OCCUPATIONAL SAFETY AND HEALTH GUIDELINE FOR ACETONITRILE

INTRODUCTION

This guideline summarizes pertinent information about acetonitrile 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 Recommendations may be superseded by new developments; readers are therefore advised to regard these recommendations as general guidelines and to determine periodically whether new information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**

C_2H_3N

- **Structure**

CH_3CN

- **Synonyms**

Methyl cyanide, cyanomethane, ethanenitrile, ethyl nitrile, methanecarbonitrile

- **Identifiers**

1. CAS No.: 75-05-8
2. RTECS No.: AL7700000
3. DOT UN: 1648 28
4. DOT labels: Flammable Liquid and Poison

- **Appearance and odor**

Acetonitrile is a flammable, colorless liquid with an aromatic odor. The odor threshold is reported to be 40 parts per million (ppm) parts of air.

CHEMICAL AND PHYSICAL PROPERTIES

- **Physical data**

1. Molecular weight: 41
2. Boiling point (at 760 mm Hg): 81.6°C (178.9°F)
3. Specific gravity (water = 1): 0.79 at 20°C (68°F)
4. Vapor density (air = 1 at boiling point of acetonitrile): 1.42
5. Melting point: -45°C (-49°F)
6. Vapor pressure at 20°C (68°F): 73 mm Hg
7. Solubility: Miscible with water, methanol, methyl acetate, ethyl acetate, alcohol, ethanol, acetone, acetamide solutions, carbon tetrachloride, chloroform, ethylene chloride, and many unsaturated hydrocarbons
8. Evaporation rate: Data not available

- **Reactivity**

1. Conditions contributing to instability: Heat, sparks, or open flame. Vapors form explosive mixtures with air.
2. Incompatibilities: Fire and explosion may result from contact of acetonitrile with perchloric acid, iron (III) salts of perchlorate, nitric acid, oleum, indium, nitrating agents, perfluorourea, chlorosulfonic acid, or other strong oxidizers.
3. Hazardous decomposition products: Toxic gases (such as oxides of nitrogen, carbon monoxide, carbon dioxide, and hydrogen cyanide) may be released in a fire involving acetonitrile.
4. Special precautions: Liquid acetonitrile attacks some coatings and some forms of plastic and rubber.

- **Flammability**

The National Fire Protection Association has assigned a flammability rating of 3 (severe fire hazard) to acetonitrile.

1. Flash point: 5.6°C (42°F) (closed cup)
2. Autoignition temperature: 523.9°C (975°F)
3. Flammable limits in air (% by volume): Lower, 4.4; upper, 16.0

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service Centers for Disease Control
National Institute for Occupational Safety and Health
Division of Standards Development and Technology Transfer

U.S. DEPARTMENT OF LABOR
Occupational Safety and Health Administration

4. Extinguishant: Use carbon dioxide, dry chemical, or foams on fires involving acetonitrile. Never direct a stream of water into burning pools of liquid acetonitrile because this may scatter and spread the flames. Water spray may be used to cool containers or to protect persons attempting to stop the leak.

Fires involving acetonitrile 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 acetonitrile 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. 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 acetonitrile. Chemical protective clothing that is specifically recommended for acetonitrile may not provide thermal protection unless so stated by the clothing manufacturer. Firefighters' protective clothing may not provide protection against permeation by acetonitrile.

EXPOSURE LIMITS

- **OSHA PEL**

The current Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for acetonitrile is 40 ppm (70 mg/m^3) as an 8-hr time-weighted average (TWA) concentration and 60 ppm (105 mg/m^3) as a short-term exposure limit (STEL) [29 CFR 1910.1000, Table Z-1-A]. A STEL is a 15-min TWA exposure that should not be exceeded at any time during the workday.

- **NIOSH REL**

The National Institute for Occupational Safety and Health (NIOSH) has established a recommended exposure limit (REL) of 20 ppm (34 mg/m^3) as a TWA for up to a 10-hr workshift and a 40-hr workweek [NIOSH 1992].

- **ACGIH TLV®**

The American Conference of Governmental Industrial Hygienists (ACGIH) has assigned acetonitrile a threshold limit value (TLV) of 40 ppm (67 mg/m^3) as a TWA for a normal 8-hr workday and a 40-hr workweek and a STEL of 60 ppm (101 mg/m^3) for periods not to exceed 15 min [ACGIH 1991b].

- **Rationale for limits**

The limits are based on the risks of organic cyanide poisoning and liver and respiratory tract injuries associated with exposure to acetonitrile.

HEALTH HAZARD INFORMATION

- **Routes of exposure**

Exposure to acetonitrile can occur through inhalation and eye or skin contact.

