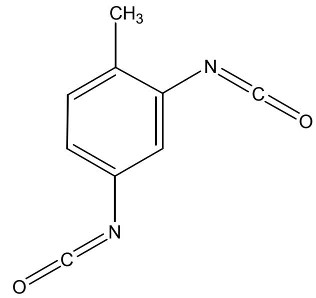
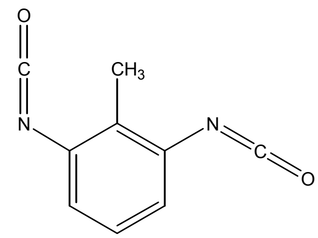
TOLUENE DIISOCYANATE
CAS No. 26471-62-5

First Listed in the *Fourth Annual Report on Carcinogens*



2,4-Toluene diisocyanate, 80%



2,6-Toluene diisocyanate, 20%

CARCINOGENICITY

Toluene diisocyanate is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (NTP 1986, IARC 1986, 1987, 1999). When administered by gavage in corn oil, commercial-grade toluene diisocyanate (analyzed as 85% 2,4-isomer and 15% 2,6-isomer) induced hemangiomas in the spleen and subcutaneous tissues, hepatocellular adenomas, and hemangiosarcomas in the liver, ovaries, and peritoneum in female mice; subcutaneous fibromas and fibrosarcomas and pancreatic acinar cell adenomas in male rats; and neoplastic nodules of the liver, pancreatic acinar cell adenomas, mammary gland fibroadenomas, and subcutaneous fibromas and fibrosarcomas in female rats. No treatment-related lesions were induced in male mice (NTP 1986). When administered by inhalation, toluene diisocyanate (80% 2,4- and 20% 2,6-isomers) induced pathological changes in the nasal cavity and lower respiratory tract; however, no significant increase in tumor incidence was observed (IARC 1986, 1999).

No adequate human studies of the relationship between exposure to toluene diisocyanate and human cancer have been reported (IARC 1999).

PROPERTIES

Toluene diisocyanate occurs as a colorless to pale yellow liquid with a sharp, pungent odor. It is sensitive to moisture, heat, and light. It is soluble in diethyl ether, acetone, and other organic solvents, and miscible with diglycol monomethyl ether, carbon tetrachloride, benzene, chlorobenzene, kerosene, and olive oil. Toluene diisocyanate may react violently with water, acids, and alcohols. Contact with bases, such as caustic soda and tertiary amines, may cause uncontrollable polymerization and the rapid evolution of heat. When heated to decomposition, it emits toxic fumes of cyanides and nitrogen oxides. Toluene diisocyanate is generally available as a mixture of 2,4- and 2,6-toluene diisocyanates in ratios of 80%:20% and 65%:35%. Other mixtures are also available commercially. 2,4-Toluene diisocyanate (CAS No. 584-84-9) is a clear to pale yellow liquid with a sharp, pungent odor. It has solubilities and reactivities similar to the mixture. It is combustible when exposed to heat or flame and darkens when exposed to sunlight. 2,4-Toluene diisocyanate is available as a >99.5% pure commercial product. 2,6-

Toluene diisocyanate (CAS No. 91-08-7) also occurs as a reactive liquid. Toluene diisocyanates may degrade to 2,6-diaminotoluene dihydrochloride, 2,6-diaminotoluene, and 2,4-diaminotoluene (see 2,4-Diaminotoluene) (NTP 1986, 2001, IARC 1999, HSDB 2000).

USE

Toluene diisocyanate is used primarily in the synthesis of polyurethane foams. This use accounts for approximately 90% of the total supply of toluene diisocyanate. Flexible polyurethane foam is used mainly in furniture (43%) and bedding (12%); rigid polyurethane foams are used primarily in insulation. Toluene diisocyanate-based rigid polyurethane foam is used in household refrigerators and, in board or laminate form, for residential sheathing or commercial roofing. "Pour-in-place" or "spray-in" rigid foam is used as insulation for truck trailers, railroad freight cars, and cargo containers. Polyurethane-modified alkyds contain approximately 6 to 7% isocyanate, mostly toluene diisocyanate, and are used as floor finishes, wood finishes, and paints. Moisture-curing coatings are used as wood and concrete sealants and floor finishes. Aircraft, truck, and passenger-car coatings are often composed of toluene diisocyanate pre-polymer systems. Castable urethane elastomers are used in applications requiring strength, flexibility, and shock-absorption, and are resistant to oil, solvents, and ultraviolet radiation. They are used in adhesive and sealant compounds and in automobile parts, shoe soles, roller skate wheels, pond liners, and blood bags. They are also used in oil fields and mines. Certain elastomer products are produced from the pure 2,4-isomer rather than the 80:20 mixture (IARC 1986, 1999, WHO 1987, HSDB 2000).

PRODUCTION

Toluene diisocyanate has been produced commercially since the late 1930s (IARC 1986). Chem Sources (2001) identified 2, 8, and 18 U.S. suppliers of toluene diisocyanate, 2,6-toluene diisocyanate, and 2,4-toluene diisocyanate, respectively. Five U.S. manufacturers are listed in the HSDB (2000). U.S. production of an 80:20 mixture of 2,4- and 2,6-toluene diisocyanate increased from 616 million lb in 1985 to 665 million lb in 1986 (USITC 1986, 1987). This production increased to an estimated 742 million lb in 1988, but showed a slight decline in 1989 to 731 million lb (USITC 1989, 1990). By 1993, the production capacity for toluene diisocyanates in North America was estimated at more than one billion lb (IARC 1999). U.S. production in 1994 and 1995 was approximately 876 million lb and 869 million lb, respectively (USITC 1996).

