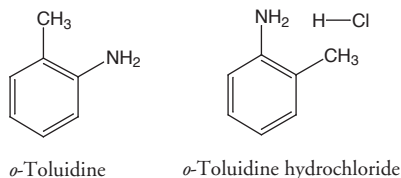


## ***o*-Toluidine and *o*-Toluidine Hydrochloride**

### **CAS Nos. 95-53-4 and 636-21-5**

Reasonably anticipated to be a human carcinogen  
First Listed in the *Third* and *Second Annual Reports on Carcinogens*, respectively (1983, 1981)



### **Carcinogenicity**

*o*-Toluidine and *o*-toluidine hydrochloride are *reasonably anticipated to be human carcinogens* based on limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals (IARC 1978, 1982a,b, 1987, 2000). When administered in the diet, *o*-toluidine hydrochloride increased the incidences of hepatocellular carcinomas or adenomas in female mice, hemangiosarcomas at multiple sites in male mice of one strain, and hemangiosarcomas and hemangiomas of the abdominal viscera in both sexes of another strain. When administered in the diet, *o*-toluidine hydrochloride increased the incidences of sarcomas of multiple organs in rats of both sexes; subcutaneous fibromas and mesotheliomas in male rats; and sarcomas of the spleen, transitional cell papillomas, carcinomas of the urinary bladder, and mammary gland fibroadenomas and adenomas in female rats. In male rats of another strain, the compound increased the incidences of subcutaneous fibromas and fibrosarcomas; a few transitional cell carcinomas of the urinary bladder were also observed. The carcinogenicity of the free base, *o*-toluidine, was investigated in one limited study in hamsters; however, no definitive conclusions were made.

There is limited evidence for the carcinogenicity of *o*-toluidine and *o*-toluidine hydrochloride in humans (IARC 2000). Although an excess of bladder cancers has been reported in four studies of workers exposed to *o*-toluidine, no population of workers exposed to *o*-toluidine only has been described (IARC 2000). An excess of bladder cancers has been reported in workers classified as being exposed primarily to *o*-toluidine, but confounding by concomitant exposure to various other potential bladder carcinogens could not be eliminated. An excess of bladder tumors was noted in workers exposed to toluene, *o*-nitrotoluene, *o*-toluidine, and 4,4-*N*-methylenebis(2-methylaniline) during the manufacture of new fuchsin and safranin (IARC 1987).

### **Properties**

*o*-Toluidine is a colorless to light yellow liquid that is slightly soluble in water, and miscible with carbon tetrachloride, diethyl ether, and ethanol (IARC 2000). When heated to decomposition, it emits toxic fumes of nitrogen oxides. It is incompatible with oxidizing materials, strong bases, or strong acids, and is sensitive to light, air, and heat (NJDHSS 2001a, HSDB 2001). *o*-Toluidine is available in the United States as a technical grade with a minimum of 99.5% purity, containing *m*- and *p*-toluidine as impurities. The commercial product may also contain a stabilizer (HSDB 2001).

*o*-Toluidine hydrochloride is a colorless to white powder that is soluble in water, dimethyl sulfoxide, and ethanol, but is insoluble in benzene and diethyl ether (IARC 2000). When heated to decomposition, it emits toxic fumes of hydrochloric acid and nitrogen oxides. It is incompatible with oxidizing agents and strong acids and is sensitive to light and heat (HSDB 2001, NJDHSS 2001b).

### **Use**

*o*-Toluidine and *o*-toluidine hydrochloride are used primarily as intermediates in the manufacture of more than 90 dyes and pigments. They are used in acid-fast dyestuffs, azo pigment dyes, triarylmethane dyes, sulfur dyes, and indigo compounds. *o*-Toluidine is also used as an intermediate for synthetic rubber and rubber vulcanizing chemicals, pharmaceuticals, and pesticides (IARC 2000, HSDB 2001). Other minor uses of *o*-toluidine and its hydrochloride salt are as an intermediate in organic synthesis and as an ingredient in a clinical laboratory reagent for glucose analysis (HSDB 2001).

