

OCCUPATIONAL SAFETY AND HEALTH GUIDELINE FOR DISULFIRAM

INTRODUCTION

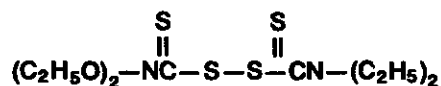
This guideline summarizes pertinent information about disulfiram for workers and employers as well as for physicians, industrial hygienists, and other occupational safety and health professionals who may need such information to conduct effective occupational safety and health programs. Recommendations may be superseded by new developments in these fields; readers are therefore advised to regard these recommendations as general guidelines and to determine periodically whether new information is available.

SUBSTANCE IDENTIFICATION

• Formula



• Structure



• Synonyms

Antabuse; bis(diethylthiocarbamoyl)disulfide; Abstensil; Alcophobin; Antethyl; Aversan; bis((diethylamino)thioxomethyl)disulphide; Disulfan; ethyl thiurad; Thiosan; tetraethylthiram disulfide; tetraethylthiuram disulfide; TTD

• Identifiers

1. CAS No.: 97-77-8
2. RTECS No.: JO1225000

3. DOT UN: None

4. DOT label: None

• Appearance and odor

Disulfiram is a yellow-white crystalline solid or gray powder that has a slight odor and a slightly bitter taste.

CHEMICAL AND PHYSICAL PROPERTIES

• Physical data

1. Molecular weight: 296.54
2. Boiling point (17 mm Hg): 117°C (242.6°F)
3. Specific gravity (water = 1): 1.3 at 20°C (68°F)
4. Vapor density: Data not available
5. Melting point: 70°C (158°F)
6. Vapor pressure: Data not available
7. Solubility: Insoluble in water; soluble in acetone, benzene, chloroform, carbon disulfide, ether, and alcohol; slightly soluble in light petroleum.
8. Evaporation rate: Data not available

• Reactivity

1. Conditions contributing to instability: None reported
2. Incompatibilities: None reported
3. Hazardous decomposition products: Toxic gases (such

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as carbon dioxide, nitrogen dioxide, and sulfur dioxide) may be released in a fire involving disulfiram.

4. Special precautions: None reported

Flammability

The National Fire Protection Association has not assigned a flammability rating to disulfiram.

1. Flash point: Not applicable

2. Autoignition temperature: Not applicable

3. Flammable limits in air: Not applicable

4. Extinguishant: Use an extinguishant that is suitable for the materials involved in the surrounding fire.

Fires involving disulfiram should be fought upwind from the maximum distance possible. Isolate the hazard area and deny access to unnecessary personnel. Emergency personnel should stay out of low areas and ventilate closed spaces before entering. Containers of disulfiram should be moved from the fire area if it is possible to do so safely. Firefighters should wear a full set of protective clothing and self-contained breathing apparatus when fighting fires involving disulfiram.

EXPOSURE LIMITS

OSHA PEL

The Occupational Safety and Health Administration (OSHA) has not promulgated a permissible exposure limit (PEL) for disulfiram [29 CFR 1910.1000, Table Z-1].

NIOSH REL

The National Institute for Occupational Safety and Health (NIOSH) has established a recommended exposure limit (REL) of 2 mg/m³ as a TWA for up to a 10-hr workday and a 40-hr workweek [NIOSH 1992].

ACGIH TLV

The American Conference of Governmental Industrial Hygienists (ACGIH) has assigned disulfiram a threshold limit value (TLV) of 2 mg/m³ as a TWA for a normal 8-hr workday and a 40-hr workweek [ACGIH 1993].

• Rationale for limits

The NIOSH limit is based on the risk of cytochrome P450 inhibition, d-amino acid inhibition, and aldehyde dehydrogenase inhibition associated with disulfiram exposure [NIOSH 1992]. The ACGIH limit is based on the risk of vasodilation, tachycardia, nausea, and hypotension associated with concomitant exposure to disulfiram and alcohol [ACGIH 1991].

HEALTH HAZARD INFORMATION

• Routes of exposure

Exposure to disulfiram can occur through inhalation, ingestion, and eye or skin contact.

• Summary of toxicology

1. *Effects on Animals:* Exposure to disulfiram produces irritation and central nervous system effects in experimental animals. The oral LD₅₀ is 500 mg/kg in rats, 1,980 mg/kg in mice, and 2,050 mg/kg in rabbits [NIOSH 1993]. The major signs of acute toxicity are ataxia, hypothermia, and paralysis [IARC 1976]. A disulfiram solution with a pH of 5.1 caused reversible and slight irritation and corneal opacity when instilled into rabbit eyes [NLM 1993]. In chronic exposure studies, rats fed disulfiram at doses of 1,000 to 2,000 mg/kg/day showed growth retardation, decreased reproductive capacity, and decreased life span [IARC 1976]. In rats exposed to disulfiram at a dose of 100 mg/kg/day from day 3 of gestation, increased fetal resorptions were seen but no teratogenic effects were observed in the surviving offspring [NLM 1993].