The United States imported 29 million lb of the compound (including mixtures) and exported 9 million lb in 1985 (USDOC 1986). Imports declined to approximately 53,000 lb (mixtures) and 102,000 lb (unmixed) while exports rose to more than 478 million lb (mixed) and 25 million lb (unmixed) in 2000 (ITA 2001).

EXPOSURE

The primary routes of potential human exposure to toluene diisocyanate are inhalation and dermal contact. Because of the high volatility of toluene diisocyanate, exposure can occur in all phases of its manufacture and use. According to a national occupational survey conducted from 1981 to 1983, approximately 40,000 workers are potentially exposed to toluene diisocyanates (CHIP 1984, IARC 1999). The occurrence of toluene diisocyanate in the work environment, primarily in air, has been associated with its commercial production; its handling and processing prior to urethane foam production; its release in stack exhaust from plants; and its release into the air from sprays, insulation materials, polyurethane foam, and coated fabrics. Analysis of the isomeric composition of atmospheric toluene diisocyanate in a plant producing polyurethane foam demonstrated a large increase in the level of the 2,6-isomer relative to that of the 2,4-isomer, particularly at the finishing end of the production process. Median air concentrations of 2,4-toluene diisocyanate were 5.0 and 2.3 $\mu g/m^3$ for the initial mixing and finishing ends of the process, respectively. The respective median values for the 2,6-isomer were 6.4 and 7.8 $\mu g/m^3$, with a maximum value greater than 450 $\mu g/m^3$ at the finishing end. These findings were attributed to enhanced emission of the less chemically active 2,6-isomer from the cured foam bats and retention of the 2,4-isomer as a polymer (IARC 1986).

Workers having potential occupational exposure to diisocyanates include adhesive workers, insulation workers, diisocyanate resin workers, lacquer workers, organic chemical synthesizers, paint sprayers, polyurethane makers, rubber workers, ship builders, textile processors, and wire coating workers (CHIP 1984). Aniline and the 2,4- and 2,6-isomers of toluene diisocyanate were detected under controlled experimental conditions in the thermodegradation fumes of polyurethane varnish used in the insulation of copper wire. Consistent with these findings, the compounds were also detected in the workplace atmosphere during the industrial production of polyurethane-coated wire (IARC 1986, 1999).

Exposure to unreacted toluene diisocyanate is associated with the spray application of polyurethane foam. The construction industry uses polyurethane formulations in thermal insulation, adhesives, lacquers, and paints. In most cases, the foam is applied through air spraying in confined spaces. In the United States, a typical modern housing unit of 1,800 ft^2 floor space, including furniture, carpet underlay, and bedding, contains 306 lb of flexible polyurethane foam. The transportation industry utilizes approximately 21% of flexible polyurethane foams with automobile seating and padding, resulting in the use of 24 to 31 lb polyurethane per automobile (IARC 1986).

Worker exposure to toluene diisocyanate is most likely to occur during sample collection, residue removal, spill clean-up, and equipment maintenance. Employees are required to use air-line respirators during these operations. The highest exposure levels have occurred during the spray application of polyurethane foam, a procedure which is usually conducted in confined spaces; exposure to concentrations above safe limits are a particular concern for the sprayers and their helpers. Studies summarized by the IARC (1986, 1999) indicate that toluene diisocyanate exposure levels of <1 to $>1,000$ $\mu g/m^3$ have been found in the workplace, as compared with the current OSHA standard of 0.02 ppm (~140 $\mu g/m^3$).

It appears that several household products that are commercially available to consumers may pose a risk of exposure to toluene diisocyanate if used indiscriminately. Consumers may also be exposed to toluene diisocyanate volatilized from polyurethane varnishes during the application of such coatings (CHIP 1984). FDA has determined that levels of toluene diisocyanate in food, food additives, or food packaging are so low that the potential daily intake is virtually nil.

The Toxic Chemical Release Inventory (TRI) listed 183, 61, and 28 industrial facilities that produced, processed, or otherwise used toluene diisocyanate (mixed isomers), 2,4-toluene diisocyanate, or 2,6-toluene diisocyanate, respectively in 1999 (TRI 2001). These facilities reported releases of 74,027 lb, 34,022 lb, and 3,818 lb of toluene diisocyanate (mixed isomers), 2,4-toluene diisocyanate, and 2,6-toluene diisocyanate, respectively.

REGULATIONS

EPA regulates toluene diisocyanate under the Clean Air Act (CAA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act, (RCRA) and Superfund Amendments and Reauthorization Act (SARA). Under the CAA, National Emission Standards for Hazardous Air Pollutants (NESHAP), EPA addresses toluene diisocyanate emissions from production and manufacturing facilities. A reportable quantity (RQ) of 100 lb (45.4 kg) has been established for this chemical under CERCLA. Toluene diisocyanate is subject to reporting and record-keeping requirements under RCRA and SARA.

FDA regulates toluene diisocyanate as an indirect food additive.

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 5 ppb (40 $\mu g/m^3$), with a ceiling of 0.02 ppm (0.14 mg/m^3) for toluene diisocyanate. NIOSH recommends that toluene diisocyanate be regarded as a potential occupational carcinogen. OSHA has set a ceiling level for exposure to toluene diisocyanate to 0.02 ppm (0.14 mg/m^3). OSHA also regulates toluene diisocyanate under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 177.

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