OCCUPATIONAL SAFETY AND HEALTH GUIDELINE
FOR ACETIC ANHYDRIDE

INTRODUCTION
This guideline summarizes pertinent information about acetic anhydride 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 Recommendations may be superseded by new developments; readers are therefore advised to regard these recommendations as general guidelines and to determine periodically whether new information is available.

SUBSTANCE IDENTIFICATION
- Formula
  \[ \text{C}_4\text{H}_6\text{O}_3 \]
- Structure
  \[ (\text{CH}_3\text{CO})_2\text{O} \]
- Synonyms
  Acetanhydride, acetic acid anhydride, acetyl ether, acetic oxide, acetyl oxide, ethanoic anhydride
- Identifiers
  1. CAS No.: 108-24-7
  2. RTECS No.: AK1925000
  3. DOT UN: 1715 39
  4. DOT labels: Corrosive, Flammable Liquid
- Appearance and odor
  Acetic anhydride is a colorless liquid with a strong, pungent, vinegarlike odor. The odor threshold is reported to be between 0.13 and 0.34 part per million (ppm) parts of air.

CHEMICAL AND PHYSICAL PROPERTIES
- Physical data
  1. Molecular weight: 102.1
  2. Boiling point (at 760 mm Hg): 139°C (282°F)
  3. Specific gravity (water = 1): 1.08 at 20°C (68°F)
  4. Vapor density (air = 1 at boiling point of acetic anhydride): 3.5
  5. Melting point: –73°C (~99.4°F)
  6. Vapor pressure at 20°C (68.8°F): 4 mm Hg
  7. Solubility: Soluble in cold water; decomposes in hot water to form acetic acid; miscible with alcohol, chloroform, ether, and ethyl acetate
  8. Evaporation rate (butyl acetate = 1): 0.46
- Reactivity
  1. Contact of acetic anhydride vapors with water or air should be avoided.
  2. Incompatibilities: Fires and explosions may result from contact of acetic anhydride with water, alcohols, strong oxidizers, chromic acid, amines, or strong caustics.
  3. Hazardous decomposition products: Toxic gases and vapors (such as carbon dioxide, carbon monoxide, various hydrocarbons, and acid aerosols) may be released when acetic anhydride is heated or decomposes.
  4. Special precautions: Acetic anhydride attacks some coatings and some forms of plastic and rubber. It is corrosive to iron, steel, and other metals.
- Flammability
  The National Fire Protection Association has assigned a flammability rating of 2 (moderate fire hazard) to acetic anhydride.
  1. Flash point: 49°C (120°F) (closed cup)
  2. Autoignition temperature: 316°C (600°F)
  3. Flammable limits in air (% by volume): Lower, 2.7; upper, 10.3
4. Extinguishment: Use carbon dioxide or dry chemical for small fires and alcohol foam for large fires. Water should be used with caution because acetic anhydride reacts with water.

Fires involving acetic anhydride should be fought upwind and 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. Vapor explosion and poison hazards may occur indoors, outdoors, or in sewers. Vapors may travel to a source of ignition and flash back. Containers of acetic anhydride may explode in the heat of the fire and should be moved from the fire area if it is possible to do so safely. If this is not possible, cool containers from the sides with water until well after the fire is out. Avoid directing water into containers of acetic anhydride. Stay away from the ends of containers. Personnel should withdraw immediately if they hear a rising sound from a venting safety device or if a container becomes discolored as a result of fire. Dikes should be used to contain fire-control water for later disposal. If a tank car or truck is involved in a fire, personnel should isolate an area of a half mile in all directions. Firefighters should wear a full set of protective clothing (including a self-contained breathing apparatus) when fighting fires involving acetic anhydride. Chemical protective clothing that is specifically recommended for acetic anhydride may not provide thermal protection unless so stated by the clothing manufacturer. Firefighters' protective clothing may not provide protection against permeation by acetic anhydride.

**HEALTH HAZARD INFORMATION**

- **Routes of exposure**

Exposure to acetic anhydride can occur through inhalation, ingestion, and eye or skin contact. Acetic anhydride also penetrates the skin.

- **Summary of toxicology**

1. **Effects on Animals:** Acetic anhydride is highly corrosive and causes severe irritation and burns of the eyes, mucous membranes, and skin of exposed animals. When instilled into the eyes, acetic anhydride can be corrosive. It can also penetrate the intact corneal epithelium in concentrations sufficiently high to cause iritis [NIOSH 1992]. Guinea pigs repeatedly challenged with dermal applications of acetic anhydride developed skin sensitization [Proctor et al. 1988]. The dermal LD₅₀ for rabbits is 4,000 mg/kg [NIOSH 1991]. Rats survived exposure to saturated vapors for 5 min [Deichmann and Gerade 1969]. Six rats exposed to 1,000 ppm of acetic anhydride for 4 hr survived, but those inhaling 2,000 ppm for the same interval died [ACGIH 1991b]. The oral LD₅₀ for rats is 1,780 mg/kg.