- **Summary of toxicology**

1. *Effects on Animals*: Acetonitrile can induce methemoglobinemia and cyanosis because it is metabolized in the body to cyanide. The 8-hr LC_{50} in rats is 7,500 ppm [NIOSH 1991]. The dermal LD_{50} in rabbits is 1,250 mg/kg [NIOSH 1991]. Acutely poisoned animals convulsed and became prostrate before death; autopsy of these animals revealed pulmonary hemorrhage [Proctor et al. 1988]. In mice exposed to 200 or 400 ppm for 6.5 hr/day, 5 days/week for 13 weeks, an increase in liver weight and pathological changes in liver cells were seen at autopsy; signs of anemia were also seen in the high-dose groups before death [ACGIH 1991a]. Dogs and monkeys exposed to a 350-ppm concentration for 7 hr/day, 3 days/week for 13 weeks showed signs of emphysema and other reactive changes in the lungs at autopsy; the monkeys also exhibited brain hemorrhage [Clayton and Clayton 1982]. The oral LD_{50} in rats is 2,730 mg/kg. Teratogenic and embryotoxic effects occurred in hamsters inhaling 5,000 or 8,000 ppm for 1 hr on day 8 of gestation, and a single oral or intraperitoneal dose of 100 to 400 mg/kg also resulted in teratogenic effects in the offspring of exposed rats [ACGIH 1991a].

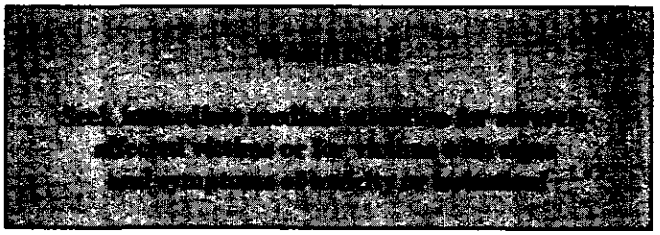
2. *Effects on Humans*: Acetonitrile is a primary irritant of the eyes, mucous membranes, skin, and upper respiratory tract of exposed workers; it has also caused methemoglobinemia and death in humans acutely overexposed. Two volunteers experienced no ill effects after inhaling 80 ppm for 4 hr; however, one of these individuals experienced bronchial irritation after an exposure to 160 ppm for the same interval [Proctor et al. 1988]. Ten painters developed signs of systemic toxicity when exposed to the vapor of a mixture containing 30% to 40% acetonitrile for 2 workdays. Four of the ten printers required hospitalization. One painter died after experiencing massive hematemesis [Proctor et al. 1988]. Several other industrial fatalities have occurred as a result of acute overexposure to acetonitrile. The lowest oral dose toxic in humans is 570 mg/kg; ingestion of this amount of acetonitrile caused gastrointestinal tract disturbances [NIOSH 1991].

- **Signs and symptoms of exposure**

1. *Acute exposure*: Acetonitrile poisoning can cause flushing or ashen-grey color; chest tightness; headache; nausea; vomiting (with or without blood); sweating; excess saliva production; lassitude; muscle weakness; painful, difficult, or irregular breathing; convulsions; stupor; coma; and cardiac and respiratory arrest.

2. *Chronic exposure*: No signs or symptoms of chronic exposure have been reported.

- **Emergency procedures**



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

1. *Eye exposure*: Tissue irritation may result from exposure to concentrated solutions, vapors, mists, or aerosols of acetonitrile. ***Immediately and thoroughly*** flush the eyes with large amounts of water, occasionally lifting the upper and lower eyelids.

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

3. *Inhalation exposure*: If vapors, mists, or aerosols of acetonitrile 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*: Do ***not*** induce vomiting.

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 uses of acetonitrile may result in worker exposures to this substance:

—Use as a solvent for extractive distillation in the manufacture of butadiene and isoprene

—Use as an extractive solvent in separation of fatty acids from fish liver oils; to remove phenol, tar, and color from petroleum hydrocarbons; to recover various alcohols, acids, and dark wood rosins; and in chemical analysis

—Use as a solvent and reactive medium for the preparation of pharmaceuticals, waterproofing compounds, antistatic agents, detergents, polymers, dyestuff intermediates, and for chemical research

—Use as an indifferent medium in physiochemical investigation and in separation of alkaloids in tissue extraction

—Use as a solvent for recrystallization and purification of salts, metals, and steroids; as a spinning solvent for synthetic fibers; as a solvent for epoxy resin coatings

—Use in organic synthesis in preparation of vitamins, perfumes, water softeners, and plasticizers, and as a catalyst to promote ionization reactions

The following methods are effective in controlling worker exposures to acetonitrile, 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:

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, placement of workers in jobs that do not jeopardize their safety and 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 acetonitrile, 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 liver and kidneys and of the cardiovascular, respiratory, and central nervous systems. Medical monitoring for respiratory disease should be conducted using the principles and methods recommended by the 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 acetonitrile 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 liver, kidney, cardiovascular, respiratory, or central nervous 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 acetonitrile exposure. The interviews, examinations, and medical screening tests should focus on identifying the adverse effects of acetonitrile on the liver, kidneys, and cardiovascular, respiratory, and central nervous 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. Acetonitrile exposure can be monitored by measurement of its metabolites, cyanide and thiocyanate, in the blood or in plasma and urine, respectively. Some sources suggest that blood cyanide levels of 0.1 mg/l or plasma or urine thiocyanate levels above 20 mg/l indicate excessive exposure. Because smokers often have higher levels of both metabolites, pre-exposure baseline measurements are suggested to establish each worker's baseline level.