2. *Effects on Humans:* The human toxicology of disulfiram may be divided into those effects related to disulfiram alone and those effects associated with the combination of disulfiram and alcohol. Disulfiram alone may produce toxic effects on the nervous system, thyroid, and skin. The combination of disulfiram and alcohol causes a toxic syndrome related to elevated acetaldehyde levels (called the "Antabuse reaction"). The lowest oral dose of disulfiram reported to be lethal in an adult male is 160 mg/kg [NIOSH 1993]. Studies have shown that a small dose of disulfiram can cause a measurable effect on thyroid iodine uptake and also can cause thyroid gland hypertrophy

[Hayes 1982]. Disulfiram can also produce acneform skin rashes, dermatitis, and urticaria [Gilman et al. 1985]. Exposure to disulfiram and concomitant ingestion of alcohol produces a syndrome that begins with a sensation of heat, facial flushing, restlessness, and anxiety and progresses to palpitations, increased heart and respiratory rates, hypotension, chest pain, sweating, nausea, vomiting, weakness, dizziness, and confusion. Atypical and severe reactions have included convulsions, cardiac arrhythmias, myocardial infarction, marked respiratory depression, and acute congestive heart failure [Gosselin et al. 1984]. This syndrome has occurred in workers who have ingested alcohol and then been exposed to disulfiram, as well as to patients exposed to disulfiram as a medication [ACGIH 1991].

• **Signs and symptoms of exposure**

1. **Acute exposure:** Acute exposure to disulfiram may cause headaches, drowsiness, fatigue, dizziness, impaired sexual functioning, a garlic or metallic taste in the mouth, mild gastrointestinal symptoms, depression, psychosis, and confusion. The signs and symptoms of disulfiram-induced peripheral neuropathy may include visual impairment, muscle weakness, numbness, and tingling, and skin reactions to disulfiram exposure may include acneform eruptions, redness, swelling, scaling, and itching.
2. **Chronic exposure:** Chronic exposure to disulfiram may cause identical signs and symptoms to those associated with acute exposure.

• **Emergency procedures**

WARNING!

Seek immediate medical attention for severely affected victims or for victims with signs and symptoms of toxicity or irritation!

Keep unconscious victims warm and on their sides to avoid choking if vomiting occurs. Initiate the following emergency procedures:

1. **Eye exposure:** Irritation may result. *Immediately and thoroughly* flush the eyes with large amounts of water, occasionally lifting the upper and lower eyelids.

2. **Skin exposure:** Irritation may result. *Immediately and thoroughly* wash contaminated skin with soap and water.

3. **Inhalation exposure:** Move the victim to fresh air *immediately*. Have the victim blow his or her nose, or use a soft tissue to remove particulates or residues from the nostrils.

If the victim is not breathing, clean any chemical contamination from the victim's lips and perform cardiopulmonary resuscitation (CPR); if breathing is difficult, give oxygen.

4. **Ingestion exposure:** Take the following steps if disulfiram or any material containing it is ingested:

—Have the victim rinse the contaminated mouth cavity several times with a fluid such as water.

—Have the victim drink a glass (8 oz) of fluid such as water.

—Induce vomiting by having the victim touch the back of the throat with a finger until productive vomiting ceases. Do *not* give syrup of ipecac because of possible onset of respiratory depression and seizures.

—Do *not* force an unconscious or convulsing person to drink fluid or to vomit.

5. **Rescue:** Remove an incapacitated worker from further exposure and implement appropriate emergency procedures (e.g., those listed on the material safety data sheet required by OSHA's hazard communication standard [29 CFR 1910.1200]). All workers should be familiar with emergency procedures, the location and proper use of emergency equipment, and methods of protecting themselves during rescue operations.

EXPOSURE SOURCES AND CONTROL METHODS

The following operations may involve disulfiram and lead to worker exposures to this substance:

—Use as a rubber accelerator and vulcanizer

—Use as a medication in the treatment of alcoholism

—Use as a seed disinfectant and fungicide

The following methods are effective in controlling worker exposures to disulfiram, depending on the feasibility of implementation:

- Process enclosure
- Local exhaust ventilation
- General dilution ventilation
- Personal protective equipment

Good sources of information on control methods are as follows:

1. ACGIH [1992]. *Industrial ventilation—a manual of recommended practice*. 21st ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
2. Burton DJ [1986]. *Industrial ventilation—a self study companion*. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
3. Alden JL, Kane JM [1982]. *Design of industrial ventilation systems*. New York, NY: Industrial Press, Inc.
4. Wadden RA, Scheff PA [1987]. *Engineering design for control of workplace hazards*. New York, NY: McGraw-Hill.
5. Plog BA [1988]. *Fundamentals of industrial hygiene*. Chicago, IL: National Safety Council.

