
1,4-Dioxane (C₄H₈O₂)

CAS 123-91-1; UN 1165

Synonyms include 1,4-diethylenedioxiide, 1,4-dioxacyclohexane, di(ethylene oxide), diethylene dioxide, diethylene ether, dioxyethylene ether, glycol ethylene ether, para-dioxane, and *p*-dioxane.

- **Persons exposed only to 1,4-dioxane vapor do not pose secondary contamination risks. Persons whose clothing or skin is contaminated with liquid 1,4-dioxane can cause secondary contamination by direct contact or through off-gassing vapor.**
- **1,4-Dioxane is a colorless liquid at room temperature with an ether-like odor that is easily ignited by heat, sparks, or flames. It is miscible with water.**
- **Exposure to high amounts can cause eye, nose, and throat irritation, as well as liver and kidney lesions. There are no data to determine whether children are more susceptible to 1,4-dioxane toxicity than adults.**

Description

1,4-Dioxane is a manufactured chemical. It is a colorless liquid at temperatures above 53 °F that dissolves well in water and in organic solvents. 1,4-Dioxane has a faint pleasant ether-like odor. The technical-grade product is >99.9% pure (ATSDR 2006). 1,4-Dioxane is easily ignited by heat, sparks or flames. Vapors can cause explosive mixtures with air (HSDB 2007). The vapors of 1,4-dioxane are heavier than air.

1,4-Dioxane must be stored in a cool, well-ventilated location away from heat, oxidizing materials, and sunlight (HSDB 2007).

Routes of Exposure

Inhalation

Inhalation is a main route of exposure among workers involved in the manufacture, processing, handling, and use of 1,4-dioxane. Inhalation exposure can also occur when using tap water contaminated with 1,4-dioxane to cook or shower. Inhalation of 1,4-dioxane can produce nose and throat irritation. Based on a reported odor threshold of 24 ppm (Ammore and Hautala 1983), odor detection may not provide adequate warning of potentially toxic levels of 1,4-dioxane in air. The absorption of 1,4-dioxane via inhalation is rapid and essentially complete (ATSDR 2006). Short-term exposure to concentrations below 50 ppm will

not result in accumulation of 1,4-dioxane or metabolites in the body.

Children exposed to the same levels of 1,4-dioxane as adults may receive a larger dose because they have greater lung surface area:body weight ratios and higher minute volumes:weight ratios. In addition, they may be exposed to higher levels than adults in the same location because of their short stature and the fact that 1,4-dioxane vapors are heavier than air.

Skin/Eye Contact

1,4-Dioxane can be absorbed through the skin, but to a much lesser degree than via inhalation. 1,4-Dioxane in the air can produce eye and nose irritation; direct contact with the liquid may cause irritation and burns (ATSDR 2006).

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants affecting the skin.

Ingestion

No data were located regarding ingestion of 1,4-dioxane in humans. 1,4-Dioxane is well absorbed from the gastrointestinal tract in animals and adverse effects following ingestion have been reported (ATSDR 2006).

Sources/Uses

1,4-Dioxane is used primarily as a solvent for chemical processing; as a laboratory reagent; in plastic, rubber, insecticides, and herbicides; as part of a polymerization catalyst; and as an extraction medium of animal and vegetable oils. 1,4-Dioxane can be found as a contaminant in ethoxylated surfactants used in cosmetics, detergents, and shampoos (ATSDR 2006).

Standards and Guidelines

OSHA PEL (permissible exposure limit) = 100 ppm (skin) as an 8-hour TWA concentration (OSHA 1999).

NIOSH IDLH (immediately dangerous to life or health) = 500 ppm (NIOSH 2005).

EPA AEGL-1 (Acute Exposure Guideline Level-1) = 17 ppm (10-minute to 8-hour) (EPA 2007).

Physical Properties

Description: Colorless liquid with a mild ether-like odor.

Warning properties: Odor (may not always provide adequate warning)

Molecular weight: 88.1 daltons (HSDB 2007).

Boiling point (760 mm Hg): 213.9 °F (101.1 °C) (HSDB 2007).

Melting point 53.2 °F (11.8 °C) (HSDB 2007).

Specific gravity: 1.0329 (water = 1) (HSDB 2007).

Water solubility: Miscible (ATSDR 2006).

Flammability limits: Lower: 2.0%; Upper: 22% (ATSDR 2006).

