HYDRAZINE AND HYDRAZINE SULFATE CAS Nos. 302-01-2 and 10034-93-2

First Listed in the Third Annual Report on Carcinogens

H₂N-----NH₂

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Hydrazine

Hydrazine Sulfate

 H_2N $--- NH_2$

CARCINOGENICITY

Hydrazine and hydrazine sulfate are *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1974, 1982, 1987, 1999). When administered orally, hydrazine induced pulmonary adenomas and adenocarcinomas in mice. Intraperitoneal injection of hydrazine induced reticulum cell sarcomas of the mediastinum and myeloid leukemias in mice of both sexes (IARC 1974). When administered by inhalation, hydrazine induced alveolarogenic carcinomas and lymphosarcomas of the spleen in female mice (MacEwen *et al.* 1974). When administered orally, hydrazine sulfate induced pulmonary adenomas and adenocarcinomas, hepatomas, and hepatocarcinomas in mice of both sexes. When administered by stomach tube, hydrazine sulfate induced lung adenomas and adenocarcinomas in rats of both sexes and hepatic cell carcinomas and spindle cell sarcomas in male rats (IARC 1974).

There is inadequate evidence for the carcinogenicity of hydrazine and hydrazine sulfate in humans (IARC 1982, 1987, 1999). Three reports on cancer mortality among workers exposed to hydrazine have been published. One case of choroidal melanoma was observed in a man who had been exposed to hydrazine for 6 years. A study of 423 men engaged in the manufacture of hydrazine initially revealed three stomach, one prostate, and one neurogenic cancers. A follow-up study of this cohort found a slight excess of lung cancer (2 cases) in the highest exposure category. Another cohort of 427 men who worked in a hydrazine plant in the UK did not find excess cancer mortality or an excess of all cause mortality. The evidence these studies provide was considered inadequate by an IARC Working Group.

PROPERTIES

Hydrazine is a white or colorless, oily, fuming liquid with an ammonia-like odor. It is miscible with water, methyl, ethyl, propyl, and isobutyl alcohols, but is insoluble in chloroform and ether (IARC 1999). Hydrazine is a flammable liquid that may spontaneously ignite on contact with oxidizers or porous materials and may explode when exposed to heat, flame, or upon chemical reaction with alkali metals. Hydrazine is available as a propellant grade with a minimum of 97.5% purity. Solutions with varying hydrazine content are available for a variety of industrial uses (HSDB 2000a).

Hydrazine sulfate occurs as a colorless crystal or white crystalline powder. It is soluble in hot water and insoluble in alcohol. When heated to decomposition, it emits toxic fumes of sulfur oxides and nitrogen oxides. Hydrazine sulfate is available in two grades of <98% and 99% purity with heavy metal and chloride impurities (HSDB 2000b).

USE

Hydrazine is used primarily as a chemical intermediate to produce agricultural chemicals, spandex fibers, and antioxidants. Hydrazine is also used as rocket fuel, an oxygen scavenger in water boilers and heating systems, a polymerization catalyst, a blowing agent, and as a scavenger for gases. Additionally, it is used for plating metals on glass and plastics and in fuel cells, solder fluxes, and photographic developers. Hydrazine is used as a reactant in fuel cells in the military, as a reducing agent in electrodless nickel plating, as a chain extender in urethane polymerizations, as a reducing agent in plutonium extraction from reactor waste, and as a water treatment chemical. Hydrazine is also used as a chemical intermediate for blowing agents, photography chemicals, pharmaceuticals, antituberculants, textile dyes, heat stabilizers, explosives, and to make hydrazine sulfate (IARC 1974, 1999, Sax 1987, ATSDR 1997, HSDB 2000a).

Hydrazine sulfate is used in refining rare metals, as an antioxidant in soldering flux for light metals, in analytical tests for blood, a reducing agent in the analysis of minerals and slag, and in the preparation of hydrazine hydrate. Hydrazine sulfate is also used as a biocide for fungi and molds; although, it is not registered for use as a biocide in the United States. Investigators have studied hydrazine sulfate as an adjunct to antineoplastic drug treatment, but extensive use is not foreseeable (IARC 1974, Sax, 1987, HSDB 2000b).

PRODUCTION

Only one current producer and 19 suppliers of hydrazine and one current producer and 28 suppliers of hydrazine sulfate were identified in the U.S. (HSDB 2000a,b, Chem Sources 2001). Annual production estimates for hydrazine ranged from 15 million lb to 38 million lb from the mid 1960s to 1984 (ATSDR 1997). U.S. production capacity estimates for hydrazine hydrate was 55 million lb in 1988 and production capacity estimates for hydrazine solutions were approximately 36.3 million lb in 1992 (IARC 1999). More recent production data were not found. In 2000, U.S. exports and imports of hydrazine and hydroxylamine and their inorganic salts were reported to be approximately 27.6 million lb and 10.7 million lb, respectively (ITA 2001). The 1979 TSCA Inventory identified four companies producing 11 million lb of hydrazine in 1977 and 13 companies importing 660,500 lb. The 1979 TSCA Inventory also identified seven companies producing 562,000 lb of hydrazine sulfate and three companies importing an unspecified amount (TSCA 1979).

EXPOSURE

Hydrazine and hydrazine sulfate may be released to the environment through production, use, and waste disposal. Hydrazine is rapidly degraded in most environmental media by oxidation. High concentrations of hydrazine are toxic to microorganisms, but at low concentrations, biodegration may occur. Use of hydrazine in boiler water treatment may result in its brief occurrence in discharged waste, but it would be rapidly oxidized (ATSDR 1997, HSDB 2000a).

