincinnati, OH. 1999.
14. National Institute for Occupational Safety and Health (NIOSH). Pocket Guide to Chemical Hazards. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.
15. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations. 29 CFR 1910.1000. 1998.