

Ethylene Oxide

75-21-8

Hazard Summary

The major use of ethylene oxide is as a chemical intermediate in the manufacture of ethylene glycol. Ethylene oxide is also used as a sterilizing agent for medical equipment and a fumigating agent for spices. The acute (short-term) effects of ethylene oxide in humans consist mainly of central nervous system depression and irritation of the eyes and mucous membranes. Chronic (long-term) exposure to ethylene oxide in humans can cause irritation of the eyes, skin, nose, throat, and lungs, and damage to the brain and nervous system. There also is some evidence linking ethylene oxide exposure to reproductive effects. EPA has concluded that ethylene oxide is carcinogenic to humans by the inhalation route of exposure. Evidence in humans indicates that exposure to ethylene oxide increases the risk of lymphoid cancer and, for females, breast cancer.

Please Note: The main sources of information for this fact sheet are, for cancer, the U.S. Environmental Protection Agency's (EPA's) Integrated Risk Information System and, for other information, the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Ethylene Oxide (1,2).

Uses

- Ethylene oxide is used mainly as a chemical intermediate in the manufacture of ethylene glycol (antifreeze), textiles, detergents, polyurethane foam, solvents, medicine, adhesives, and other products. (1,2)
- Relatively small amounts of ethylene oxide are used as a fumigant, as a sterilant for food (spices) and cosmetics, and in hospital sterilization of surgical equipment and plastic devices that cannot be sterilized by steam. (1,2)

Sources and Potential Exposure

- Sources of ethylene oxide emissions to the air include uncontrolled emissions or venting with other gases in industrial settings. (2)
- Other sources of ethylene oxide air emissions include its use as a sterilizer of medical equipment and its release from commodity-fumigated materials. (2)
- The general population may be exposed to ethylene oxide through breathing contaminated air or from smoking tobacco or being near someone who is smoking. Certain occupational groups (e.g., workers in ethylene oxide manufacturing or processing plants, sterilization technicians, and workers involved in fumigation) may be exposed in the workplace. (2)

Assessing Personal Exposure

- Tests are available to determine personal exposure to ethylene oxide, such as the determination of ethylene oxide in the blood or the amount breathed out of the lungs. (2)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure of workers to high levels of ethylene oxide has resulted in nausea, vomiting, neurological disorders, bronchitis, pulmonary edema, and emphysema. (2)
- Dermal or ocular contact with solutions of ethylene oxide has caused irritation of the skin and eyes in humans. (2)
- Tests involving acute exposure of animals have shown ethylene oxide to have **high** acute toxicity from inhalation exposures. (2)

Chronic Effects (Noncancer):

- Major effects observed in workers exposed to ethylene oxide at low levels for several years are irritation of the eyes, skin, and respiratory passages and effects to the nervous system (e.g., headache, nausea, memory loss, numbness). (2)
- EPA has not established a Reference Dose (RfD) or a Reference Concentration (RfC) for ethylene oxide.
- The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference exposure level of 0.03 milligrams per cubic meter (mg/m^3) (18 parts per billion [ppb]) for ethylene oxide based on nervous system effects in mice. 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 estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (3)
- ATSDR has established an intermediate inhalation minimal risk level (MRL) of $0.2 \text{ mg}/\text{m}^3$ (0.09 parts per million [ppm]) based on an exposure below that associated with renal effects in mice. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. The exposure period for an intermediate MRL is from two weeks to a year. (2)

Reproductive/Developmental Effects:

- Some evidence exists indicating that inhalation exposure to ethylene oxide can cause an increased rate of miscarriages in female workers. (2)
- Various reproductive effects have been noted in inhalation exposure studies of animals, including decreased number of implantation sites, decreased testicular weights and sperm concentration, and testicular degeneration. (2)

Cancer Risk:

- Human occupational studies have shown elevated cases of lymphoid cancer and, also breast cancer in female workers. (1)
- Ethylene oxide has been shown to cause lymphoid cancer and tumors of the brain, lung, connective tissue, uterus, and mammary gland in animals exposed to ethylene oxide by inhalation. (1)
- EPA has concluded that ethylene oxide is carcinogenic to humans by the inhalation route of exposure. (1)
- EPA additionally concludes that the weight of evidence supports a mutagenic mode of action for ethylene oxide toxicity. (1)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated an inhalation unit cancer risk estimate of 3×10^{-3} per $\mu\text{g}/\text{m}^3$ (6×10^{-3} per ppb) for ethylene oxide for both cancer types combined (lymphoid cancer and, in females, breast cancer). Taking into account the mode of action conclusion, EPA estimates that if an individual were to continuously breathe air containing ethylene oxide at an average of $2 \times 10^{-4} \mu\text{g}/\text{m}^3$ (1×10^{-4} ppb) over his or her entire lifetime, that person theoretically would have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that a lifetime of continuously breathing air containing $2 \times 10^{-3} \mu\text{g}/\text{m}^3$ (1×10^{-3} ppb) ethylene oxide would result in not greater than one-in-a-hundred thousand

increased chance of developing cancer, and for air containing $2 \times 10^{-2} \mu\text{g}/\text{m}^3$ (1×10^{-2} ppb) ethylene oxide 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 estimates, see EPA's Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide. (1)

Physical Properties

- The chemical formula for ethylene oxide is $\text{C}_2\text{H}_4\text{O}$, and the molecular weight is 44.1 g/mol. (2)
- The vapor pressure for ethylene oxide is 1,095 mm Hg at 20°C, and it has an octanol/water partition coefficient (log Kow) of -0.22. (2)
- Ethylene oxide has a solubility in water of 1×10^6 mg/L at 20°C and is soluble in alcohol, ether, acetone, and benzene. (2)
- Ethylene oxide has an odor threshold of 787 mg/m³. (2)
- Ethylene oxide has an estimated half-life in air ranging from 69 to 149 days, while its half-life in water ranges from 12 to 14 days in sterile, deionized, and natural river water. (2)

Conversion Factors:

To convert concentrations in air (at 25°C) from ppm to mg/m³:

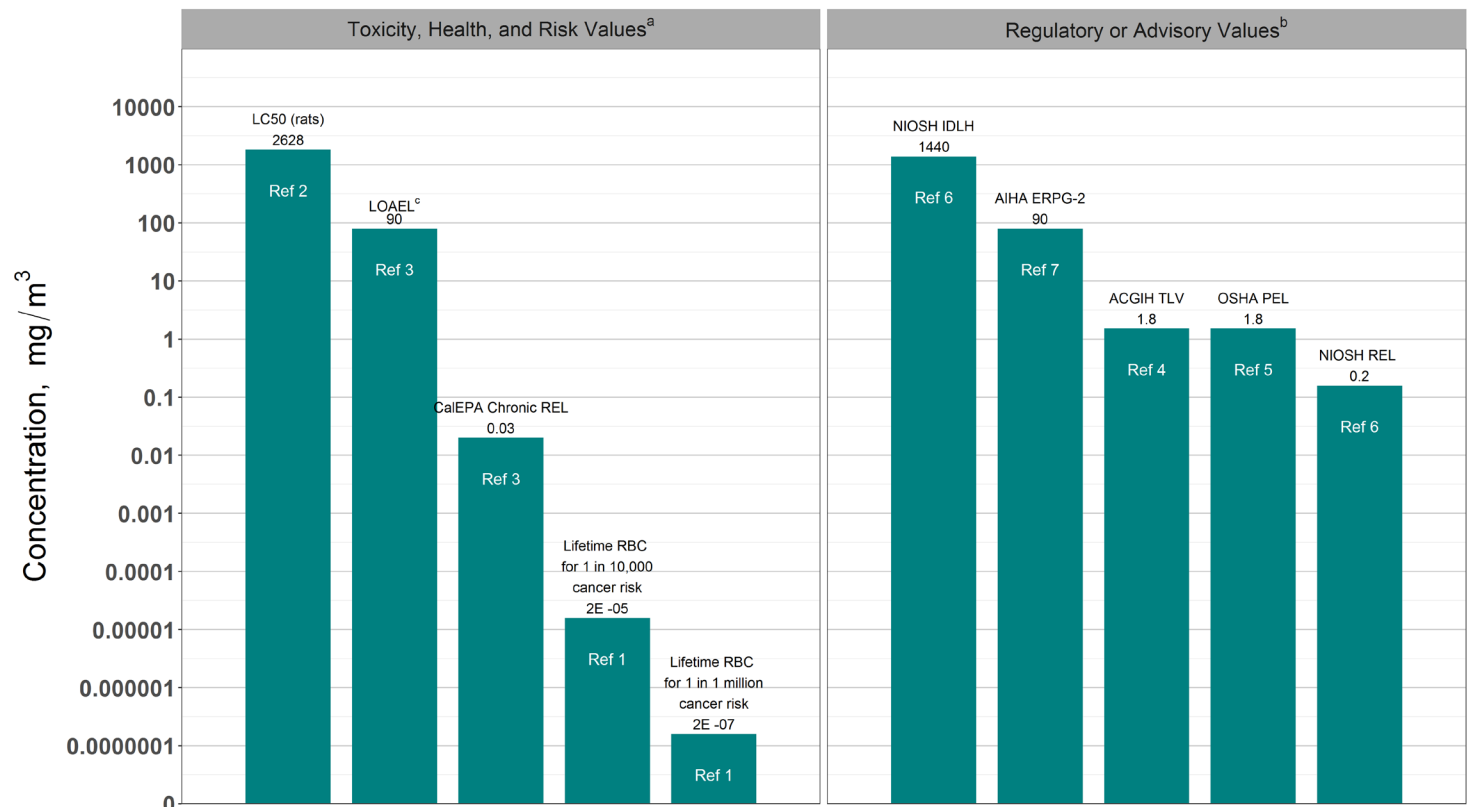
$$\text{mg}/\text{m}^3 = (\text{ppm}) \times (\text{molecular weight of the compound}) / (24.45).$$