2. **Effects on Humans:** Exposure to acetic anhydride in either the liquid or vapor form causes severe irritation of the eyes, skin, and mucous membranes in humans. Eye contact can lead to corneal burns, erosion, edema, scarring, cataracts with temporary or permanent visual impairment, and inflammation and structural damage of the iris [Grant 1986; Klagesen et al. 1986]. In contact with the skin, acetic anhydride causes delayed burns that may be slow to heal [Grayson 1985; Sittig 1985]. The vapor of this substance is reported to be irritating even at a concentration as low as 0.09 ppm [NIOSH 1992]. Workers exposed to concentrations of acetic anhydride greater than 5 ppm experienced acute eye and upper respiratory tract irritation; their symptoms included severe eye pain and difficult breathing [Proctor et al. 1988]. Inhalation of high concentrations of this substance can cause bronchoespasm and ulceration of the nasal mucosa [Proctor et al. 1988]. Humans exposed to the vapor of acetic anhydride occasionally become sensitized to this substance [Proctor et al. 1988]. Inhalation of acetic anhydride can cause corrosion of oral, esophageal, and gastric tissues as well as hemorrhages, strictures, and stenoses but rarely perforations [NIOSH 1992].

- **Signs and symptoms of exposure**

1. **Acute exposure:** Acetic anhydride is corrosive to tissues. It can cause a burning sensation in the nose and throat, cough, pain in the chest, difficult breathing, dyspnea, and pulmonary edema. Exposure of the eye to liquid or vaporous acetic anhydride results in excessive tearing, redness, pain, and photophobia. In contact with the skin, acetic anhydride can cause corrosion, burns, and blisters. Ingestion can also induce clammy skin, weak and rapid pulse, nausea, vomiting,
shallow respiration, and decreased urine output. In cases where circulatory collapse has occurred and gone uncorrected for several hours, renal failure and ischemic liver and heart lesions have resulted. Death following ingestion can result from glottic edema or circulatory shock.

2. Chronic exposure: Acetic anhydride can cause conjunctivitis, pulmonary edema with coughing and difficult breathing, and skin sensitization with redness, itching, and wheals.

- Emergency procedures

Keep unconscious victims warm and on their sides to avoid choking if vomiting occurs. Immediately initiate the following emergency procedures, continuing them as appropriate en route to the emergency medical facility:

1. Eye exposure: Tissue destruction and blindness may result from exposure to concentrated solutions, vapors, mists or aerosols of acetic anhydride! Immediately but gently flush the eyes with large amounts of water for at least 15 min, occasionally lifting the upper and lower eyelids.

2. Skin exposure: Severe burns and skin corrosion may result! Immediately remove all contaminated clothing! Immediately and gently wash skin for at least 15 min. Use soap and water if skin is intact; use only water if skin is not intact.

3. Inhalation exposure: If vapors, mists, or aerosols of acetic anhydride are inhaled, move the victim to fresh air immediately.

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 acetic anhydride or a solution containing it is ingested:

- Do not induce vomiting.

- Have the victim rinse the contaminated mouth cavity several times with a fluid such as water. Immediately after rinsing, have the victim drink one cup (8 oz) of fluid and no more.

- Do not permit the victim to drink milk or carbonated beverages!

- Do not permit the victim to drink any fluid if more than 60 min have passed since initial ingestion.

NOTE: These instructions must be followed exactly. Drinking a carbonated beverage or more than one cup of fluid could create enough pressure to perforate already damaged stomach tissue. The tissue-coating action of milk may impede medical assessment of tissue damage. Ingestion of any fluid more than 60 min after initial exposure could further weaken damaged tissue and result in perforation.

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 and the location and proper use of emergency equipment.

EXPOSURE SOURCES AND CONTROL METHODS

The following operations may involve acetic anhydride and may result in worker exposures to this substance:

- Manufacture of acetyl compounds, cellulose acetate, cellulose esters, chloroacetic acid, acetyl chloride, triacetate fibers, and vinyl acetate

- Processing of dyes, perfumes, explosives, and flavorings

- Electropolishing of metals and processing of semiconductors

- Use of acetic anhydride as an acetylizer and solvent in examining wool fat, glycerol, fatty and volatile oils, and resins, and in detecting rosins

- Use of acetic anhydride as a dehydrating agent in nitra-

- Use of acetic anhydride in the manufacture of pharmaceuticals, including aspirin, and as an intermediate in the synthesis of pesticides

- Use of acetic anhydride as an esterifying agent for food starch

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

- Process enclosure

- Local exhaust ventilation

- General dilution ventilation

- Personal protective equipment

Good sources of information about control methods are as follows:

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**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, placement of workers in jobs that do not jeopardize their safety or health, 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 must 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 acetic anhydride, 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 the function and integrity of the eyes, skin, and respiratory system. Medical monitoring for respiratory disease should be conducted using the principles and methods recommended by American Thoracic Society [ATS 1987].

A preplacement medical evaluation is recommended to assess an individual's suitability for employment at a specific job and to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is exposed to acetic anhydride at or below the prescribed exposure limit. The licensed 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 eye, skin, or respiratory system diseases.