Incompatibilities

1,4-Dioxane is incompatible with decaborane, triethynyl aluminum, oxygen, halogens, reducing agents, moisture and heat. 1,4-Dioxane must be stored to avoid contact with oxidizing agents (such as perchlorates, peroxides, permanganates, chlorates, nitrates, chlorine, bromine, and fluorine) since violent reactions occur (NJDHSS 2002).

Health Effects

- **1,4-Dioxane is irritating to the skin, eyes, and respiratory tract. These effects can result from inhalation or dermal exposure to 1,4-dioxane.**
- **The main systemic targets for 1,4-dioxane toxicity are the liver and kidney and deaths following acute inhalation exposure to high amounts of 1,4-dioxane may have been due to serious damage to these organs. The mechanism of 1,4-dioxane toxicity has not been elucidated.**
- **Little is known about long-term exposure to lower concentrations of 1,4-dioxane.**

Acute Exposure

1,4-Dioxane induces eye, nose, throat, and skin irritation. Short-term exposure to relatively high amounts of 1,4-dioxane results in liver and kidney toxicity (regardless of the route of exposure) and may be lethal. Mechanisms of 1,4-dioxane toxicity have not been elucidated (ATSDR 2006).

Children do not always respond to chemicals in the same manner as adults. In addition, children of different ages (e.g., in-utero, infants, toddlers, older children) may have different responses to certain chemical exposure, and thus different protocols for managing their care may be needed.

Gastrointestinal

Workers exposed to high amounts of 1,4-dioxane in the air often complained of gastrointestinal pain (ATSDR 2006).

Hepatic

Serious liver injuries resulted from acute exposure to high amounts of 1,4-dioxane in the air (ATSDR 2006). Liver injuries may have been a major contributor to the death of some subjects.

Renal

Renal failure has been described following acute 1,4-dioxane intoxication (ATSDR 2006). Kidney injuries were likely a major contributor to the death of some subjects.

Respiratory

Subjects exposed to controlled amounts (as low as 50 ppm) of 1,4-dioxane in the air for short periods of time complained of nose and throat irritation (ATSDR 2006).

Children may be more vulnerable because of increased minute ventilation per kg and failure to recognize the need to promptly evacuate an area when exposed.

Pneumonitis may be a problem in children.

Ocular

Subjects exposed to 1,4-dioxane (at concentrations as low as 50 ppm) in the air for short periods of time complained of eye irritation and lacrimation (ATSDR 2006).

Potential Sequelae

No information was located regarding potential sequelae following exposure to 1,4-dioxane.

Chronic Exposure

There is very limited information regarding chronic exposure of humans to 1,4-dioxane. A single study of workers exposed to relatively low amounts of 1,4-dioxane for an average of 25 years found no evidence of liver or kidney disease or any other clinical effect (Theiss et al. 1976).

Chronic exposure may be more serious for children because of their potential longer latency period.

Carcinogenicity

The Department of Health and Human Services (DHHS) considers 1,4-dioxane as reasonably anticipated to be a human carcinogen on the basis of sufficient evidence of carcinogenicity in experimental animals (NTP 2005). The EPA has established that 1,4-dioxane is a probable human carcinogen on the basis of inadequate evidence in humans and sufficient evidence in animals (IRIS 2007). The International Agency for Research on Cancer (IARC) has determined that 1,4-dioxane is possibly carcinogenic to humans (IARC 1999).

*Reproductive and
Developmental Effects*

No data were located regarding reproductive and developmental effects in humans. A single oral study in rats exposed to 1,4-dioxane during gestation reported slight fetotoxicity at doses that also affected the mothers (ATSDR 2006).

Prehospital Management

- **Victims exposed only to 1,4-dioxane vapor do not pose contamination risks to rescuers. Victims whose clothing or skin is contaminated with liquid 1,4-dioxane can secondarily contaminate response personnel by direct contact or through off-gassing vapor. 1,4-Dioxane vapor may also off-gas from vomitus of victims who have ingested the chemical.**
- **1,4-Dioxane can cause skin, eye, and respiratory tract irritation as well as liver and kidney lesions. There is no antidote for 1,4-dioxane. Treatment consists of supportive measures.**

Hot Zone

Rescuers should be trained and appropriately attired before entering the Hot Zone. If the proper equipment is not available, or if rescuers have not been trained in its use, assistance should be obtained from a local or regional HAZMAT team or other properly equipped response organization.

Rescuer Protection

1,4-Dioxane vapor is absorbed well by inhalation and is a respiratory tract irritant. The liquid is a skin irritant with moderate skin absorption (ATSDR 2006).

