

# 2-Methylaniline ( o-Toluidine)

95-53-4

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## Hazard Summary

o-Toluidine is primarily used in the manufacture of dyes. o-Toluidine is highly toxic to humans when absorbed through the skin, inhaled as vapor, or swallowed. Acute (short-term) exposure of humans to o-toluidine affects the blood (i.e., methemoglobinemia), with clinical signs of central nervous system depression. The chronic (long-term) effects in workers exposed to o-toluidine include anemia, anorexia, weight loss, skin lesions, central nervous system depression, cyanosis, and methemoglobinemia. Animal studies indicate that chronic exposure to o-toluidine causes effects on the spleen, liver, urinary bladder, and blood. Occupational exposure to dyestuffs (including o-toluidine) is associated with an increased risk of bladder cancer. 2-Methylaniline hydrochloride (the hydrochloride salt of o-toluidine) was carcinogenic in rats and mice. o-Toluidine has been classified by EPA as a Group B2, probable human carcinogen.

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Please Note: The main source of information for this fact sheet is EPA's Health and Environmental Effects Profile for 2-Methylaniline and 2-Methylaniline Hydrochloride. (2) Other secondary sources include the Hazardous Substances Data Bank (HSDB) (3), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS) (5), a database of toxic effects that are not peer reviewed.

## Uses

- The principal commercial use of o-toluidine is in the manufacture of dyes. It is also used in the manufacture of rubber vulcanization accelerators, hypnotic and anesthetic pharmaceuticals, and pesticides.(1,2)

## Sources and Potential Exposure

- Occupational exposure via inhalation or skin contact is possible in work environments utilizing o-toluidine.(2)
- o-Toluidine has been found in tobacco smoke and in steam volatiles from the distillation of one type of tobacco leaves. (1)
- o-Toluidine has been detected in a variety of foods including fresh kale, celery and carrots, and in shelled peas, red cabbage, and black tea aroma. (2)

## Assessing Personal Exposure

- There is a medical test available to determine whether someone has been exposed to o-toluidine via analysis of blood or urine. (3)

## Health Hazard Information

### Acute Effects:

- o-Toluidine is highly toxic to humans when absorbed through the skin, inhaled as vapor, or swallowed. o-Toluidine changes hemoglobin (which carries oxygen in the blood) to methemoglobin; methemoglobinemia results in a decreased supply of oxygen to peripheral tissues. (3,4)
- Tests involving acute oral exposure of rats, have shown o-toluidine to have moderate acute toxicity. (5)

#### Chronic Effects (Noncancer):

- The long-term effects experienced by workers exposed to o-toluidine include anemia, anorexia, weight loss, cyanosis, methemoglobinemia, skin lesions, and central nervous system depression including dizziness, headache, and confusion. (3)
- Effects on the spleen, liver, urinary bladder, and body weight were reported in rats chronically exposed to 2-methylaniline hydrochloride in their feed. Other animal studies indicate that chronic exposure to o-toluidine causes effects to the blood, including methemoglobinemia, reticulocytosis, and anemia. (1,2,3,10)
- EPA has not established a Reference Concentration (RfC) or Reference Dose (RfD) for o-toluidine.

#### Reproductive/Developmental Effects:

- Limited information regarding the reproductive or developmental effects of inhaled or ingested o-toluidine was located. One Russian study reported an increased frequency of tumors in offspring of mice injected with o-toluidine during gestation. (2)

#### Cancer Risk:

- An increased risk of bladder cancer has been reported among workers exposed to dyestuffs and dyestuff intermediates (including o-toluidine). However, no population of workers exposed only to o-toluidine has been described. Occasional cases of bladder tumors have been reported in workers exposed primarily to o-toluidine. (11)
- 2-Methylaniline hydrochloride (the hydrochloride salt of o-toluidine) was carcinogenic in both rats and mice. A National Cancer Institute (NCI) study, in which animals were exposed to 2-methylaniline hydrochloride in feed, reported increased incidences of sarcomas of the spleen and other organs in male and female rats; mesotheliomas of the abdominal cavity and scrotum and fibromas of subcutaneous tissue in male rats; transitional-cell carcinomas of the urinary bladder and fibroadenomas or adenomas of the mammary gland in female rats; hepatocellular or adenomas in female mice; and hemangiosarcomas at various sites in male mice. These tumors have also been reported in other studies in which animals were exposed to 2-methylaniline hydrochloride in their diet. (2,3,10)
- The International Agency for Research on Cancer (IARC) has stated that there is sufficient evidence for the carcinogenicity of 2-methylaniline hydrochloride in experimental animals. (1)
- EPA has classified o-toluidine as a Group B2, probable human carcinogen. (6)
- EPA has calculated an oral cancer slope factor of  $0.24 \text{ (mg/kg/d)}^{-1}$ . (6)