- 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 acetic anhydride exposure. The interviews, examinations, and medical screening tests should focus on identifying the adverse effects of acetic anhydride on the eyes, skin, and respiratory system. 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. No biological monitoring test acceptable for routine use has yet been developed for acetic anhydride.

- 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 job placement should be repeated at the time of job transfer or termination. Any changes in the worker's health status should be compared with those expected for a suitable reference population.

**WORKPLACE MONITORING AND MEASUREMENT**

A worker's exposure to airborne acetic anhydride is determined by using a standard midget bubbler containing 10 ml of alkaline hydroxylamine hydrochloride solution. The absorbing solution is made up of equal volumes of hydroxylamine hydrochloride (200 g in 1 liter distilled water) and sodium hydroxide (200 g in 1 liter distilled water). The solution is mixed just before use and is stable for only 2 hr. Samples are collected at a recommended flow rate of 0.2 to 1 liter/min until a recommended air volume of 25 to 100 liters is collected. Analysis is performed colorimetrically using...
visible absorption spectrophotometry. A purple-colored complex is formed by adding ferric chloride solution to the sample. The limit of detection for this procedure is 0.05 mg/sample. This method is described in Method 3506 of the NIOSH Manual of Analytical Methods [NIOSH 1984].

PERSONAL HYGIENE

If acetic anhydride contacts the skin, workers should flush the affected areas immediately with plenty of water for 15 min and then wash with soap and water. Get medical help immediately.

Clothing and shoes contaminated with acetic anhydride should be removed immediately and provisions should be made for safely removing this chemical from these articles. If gross exposure occurs, remove contaminated clothing under a safety shower. Speed in removing the contaminated material from the skin is extremely important. Persons laundering contaminated clothing should be informed about the hazardous properties of acetic anhydride, particularly its potential to be corrosive to the skin.

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

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

STORAGE

Acetic anhydride 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]. Outside or detached storage is preferred. Inside storage must be in a standard flammable liquids storage room or cabinet. Steel, galvanized tin, tinned iron, copper, or copper alloys should not be used for piping or valves that will be in contact with acetic anhydride. Containers of acetic anhydride should be protected from physical damage and should be separated from water, alcohols, strong oxidizers, chromic acid, amines, strong caustics, heat, sparks, and open flame. Because containers that formerly contained acetic anhydride may still hold product residues, they should be handled appropriately.

SPILLS AND LEAKS

In the event of a spill or leak involving acetic anhydride, persons not wearing protective equipment and clothing should be restricted from contaminated areas until cleanup is complete. The following steps should be undertaken following a spill or leak:

1. Do not touch the spilled material; stop the leak if it is possible to do so without risk.
2. Notify safety personnel.
3. Remove all sources of heat and ignition.
4. Ventilate potentially explosive atmospheres.
5. If the leak or spill has not ignited, water spray may be used to reduce vapors.
6. Absorb small liquid spills with sand or other noncombustible absorbent material and place the material in a covered container for later disposal. Wash the site with soda ash solution and flush with plenty of water.
7. For large liquid spills, build dikes far ahead of the spill to contain the acetic anhydride for later reclamation or disposal.

SPECIAL REQUIREMENTS

U.S. Environmental Protection Agency (EPA) requirements for emergency planning, reportable quantities of 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

Acetic anhydride 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

A hazardous substance release is defined by EPA as any spilling, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping, or disposing of hazardous substances into the environment (including the abandonment or discarding of contaminated containers). In the event of a release that is equal to or greater than the reportable quantity for that chemical, employers are required by the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 CFR 355.40] to notify the proper Federal, State, and local authorities.

The reportable quantity for acetic anhydride is 5,000 lb. If an amount equal to or greater than this quantity is released within a 24-hr period in a manner that will expose persons outside the facility, employers are required to do the following:

—Notify the National Response Center immediately at (800) 424–8802 or at (202) 426–2675 in Washington, D.C. [40 CFR 302.6].

—Notify the emergency response commission of the State likely to be affected by the release [40 CFR 355.40].
---Notify the community emergency coordinator of the local emergency planning committee (or relevant local emergency response personnel) of any area likely to be affected by the release [40 CFR 355.40].

**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 acetic anhydride 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 acetic anhydride 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 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 acetic anhydride 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, 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 on the selection and use of respirators and on 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 clothing should be worn to prevent any possibility of skin contact with acetic anhydride. 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. The following materials have been tested against permeation by acetic anhydride and have demonstrated protection for more than 4 but fewer than 8 hr: butyl rubber and Teflon®. Polyvinyl chloride, nitrile rubber, Viton®, and natural rubber have all demonstrated poor resistance to permeation by acetic anhydride.

If acetic anhydride is dissolved in water or 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 acetic anhydride might contact the eyes (e.g., through vapors 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 acetic anhydride. Contact lenses should not be worn if the potential exists for acetic anhydride exposure.

**REFERENCES CITED**