### **Production**

Commercial production was first reported in the United States in 1922 for *o*-toluidine and in 1956 for *o*-toluidine hydrochloride (IARC 1982a,b, 2000). In the late 1970s, production volumes were estimated to be 1.1 to 11 million lb/yr, but increased to 14.5 to 28.2 million lb/yr by the early 1990s (IARC 2000). *o*-Toluidine was manufactured by six U.S. companies in 1999 and was available from 24 suppliers (IARC 2000, Chem Sources 2001). *o*-Toluidine hydrochloride has not been commercially produced in the United States since 1975 (HSDB 2001b); however, the Chem Sources USA directory identified 12 suppliers in 1986 (Chem Sources 1986) and four suppliers in 2001 (Chem Sources 2001). The United States imported 35,700 lb of *o*-toluidine and 992 lb of its hydrochloride salt in 1983 (EPA 1984). Recent import and export data specifically for *o*-toluidine and *o*-toluidine hydrochloride were not found; however, U.S. imports in 2000 of "toluidines and their derivatives, salts thereof" and "other toluidines and their derivatives, and salts thereof" were reported at 2.3 and 20.9 million lb, respectively. Exports in 2000 of "toluidines (aminotoluenes) and their derivatives, salts thereof" were 6.8 million lb (ITA 2001).

### **Exposure**

Occupational exposure to *o*-toluidine and *o*-toluidine hydrochloride is most likely to occur through inhalation and dermal contact. The general population may be exposed to low concentrations in ambient air, tobacco smoke, food, or dermal contact with commercial products (HSDB 2001a). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 13,053 workers were potentially exposed to *o*-toluidine in the workplace (NIOSH 1976). The National Occupational Exposure Survey (1981-1983) indicated that approximately 30,000 workers, including approximately 15,500 women, potentially were exposed to *o*-toluidine (NIOSH 1984, IARC 2000, HSDB 2001a). Occupations with the greatest potential for exposure to the compounds include dye makers and pigment makers.

*o*-Toluidine residues are present in products used as acid inhibitors at concentrations of <0.5%; further, concentrations in the air at a facility producing dyes and pigments ranged from 0.004 to 0.26 ppm. In area samples taken in the air at two coal liquification pilot facilities, the mean concentration of *o*-toluidine was <0.1 ppm. Although medical and laboratory personnel represent a significant population of workers potentially exposed to *o*-toluidine, air concentrations have been determined to be below 22 µg/l (CHIP 1984). Consumer exposure to *o*-toluidine may possibly occur from residues present in commercial dyes used on textiles. Also, *o*-toluidine is reported to be present in cigarette smoke at a concentration of 32 ng/cigarette (OSH 1982).

*o*-Toluidine has been detected in the effluents from refineries and production facilities, in river water, process water, and ground water (CHIP 1984, IARC 2000). The Toxic Chemical Release Inventory (TRI99) listed 25 and 3 industrial facilities that produced, processed, or otherwise used *o*-toluidine and *o*-toluidine hydrochloride, respectively. These facilities reported releases of 18,383 lb of *o*-toluidine and 175 lb of *o*-toluidine hydrochloride to the environment in 1999. Yearly releases between 1988 and 1999 ranged from approximately 18,000 lb to 55,000 lb (TRI99 2001).

## Regulations

### EPA

#### Clean Air Act

NESHAP: *o*-Toluidine listed as a Hazardous Air Pollutant (HAP)

#### Comprehensive Environmental Response, Compensation, and Liability Act

Reportable Quantity (RQ) = 100 lb (for each substance)

#### Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substances subject to reporting requirements

#### Resource Conservation and Recovery Act

Both are Listed Hazardous Wastes: Waste codes for which listing is based wholly or partly on either substance - U222, U328, K112, K113, K114

Both are listed as Hazardous Constituents of Waste

### OSHA

Permissible Exposure Limit (PEL) = 5 ppm (22 mg/m<sup>3</sup>)

## Guidelines

### ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 2 ppm (*o*-Toluidine)

### NIOSH

Immediately Dangerous to Life and Health (IDLH) = 50 ppm (*o*-Toluidine)

Listed as a potential occupational carcinogen (*o*-Toluidine)

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