- **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 acetonitrile is determined by using coconut shell charcoal tubes (400/200-mg sections, 20/40 mesh). Samples are collected at a maximum flow rate of 0.2 liter/min until a maximum air volume of 25 liters is collected. The sample is then treated with benzene to extract the acetonitrile. Analysis is conducted by gas chromatography using a flame ionization detector. The limit of detection for this procedure is 0.01 mg per sample. This method is described in Method 1606 of the *NIOSH Manual of Analytical Methods* [NIOSH 1984].

PERSONAL HYGIENE

Clothing and shoes contaminated with acetonitrile should be removed immediately, and provisions should be made for safely removing this chemical from these articles. Work clothing should not be taken home for laundering. Persons laundering contaminated clothing should be informed about the hazardous properties of acetonitrile, particularly its potential for being absorbed through the skin in toxic amounts.

A worker who handles acetonitrile 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 acetonitrile or a solution containing this substance is handled, processed, or stored.

STORAGE

Acetonitrile 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 area. All electrical service in the storage area should meet code requirements for flammable atmospheres. Containers of acetonitrile should be protected from physical damage and should be stored separately from perchloric acid, iron (III) salts of perchlorate, nitric acid, oleum, indium, nitrating agents, perfluorourea, chlorosulfonic acid, other strong oxidizers, heat, sparks, and open flame. To prevent static sparks, conveying equipment and storage containers should be electrically grounded and bonded during transfer. Because containers that formerly contained acetonitrile may still hold product residues, they should be handled appropriately.

SPILLS AND LEAKS

In the event of a spill or leak involving acetonitrile, persons not wearing protective equipment and clothing should be restricted from contaminated areas until the 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. Isolate and ventilate the area of the spill or leak.

5. Absorb small liquid spills with sand or other noncombustible absorbent material and place the material in a covered, vapor-tight container for later disposal.

6. Large quantities of acetonitrile can be collected and atomized in a suitable combustion chamber equipped with an appropriate effluent gas cleaning device.

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**

Acetonitrile 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 above the reportable quantity for that chemical, employers are required by the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [40 CFR 355.40] to notify the proper Federal authorities.

The reportable quantity for acetonitrile 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 who own or operate facilities in SIC codes 20 to 39, who employ 10 or more workers, and who manufacture 25,000 lb or more or otherwise use 10,000 lb or more of this substance per calendar year are required by EPA [49 CFR 372.30] to submit a Toxic Chemical Release Inventory Form (Form R) to EPA reporting the amount of acetonitrile 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. Acetonitrile is listed as a hazardous waste under the Resource Conservation and Recovery Act (RCRA) [40 USC 6901 et seq.] and has been assigned EPA Hazardous Waste No. U003. This substance has been banned from land dis-

posal and may be treated by incineration. Acetonitrile also may be disposed of in an organometallic or organic lab pack that meets the requirements of 40 CFR 264.316 or 265.316.

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 acetonitrile 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

Gloves, boots, aprons, and gauntlets should be worn as necessary to prevent skin contact either with the vapor or the liquid. 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 acetonitrile and have demonstrated good-to-excellent resistance for periods of at least 8 hr: butyl rubber, polyvinyl alcohol, and Teflon®. Natural rubber, neoprene, nitrile, polyvinyl chloride, and Viton® have demonstrated poor resistance to permeation.

If acetonitrile 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 acetonitrile might contact the eyes (e.g., through 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 acetonitrile. Contact lenses should not be worn if the potential exists for acetonitrile exposure.

REFERENCES CITED

ACGIH [1991a]. Documentation of the threshold limit values and biological exposure indices. 6th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

ACGIH [1991b]. 1991-1992 Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

ATS [1987]. Standardization of spirometry—1987 update. American Thoracic Society. Am Rev Respir Dis *136*:1285-1296.

Clayton G, Clayton F, eds. [1982]. Patty's industrial hygiene and toxicology. 3rd rev. ed. New York, NY: John Wiley & Sons.

CFR. Code of Federal regulations. Washington, DC: U.S. Government Printing Office, Office of the Federal Register.

NIOSH [1984]. Acetonitrile: Method 1606. In: Eller PM, ed. NIOSH manual of analytical methods. 3rd rev. ed. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 84-100.

NIOSH [1987a]. NIOSH guide to industrial respiratory protection. Cincinnati, OH: U.S. Department of Health and

Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-116.

NIOSH [1987b]. Respirator decision logic. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-108.

NIOSH [1991]. Registry of toxic effects of chemical substances database: acetonitrile. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer, Technical Information Branch.

NIOSH [1992]. NIOSH recommendations for occupational safety and health: compendium of policy documents and statements. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 92-100.

Proctor NH, Hughes JP, Fischman ML [1988]. Chemical hazards of the workplace. 2nd ed. Philadelphia, PA: J.B. Lippincott Company.