Respiratory Protection: Positive-pressure, self-contained breathing apparatus (SCBA) is recommended in response situations that involve exposure to potentially unsafe levels of 1,4-dioxane (HSDB 2007).

Skin Protection: Chemical-protective clothing is recommended because 1,4-dioxane can cause skin irritation. Fully encapsulating, vapor protective clothing should be worn to deal with spills or leaks with no fire (HSDB 2007).

ABC Reminders

Quickly establish a patent airway, ensure adequate respiration and pulse. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible.

Victim Removal

If victims can walk, lead them out of the Hot Zone to the Decontamination Zone. Victims who are unable to walk may be removed on backboards or gurneys; if these are not available, carefully carry or drag victims to safety.

Victims with chemically-induced acute disorders may suffer from anxiety, especially children who may be separated from a parent or other adult.

Decontamination Zone

Patients exposed to 1,4-dioxane who have no skin or eye irritation may be transferred immediately to the Support Zone. Other patients will require decontamination as described below.

Rescuer Protection

If exposure levels are determined to be safe, decontamination may be conducted by personnel wearing a lower level of protection than that worn in the Hot Zone (described above).

ABC Reminders

Quickly establish a patent airway, ensure adequate respiration and pulse. Stabilize the cervical spine with a collar and a backboard if trauma is suspected. Administer supplemental oxygen as required. Assist ventilation with a bag-valve-mask device if necessary.

Basic Decontamination

Victims who are able may assist with their own decontamination. Quickly remove and double-bag contaminated clothing and personal belongings.

Flush exposed skin and hair with copious amounts of water for at least 20 minutes. Wash with soap and rinse thoroughly with water (HSDB 2007). Use caution to avoid hypothermia when decontaminating victims, particularly children or the elderly. Use blankets or warmers after decontamination as needed.

Flush exposed or irritated eyes with tepid water for 15 minutes. Remove contact lenses if easily removable without additional trauma to the eye. Continue eye irrigation during other basic care and transport. If pain or injury is evident, continue irrigation while transferring the victim to the Support Zone.

Gastric lavage may be performed soon after ingestion of life-threatening amounts of liquid or powdered products.

Provide reassurance to chemically-contaminated victims during decontamination, particularly children who may suffer separation anxiety if separation from a parent occurs.

Transfer to Support Zone

As soon as basic decontamination is complete, move the victim to the Support Zone.

Support Zone

Be certain that victims have been decontaminated properly (see *Decontamination Zone*, above). Victims who have undergone decontamination pose no serious risks of secondary contamination to rescuers. In such cases, Support Zone personnel require no specialized protective gear.

ABC Reminders

Quickly establish a patent airway, ensure adequate respiration and pulse. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible. Administer supplemental oxygen as required and establish intravenous access if necessary. Place on a cardiac monitor.

Additional Decontamination

Continue irrigating exposed skin and eyes, as appropriate.

Advanced Treatment

In cases of respiratory compromise, secure airway and support respiration according to advanced life support (ALS) protocols.

Treat patients who have bronchospasm with an aerosolized bronchodilator such as albuterol. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). 1,4-Dioxane poisoning is not known to pose

additional risk during the use of bronchial or cardiac sensitizing agents and sympathomimetic bronchodilators may reverse bronchospasm in patients exposed to 1,4-dioxane.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution; repeat every 20 minutes as needed while observing for myocardial variability.

Patients who are comatose, hypotensive, or having seizures or cardiac arrhythmias should be treated according to ALS protocols.

Transport to Medical Facility

Only decontaminated patients or patients not requiring decontamination should be transported to a medical facility. “Body bags” are not recommended.

Report to the base station and the receiving medical facility the condition of the patient, treatment given, and estimated time of arrival at the medical facility.

If 1,4-dioxane has been ingested, prepare the ambulance in case the victim vomits. Have ready several towels and open plastic bags to quickly clean up and isolate vomitus.

Multi-Casualty Triage

Consult with the base station physician or the regional poison control center for advice regarding triage of multiple victims.

Asymptomatic patients who have not had a significant exposure may be discharged at the scene after their names, addresses, and telephone numbers are recorded. Those discharged should be advised to seek medical care promptly if symptoms develop (see *Patient Information Sheet* below). Patients who had significant exposure and all patients who have ingested 1,4-dioxane should be transported to a medical facility for evaluation.

