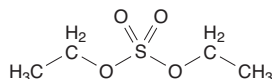


Diethyl Sulfate

CAS No. 64-67-5

Reasonably anticipated to be a human carcinogen

First listed in the *Fourth Annual Report on Carcinogens* (1985)



Carcinogenicity

Diethyl sulfate is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Diethyl sulfate caused tumors in rats at several different tissue sites and by several different routes of exposure. Administration of diethyl sulfate by stomach tube caused benign or malignant forestomach tumors (papilloma or squamous-cell carcinoma) in rats of unspecified sex. Prenatal exposure to diethyl sulfate caused cancer of the nervous system, and cancer at the injection site (malignant sarcoma) was observed after subcutaneous injection (IARC 1974, 1982).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to diethyl sulfate. Exposure to diethyl sulfate occurs mainly during ethanol production. In most studies of ethanol production workers, diethyl sulfate was not measured, making it difficult to evaluate the contribution of diethyl sulfate to cancer risk. A retrospective cohort study of morbidity and mortality among 355 ethanol and isopropanol production workers found a significant excess of laryngeal cancer (4 deaths) (Lynch *et al.* 1979). When the cohort was expanded to include maintenance workers and supervisors (a total of 740 workers and 7 deaths), the excess of laryngeal cancer was smaller but still statistically significant. Within the expanded cohort, a nested case-control study of 50 cases of throat cancer found a relationship between cancer and the level of exposure to sulfuric acid; however, the increased risk persisted after workers in the ethanol and isopropanol units were excluded (Soskolne *et al.* 1984). A nested case-control study of 17 benign brain tumors (glioma) among workers at a petrochemical plant found the risk of brain cancer to be associated with estimated exposure to diethyl sulfate (Leffingwell *et al.* 1983); however, no increased risk was found in an overlapping study of 21 cases (including the 17 cases of the Leffingwell study) with a different series of controls (Austin and Schnatter 1983).

Properties

Diethyl sulfate is the diethyl ester of sulfuric acid and exists at room temperature as a colorless oily liquid with a faint peppermint odor. It is slightly soluble in water, but miscible with alcohol, diethyl ether, and most polar solvents. Diethyl sulfate readily decomposes in hot water to ethyl hydrogen sulfate and ethyl alcohol (IARC 1974, 1992). Physical and chemical properties of diethyl sulfate are listed in the following table.

Property	Information
Molecular weight	154.2
Density	1.17 g/cm ³ at 25°C
Melting point	-25°C
Boiling point	210°C with decomposition
Log <i>K</i> _{ow}	1.14
Water solubility	7.0 g/L at 20°C
Vapor pressure	0.212 mm Hg at 25°C
Vapor density relative to air	5.31

Source: HSDB 2009.

Use

The primary use of diethyl sulfate is as a chemical intermediate (ethylating agent) in synthesis of ethyl derivatives of phenols, amines, and thiols; as an accelerator in the sulfation of ethylene; and in some sulfonation processes. It is used to manufacture dyes, pigments, carbonless paper, and textiles. It is an intermediate in the indirect hydration (strong acid) process for the preparation of synthetic ethanol from ethylene. Smaller quantities are used in household products, cosmetics, agricultural chemicals, pharmaceuticals, and laboratory reagents (IARC 1992, 1999, HSDB 2009). In 1966, it was used as a mutagen to create the Luther variety of barley (IARC 1974).

Production

Diethyl sulfate has been produced commercially in the United States since at least the 1920s (IARC 1974). In 2009, diethyl sulfate was produced by two manufacturers in East Asia, and four each in the United States and India (SRI 2009) and was available from 28 suppliers, including 13 U.S. suppliers (ChemSources 2009). No data on U.S. exports or imports specifically of diethyl sulfate were found. Reports filed under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of diethyl sulfate totaled 1 million to 10 million pounds between 1986 and 2006, except in 1994, when the quantity increased to 10 million to 50 million pounds (EPA 2004, 2009).

Exposure

The routes of potential human exposure to diethyl sulfate are inhalation, ingestion, and dermal contact during its production and use. Diethyl sulfate can be released to the environment during its production and use in the synthesis of various intermediates and products (IARC 1992, HSDB 2009). According to EPA's Toxics Release Inventory, environmental releases of diethyl sulfate since 1988 have ranged from a high of over 38,000 lb in 1999 (including 34,500 lb sent to an off-site landfill) to a low of 4,000 lb in 1991. Most of the releases from 1988 to 2007 ($\geq 93\%$) were to air, and the remainder were to off-site landfills. In 2007, seven facilities released 5,346 lb of diethyl sulfate, all to air (TRI 2009). If released to air, diethyl sulfate will exist as a vapor, with a half-life of 9 days by reaction with photochemically produced hydroxyl radicals and a half-life of less than 1 day by hydrolysis. In soil and water, diethyl sulfate will hydrolyze rapidly, with a half-life in water of 1.7 hours. Because of its sensitivity to hydrolysis, the processes of volatilization, adsorption to soil and sediment, biodegradation, and bioaccumulation are not expected to be significant. Hydrolysis of diethyl sulfate produces monoethyl sulfate and ethanol (IARC 1992).

Workers involved in the production of ethanol by the strong-acid process frequently were exposed to diethyl sulfate, which is formed as a by-product of the reaction between ethylene and sulfuric acid (Lynch *et al.* 1979). Analysis of the history of an ethanol plant and interviews with present and former supervisors indicated that exposure to diethyl sulfate vapor was likely from leaky pump seals and when

process equipment was opened for manual cleaning, which had to be done frequently. The strong-acid-process workers were also exposed to sulfuric acid mist, coke, tar, heat-transfer-fluid vapor, sulfur trioxide, and ethyl ether. Based on the presence of approximately 30% diethyl sulfate in acid extracts, the maximum vapor concentration over a spill was calculated as 2,000 ppm; however, the actual exposures to workers most likely were much less, because of dilution due to ventilation or air movement. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 2,260 workers, including 165 women, potentially were exposed to diethyl sulfate in the Textile, Lumber, and Wood Products industries (NIOSH 1990).

Regulations

Coast Guard (Dept. of Homeland Security)

Minimum requirements have been established for safe transport of diethyl sulfate on ships.

Department of Transportation (DOT)

Diethyl sulfate is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.

New Source Performance Standards: Manufacture or use is subject to certain provisions for the control of volatile organic compound emissions.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

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