MEDICAL MONITORING

Workers who may be exposed to chemical hazards should be monitored in a systematic program of medical surveillance that is intended to prevent occupational injury and disease. The program should include education of employers and workers about work-related hazards, early detection of adverse health effects, and referral of workers for diagnosis and treatment. The occurrence of disease or other work-related adverse health effects should prompt immediate evaluation of primary preventive measures (e.g., industrial hygiene monitoring, engineering controls, and personal protective equipment). A medical monitoring program is intended to supplement, not replace, such measures. To place workers effectively and to detect and control work-related health effects, medical evaluations

should be performed (1) before job placement, (2) periodically during the term of employment, and (3) at the time of job transfer or termination.

• Preplacement medical evaluation

Before a worker is placed in a job with a potential for exposure to disulfiram, a licensed health care professional should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories, a physical examination, and physiologic and laboratory tests appropriate for the anticipated occupational risks. These should concentrate on a history of skin allergies and excessive alcohol intake and on the function and integrity of the central and peripheral nervous systems, eyes, skin, liver, and thyroid.

A preplacement medical evaluation is recommended to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is exposed to disulfiram at or below the prescribed exposure limit. The health care professional should consider the probable frequency, intensity, and duration of exposure as well as the nature and degree of any applicable medical condition. Such conditions (which should not be regarded as absolute contraindications to job placement) include a history and other findings consistent with excessive alcohol intake or with diseases of the eyes, skin, nervous system, liver, or thyroid.

• Periodic medical examinations and biological monitoring

Occupational health interviews and physical examinations should be performed at regular intervals during the employment period, as mandated by any applicable Federal, State, or local standard. Where no standard exists and the hazard is minimal, evaluations should be conducted every 3 to 5 years or as frequently as recommended by an experienced occupational health physician. Additional examinations may be necessary if a worker develops symptoms attributable to disulfiram exposure. The interviews, examinations, and medical screening tests should focus on identifying the adverse effects of disulfiram on the eyes, skin, nervous system, liver, or thyroid. Current health status should be compared with the baseline health status of the individual worker or with expected values for a suitable reference population.

Biological monitoring involves sampling and analyzing body tissues or fluids to provide an index of exposure to

a toxic substance or metabolite. Disulfiram and its metabolites can be detected in the blood, urine, and breath of exposed individuals. However, no method of correlating airborne concentrations of disulfiram with concentrations in the blood, urine, or breath has been developed. Therefore, no biological monitoring test acceptable for routine use has yet been developed for disulfiram.

- **Medical examinations recommended at the time of job transfer or termination**

The medical, environmental, and occupational history interviews, the physical examination, and selected physiologic or laboratory tests that were conducted at the time of placement should be repeated at the time of job transfer or termination to determine the worker's medical status at the end of his or her employment. Any changes in the worker's health status should be compared with those expected for a suitable reference population.

WORKPLACE MONITORING AND MEASUREMENT

Determination of a worker's exposure to airborne disulfiram is made using a glass fiber filter (37 mm). Samples are collected at a recommended flow rate of 1.0 liter/min until a recommended air volume of 120 liters is collected. Samples are extracted with methanol, and analysis is conducted by high-performance liquid chromatography using ultraviolet detection. This method is described in the OSHA Computerized Information System [OSHA 1992] and the *OSHA Chemical Information Manual* [OSHA 1987].

PERSONAL HYGIENE

If disulfiram contacts the skin, workers should flush the affected areas immediately with plenty of water for 15 minutes, and then wash with soap and water.

Clothing contaminated with disulfiram should be removed immediately, and provisions should be made for the safe removal of the chemical from the clothing.

A worker who handles disulfiram should thoroughly wash hands, forearms, and face with soap and water before eating, using tobacco products, using toilet facilities, or applying cosmetics.

Workers should not eat, drink, use tobacco products, or apply cosmetics in areas where disulfiram or a solution containing disulfiram is handled, processed, or stored.

STORAGE

Disulfiram should be stored in a cool, dry, well-ventilated area in tightly sealed containers that are labeled in accordance with OSHA's hazard communication standard [29 CFR 1910.1200]. Containers of disulfiram should be protected from physical damage and should be stored separately from phenols, flammable substances, heat, sparks, and open flame. Because containers that formerly contained disulfiram may still hold product residues, they should be handled appropriately.