Emergency Department Management

- **Patients do not pose contamination risks after contaminated clothing is removed and the skin is washed.**
- **Exposure to high amounts of 1,4-dioxane may induce liver and kidney effects which may cause death days after exposure.**
- **There is no antidote for 1,4-dioxane; treatment consists of supportive measures.**

Decontamination Area

Previously decontaminated patients and patients who have no skin or eye irritation may be transferred immediately to the Critical Care Area. Others require decontamination as described below.

Be aware that use of protective equipment by the provider may cause anxiety, particularly in children, resulting in decreased compliance with further management efforts.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants that react with the skin. Also, emergency room personnel should examine children's mouths because of the frequency of hand-to-mouth activity among children.

ABC Reminders

Evaluate and support airway, breathing, and circulation according to ALS protocols.

Treat patients who have bronchospasm with an aerosolized bronchodilator such as albuterol. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). 1,4-Dioxane poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents and sympathomimetic

bronchodilators may reverse bronchospasm in patients exposed to 1,4-dioxane.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution; repeat every 20 minutes as needed while observing for myocardial variability.

Patients who are comatose, hypotensive, or have seizures or ventricular arrhythmias should be treated in the conventional manner.

Basic Decontamination

Patients who are able may assist with their own decontamination. Remove and double-bag contaminated clothing and all personal belongings.

Flush exposed skin and hair with water for 2–3 minutes (preferably under a shower), then wash thoroughly with mild soap. Rinse thoroughly with water. Use caution to avoid hypothermia when decontaminating victims, particularly children or the elderly. Use blankets or warmers after decontamination as needed.

Flush exposed eyes with plain tepid water for at least 15 minutes (HSDB 2007). Remove contact lenses if easily removable without additional trauma to the eye. Continue irrigation during other basic care and transport. If pain or injury is evident, continue irrigation while transferring the victim to the Critical Care Area.

If 1,4-dioxane has been ingested and the victim is alert, asymptomatic, and has a gag reflex, consider administering a slurry of activated charcoal at a dose of 1 g/kg (infant, child, and adult dose) (HSDB 2007).

Critical Care Area

Be certain that appropriate decontamination has been carried out (see *Decontamination Area* above).

ABC Reminders

Evaluate and support airway, breathing, and circulation as in ABC Reminders above under *Decontamination Zone*. Establish intravenous access in seriously ill patients if this has not been done previously. Continuously monitor cardiac rhythm.

Patients who are comatose, hypotensive, or have seizures or cardiac arrhythmias should be treated in the conventional manner.

Inhalation Exposure

Administer supplemental oxygen by mask to patients who have respiratory symptoms. Treat patients who have bronchospasm with an aerosolized bronchodilator such as albuterol. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). 1,4-Dioxane poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents and sympathomimetic bronchodilators may reverse bronchospasm in patients exposed to 1,4-dioxane.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution; repeat every 20 minutes as needed while observing for myocardial variability.

Skin Exposure

If the skin was in contact with liquid 1,4-dioxane, wash the exposed skin with soap and water to remove any residual amount.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants affecting the skin.

Eye Exposure

Continue irrigation for at least 15 minutes. Test visual acuity. Examine the eyes for corneal damage and treat appropriately. Immediately consult an ophthalmologist for patients who have corneal injuries.

Ingestion Exposure

If 1,4-dioxane has been ingested and the victim is alert, asymptomatic, and has a gag reflex, and charcoal has not been given previously, consider administering a slurry of activated charcoal at a dose of 1 g/kg (infant, child, and adult dose) (HSDB 2007).

Consider gastric lavage with a small nasogastric (NG) tube if: (1) a large dose has been ingested; (2) the patient's condition is evaluated within 30 minutes; (3) the patient has oral lesions or persistent esophageal and/or gastric discomfort; and (4) the lavage can be administered within 1 hour of ingestion. Care must be taken when placing the gastric tube because blind-tube placement may further injure the chemically damaged esophagus or stomach.

Gastric lavage is useful in certain circumstances to remove caustic material and prepare for endoscopic examination. Because the risk of perforation from NG intubation is relatively high in children, lavage is discouraged in children unless intubation is performed under endoscopic guidance.

Consider endoscopy to evaluate the extent of gastrointestinal tract injury. Extreme throat swelling may require airway management using ALS protocols.

Antidotes and Other Treatments

There is no antidote for 1,4-dioxane. Treatment of 1,4-dioxane poisoning is supportive.