For ethylene oxide: 1 ppm = 1.8 mg/m³

To convert concentrations in air from $\mu\text{g}/\text{m}^3$ to mg/m³:

$$\text{mg}/\text{m}^3 = (\mu\text{g}/\text{m}^3) \times (1 \text{ mg}/1,000 \mu\text{g})$$

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.

AIHA ERPG — American Industrial Hygiene Association's emergency response planning guidelines. ERPG-1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG-2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

CalEPA Chronic REL — California EPA Office of Environmental and Human Health Assessment (OEHHA) chronic reference exposure level is the concentration at or below which no adverse health effect is anticipated for a lifetime exposure.

LC₅₀ (Lethal Concentration₅₀) — 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.

LOAEL (Lowest Observed Adverse Effect Level) — The lowest dose or concentration at which there was an observed toxic or adverse effect of a target organism distinguished from a normal or untreated organism of the same species.

NIOSH IDLH Value — National Institute of Occupational Safety and Health's immediately dangerous to life or health air concentration value; NIOSH IDLH value is a 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 health effects or prevent escape from the environment.

NIOSH REL — NIOSH's recommended exposure limit; the recommended exposure limit for an 8- or 10-hour time-weighted average exposure and/or ceiling.

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-hour workday or a 40-hour workweek.

RBC (Cancer risk-based concentration) — A calculated concentration of a chemical in air to which continuous exposure over a lifetime is estimated to be associated with a risk of contracting cancer not greater than the specified probability (e.g., 1 in a million). The RBCs for ethylene oxide in the above graph are calculated using age-dependent adjustment factors (ADAFs).

^aToxicity, Health, and Risk numbers are toxicological values from animal testing or risk assessment values developed by EPA.

^bRegulatory 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, ACGIH, and AIHA numbers are advisory.

^cThe LOAEL is from the critical study used as the basis for the CalEPA chronic REL.

Summary updated December 2018.

References

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3. California Environmental Protection Agency (CalEPA). Air Toxics Hot Spots Program Technical Support Document for the Derivation of Noncancer Reference Exposure Levels Appendix D3. Chronic RELs and Toxicity Summaries Using the Previous Version of the Hot Spots Risk Assessment Guidance (OEHHA 1999). Dec 19, 2008. <https://oehha.ca.gov/media/downloads/crn/appendixd3final.pdf>
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5. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations. 29 CFR 1910.1000. 1998. Available at https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=10099.
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7. American Industrial Hygiene Association (AIHA). The AIHA 2013 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook. 2013. <https://www.aiha.org/get-involved/AIHAGuidelineFoundation/EmergencyResponsePlanningGuidelines/Documents/2013ERPGValues.pdf>