SPILLS AND LEAKS

In the event of a spill or leak involving disulfiram, persons not wearing protective equipment and clothing should be restricted from contaminated areas until cleanup has been completed. The following steps should be undertaken following a spill or leak:

1. Notify safety personnel.
2. Remove all sources of heat and ignition.
3. Ventilate the area of the spill or leak.
4. Collect powdered material in the most convenient manner and deposit in sealed containers.

SPECIAL REQUIREMENTS

U.S. Environmental Protection Agency (EPA) requirements for emergency planning, reportable quantities for hazardous releases, community right-to-know, and hazardous waste management may change over time. Users are therefore advised to determine periodically whether new information is available.

- **Emergency planning requirements**

Disulfiram is not subject to EPA emergency planning requirements under the Superfund Amendments and Reauthorization Act (SARA) [42 USC 11022].

- **Reportable quantity requirements for hazardous releases**

Employers are not required by the emergency release notification provisions of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [40 CFR 355.40] to notify the National Response Center of an accidental release of disulfiram; there is no reportable quantity for this substance.

- **Community right-to-know requirements**

Employers are not required by Section 313 of SARA to submit a Toxic Chemical Release Inventory form (Form R) to EPA reporting the amount of disulfiram emitted or released from their facility annually.

- **Hazardous waste management requirements**

EPA considers a waste to be hazardous if it exhibits any of the following characteristics: ignitability, corrosivity, reactivity, or toxicity as defined in 40 CFR 261.21-261.24. Although disulfiram is not specifically listed as a hazardous waste under the Resource Conservation and Recovery Act (RCRA) [40 USC 6901 et seq.], EPA requires employers to treat any waste as hazardous if it exhibits any of the characteristics discussed above.

Providing detailed information about the removal and disposal of specific chemicals is beyond the scope of this guideline. The U.S. Department of Transportation, EPA, and State and local regulations should be followed to ensure that removal, transport, and disposal of this substance are conducted in accordance with existing regulations. To be certain that chemical waste disposal meets EPA regulatory requirements, employers should address any questions to the RCRA hotline at (800) 424-9346 or at (202) 382-3000 in Washington, D.C. In addition, relevant State and local authorities should be contacted for information about their requirements for waste removal and disposal.

RESPIRATORY PROTECTION

- **Conditions for respirator use**

Good industrial hygiene practice requires that engineering controls be used where feasible to reduce workplace concentrations of hazardous materials to the prescribed exposure limit. However, some situations may require the use of respirators to control exposure. Respirators must be worn if the ambient concentration of disulfiram

exceeds prescribed exposure limits. Respirators may be used (1) before engineering controls have been installed, (2) during work operations such as maintenance or repair activities that involve unknown exposures, (3) during operations that require entry into tanks or closed vessels, and (4) during emergencies. Workers should use only respirators that have been approved by NIOSH and the Mine Safety and Health Administration (MSHA).

- **Respiratory protection program**

Employers should institute a complete respiratory protection program that, at a minimum, complies with the requirements of OSHA's respiratory protection standard [29 CFR 1910.134]. Such a program must include respirator selection, an evaluation of the worker's ability to perform the work while wearing a respirator, the regular training of personnel, respirator fit testing, periodic workplace monitoring, and regular respirator maintenance, inspection, and cleaning. The implementation of an adequate respiratory protection program (including selection of the correct respirator) requires that a knowledgeable person be in charge of the program and that the program be evaluated regularly. For additional information about the selection and use of respirators and about the medical screening of respirator users, consult the *NIOSH Respirator Decision Logic* [NIOSH 1987b] and the *NIOSH Guide to Industrial Respiratory Protection* [NIOSH 1987a].

PERSONAL PROTECTIVE EQUIPMENT

Protective gloves and clothing should be worn to prevent any skin contact with disulfiram. Chemical protective clothing should be selected on the basis of available performance data, manufacturers' recommendations, and evaluation of the clothing under actual conditions of use. No reports have been published on the resistance of various protective clothing materials to disulfiram permeation. If permeability data are not readily available, protective clothing manufacturers should be requested to provide information on the best chemical protective clothing for workers to wear when they are exposed to disulfiram.

If disulfiram is dissolved in an organic solvent, the permeation properties of both the solvent and the mixture must be considered when selecting personal protective equipment and clothing.

Safety glasses, goggles, or face shields should be worn during operations in which disulfiram might contact the

eyes (e.g., through dust particles or splashes of solution). Eyewash fountains and emergency showers should be available within the immediate work area whenever the potential exists for eye or skin contact with disulfiram. Contact lenses should not be worn if the potential exists for disulfiram exposure.

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