The primary routes of potential human exposure to hydrazine are ingestion, inhalation, and dermal contact. The exposure potential for the general population is low, but it may occur through inhalation of cigarette smoke or ingestion of trace amounts in processed foods. Hydrazine has been detected in cigarette smoke at a concentration of 32 μ g/cigarette (OSH 1982). Occupational exposure is more likely to occur by inhalation or dermal contact (HSDB 2000a). The National Occupational Exposure Survey estimated that 59,147 workers, including 2,840 females, were potential exposed to hydrazine in the U.S. between 1981 and 1982 (IARC 1999). NIOSH estimated that about 11,000 workers were possibly exposed to hydrazine in the workplace between 1972 and 1974 (NIOSH 1976). In 1978, NIOSH estimated that 9,000 workers in the United States may have been potentially exposed to hydrazine and that over 90,000 may have been exposed to various hydrazine salts (NIOSH 1978).

The most recent Toxic Chemical Release Inventory (TRI99 2001) listed 36 industrial facilities that reported releases of hydrazine in 1999. The facilities reported releases of hydrazine to the environment which were estimated to total 143,727 lb (10,278 lb total on-site air release, 642 lb surface water discharges, 88,378 lb underground injections, 372 lb total land release, and 44,057 off-site releases). Only 1 industrial facility reported environmental releases of hydrazine sulfate in 1999 (TRI99 2001). This facility reported that 190,000 lb were disposed by underground injection.

REGULATIONS

In 1980, The U.S. Consumer Product Safety Commission (CPSC) preliminarily determined that hydrazine and hydrazine sulfate were not present in consumer products under its jurisdiction. Subsequently, public comment was solicited to verify the accuracy of this information; no comments were received. Pending receipt of new information, CPSC plans no action on this chemical.

EPA regulates hydrazine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Food, Drug, and Cosmetic Act (FD&CA), Resource Conservation and Recovery Act (RCRA), and Superfund Amendments and Reauthorization Act (SARA). Hydrazine is subject to reporting and record-keeping requirements under CERCLA, RCRA, and SARA. A 1 lb statutory reportable quantity (RQ) has been established under CERCLA for hydrazine. Under FD&CA, hydrazine is subject to regulations and data labeling requirements for its use as an inert ingredient of pesticides. If the threshold planning quantity of 1,000 lb established under SARA is reached, local response plans must be prepared. EPA regulates hydrazine sulfate under SARA, subjecting it to reporting requirements.

FDA regulates hydrazine under FD&CA requiring that steam in contact with food contain no hydrazine.

ACGIH recommends a threshold limit value (TLV) of 0.01 ppm (0.013 mg/m³) for hydrazine. NIOSH has set the recommended a 0.03 ppm (0.04 mg/m³) for a 120 minute short-term ceiling value for hydrazine and hydrazine sulfate. OSHA has set the permissible exposure limit (PEL) at 1 ppm (1.3 mg/m³) as an 8-hr time-weighted average (TWA); the potential for absorption through the skin was noted. OSHA also regulates hydrazine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 96.

REFERENCES

ATSDR. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Hydrazine. (Final Report). Atlanta, GA: ATSDR, Public Health Service, U.S. Department of Health and Human Services. 1997. 203 pp. NTIS Accession No PB98-101025.

Chem Sources. Chemical Sources International, Inc. http://www.chemsources.com, 2001.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. Hydrazine. Profile last updated March 22, 2000a. Last review date, January 23, 1997.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. Hydrazine Sulfate. Profile last updated February 11, 2000b. Last review date, January 23, 1997.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Some Aromatic Amines, Hydrazine and Related Substances, N-Nitroso Compounds and Miscellaneous Alkylating Agents. Vol. 4. 286 pp. Lyon, France: IARC, 1974.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. Supplement 4. 292 pp. Lyon, France: IARC, 1982.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity. Supplement 7. 440 pp. Lyon, France: IARC, 1987.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. Vol. 71, Part 3. 1,589 pp. Lyon, France: IARC, 1999.

ITA. International Trade Administration. U.S. Department of Commerce. Subheading 282510: Hydrazine and Hydroxylamine and their Inorganic Salts. http://www.ita.doc.gov/td/industry/otea/Trade-Detail/, 2001.

MacEwen, J.D., E.E. McConnell, and K.C. Back. The Effect of a Six Month Chronic Level Inhalation Exposure to Hydrazine on Animals. L-Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio. AMRL-FR-74-125, Paper No. 16. Distributed by National Technical Information Service, U.S. Department of Commerce, Publication No. AD-A-011865. Springfield, VA, 1974.

NIOSH. National Institute for Occupational Safety and Health. National Occupational Hazard Survey (1972-74). Cincinnati, OH: Department of Health, Education, and Welfare, 1976.

NIOSH. National Institute for Occupational Safety and Health. Criteria for a Recommended Standard -- Occupational Exposure to Hydrazines. DHEW (NIOSH) Publication No. 78-172. Cincinnati, OH: Department of Health, Education, and Welfare, 1978.

OSH. Office on Smoking and Health, Public Health Service. The Health Consequences of Smoking, Cancer, a Report of the Surgeon General. 322 pp. DHHS (PHS) Publication No. 82-50179. Department of Health and Human Services, Rockville, MD, 1982.

Sax, N.I. Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Corporation, 1987, pp. 276, 490, 633, 635, and 732.

TSCA. Toxic Substances Control Act, Chemical Substance Inventory, 1979: public record.

TRI99. Toxic Chemical Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). Available from the U.S. Environmental Protection Agency Office of Environmental Information, <u>http://www.epa.gov/triexplorer/reports.htm</u>, 2001.