Laboratory Tests

Routine laboratory studies for all exposed patients include CBC, glucose, and electrolyte determination. Additional testing for liver and kidney function may be indicated for patients exposed to high levels of 1,4-dioxane (NJDHSS 2002). Prompt testing for 1,4-dioxane and its breakdown products may be beneficial for assessment of the extent of exposure.

Disposition and Follow-up

Consider hospitalizing patients who have a suspected severe exposure to 1,4-dioxane.

Delayed Effects

Patients who have substantial ingestion exposure may develop aspiration pneumonitis or renal failure and should be admitted to an intensive care unit for observation.

Patients who have inhalation exposure and who complain of chest pain, chest tightness, or cough should be observed and examined periodically for 6–12 hours to detect delayed onset pulmonary edema or respiratory failure.

Patient Release

Patients may be discharged with instructions to seek medical care promptly if symptoms develop (see the *1,4-Dioxane—Patient Information Sheet* below).

Follow-up

Obtain the name of the patient’s primary care physician so that the hospital can send a copy of the emergency department (ED) visit to the patient’s doctor.

Severely exposed patients should be monitored as needed for liver and kidney damage. Patients who have skin burns or corneal injuries should be reexamined within 24 hours.

Reporting

If a work-related incident has occurred, you may be legally required to file a report; contact your state or local health department.

Other persons may still be at risk in the setting where this incident occurred. If the incident occurred in the workplace, discussing it with company personnel may prevent future incidents. If a public health risk exists, notify your state or local health department or other responsible public agency. When appropriate, inform patients that they may request an evaluation of their workplace from OSHA or NIOSH. See Appendix III for a list of agencies that may be of assistance.

1,4-Dioxane Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to 1,4-dioxane.

What is 1,4-dioxane?

1,4-Dioxane is a colorless liquid at ambient temperatures with a faint pleasant odor. It does not occur naturally in the environment; it is man-made. Its main use is as a solvent for chemical processing; as a laboratory reagent; in plastic, rubber, insecticides, and herbicides; as part of a polymerization catalyst; and as an extraction medium of animal and vegetable oils. 1,4-Dioxane can be found as a contaminant in some consumer products such as cosmetics, detergents, and shampoos.

What immediate health effects can be caused by exposure to 1,4-dioxane?

Acute exposure to high amounts of vapors of 1,4-dioxane produces eye, nose, and throat irritation, as well as liver and kidney damage. Deaths have been reported after acute exposure to high levels of 1,4-dioxane. Skin contact with liquid 1,4-dioxane can produce skin irritation and burns. Ingestion of liquid 1,4-dioxane can produce internal burns. Little is known about long-term exposure to low levels of 1,4-dioxane. Workers exposed to relative low levels of 1,4-dioxane for years had no health problems.

Can 1,4-dioxane poisoning be treated?

There is no antidote for 1,4-dioxane, but its effects can be treated. Seriously exposed persons may need to be hospitalized.

Are any future health effects likely to occur?

It is not known whether short-term exposure to high-levels of 1,4-dioxane will result in future health effects. However, the possibility exists that repeated exposures to low or moderate levels may cause liver and/or kidney problems in the future.

What tests can be done if a person has been exposed to 1,4-dioxane?

1,4-Dioxane and some of its breakdown products can be measured in blood and urine. Identification of 1,4-dioxane indicates that you have been exposed to 1,4-dioxane, but some of the breakdown products also can be produced by exposure to chemicals other than 1,4-dioxane. The tests need to be conducted within days after the exposure because 1,4-dioxane and its breakdown products leave the body fairly rapidly. These tests are available at specially-equipped laboratories.

Where can more information about 1,4-dioxane be found?

More information about 1,4-dioxane can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational and environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety and Health Administration (OSHA), or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- Severe eye irritation, blurred vision
- Abdominal pain, nausea, anuria

No follow-up appointment is necessary unless you develop any of the symptoms listed above.

Call for an appointment with Dr. _____ in the practice of _____.

When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.

Return to the Emergency Department/_____ Clinic on (date) _____ at _____ AM/PM for a follow-up examination.

Do not perform vigorous physical activities for 1 to 2 days.

You may resume everyday activities including driving and operating machinery.

Do not return to work for _____ days.

You may return to work on a limited basis. See instructions below.

Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.

Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.

Avoid taking the following medications: _____

You may continue taking the following medication(s) that your doctor(s) prescribed for you:

 Other instructions: _____

• Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

• You or your physician can get more information on the chemical by contacting: _____ or _____, or by checking out the following Internet Web sites: _____;

Signature of patient _____ Date _____

Signature of physician _____ Date _____

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