## Physical Properties

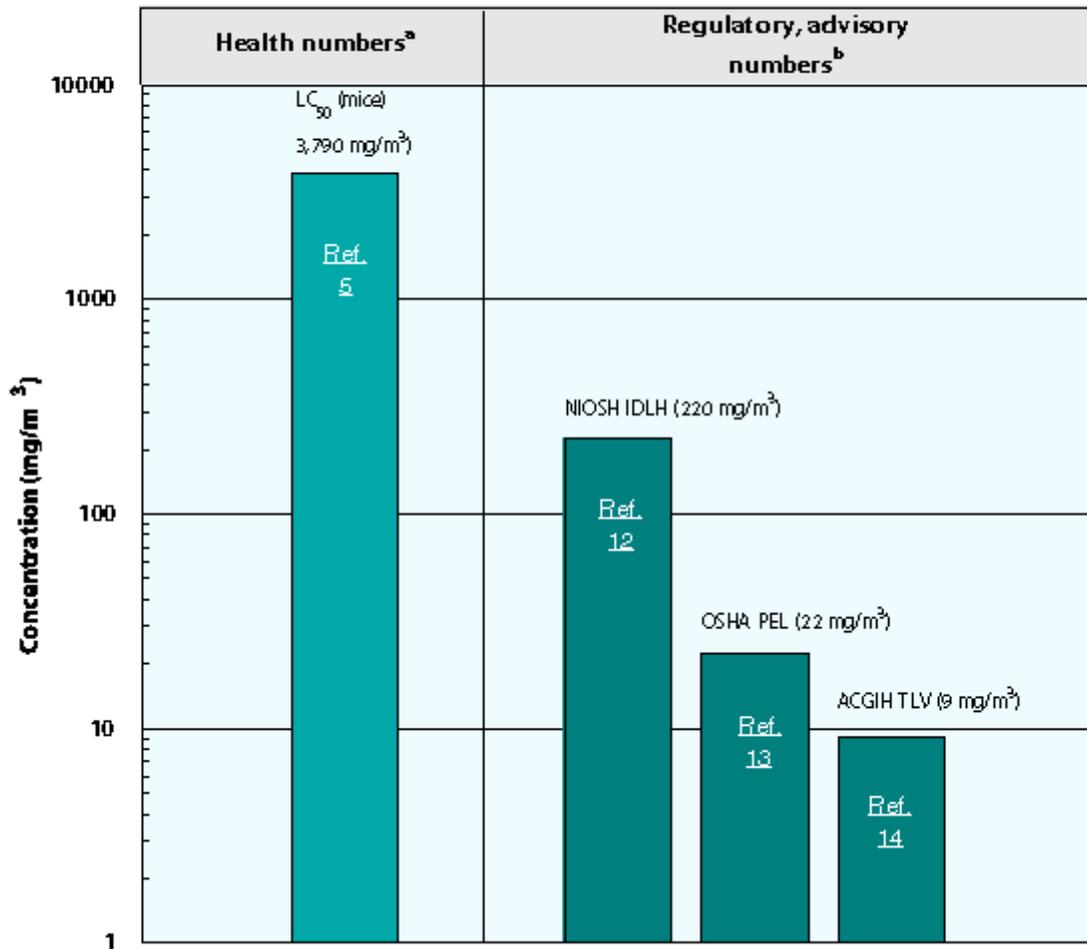
- 2-Methylaniline is another name for o-toluidine.
  - o-Toluidine is a colorless to light yellow liquid. (2)
  - o-Toluidine has an odor threshold of 0.25 parts per million (ppm). (7)
  - o-Toluidine is slightly soluble in water. (2)
  - The chemical formula for o-toluidine is  $\text{C}_7\text{H}_9\text{N}$ , and it has a molecular weight of 107.15 g/mol. (2,8) The vapor pressure for o-toluidine is  $0.31 \text{ mm Hg}$  at  $25^\circ\text{C}$ , and the log octanol/water partition coefficient ( $\log K_{ow}$ ) is 1.56. (9)
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#### Conversion Factors:

To convert concentrations in air (at  $25^\circ\text{C}$ ) from ppm to  $\text{mg}/\text{m}^3$ :  $\text{mg}/\text{m}^3 = (\text{ppm}) \times (\text{molecular weight of the compound}) / (24.45)$ . For o-toluidine:  $1 \text{ ppm} = 4.4 \text{ mg}/\text{m}^3$ . To convert from  $\mu\text{g}/\text{m}^3$  to  $\text{mg}/\text{m}^3$ :  $\text{mg}/\text{m}^3 = (\mu\text{g}/\text{m}^3) \times (1 \text{ mg}/1,000 \mu\text{g})$ .

## Health Data from Inhalation Exposure

## 2-Methylaniline



ACGIH TLV --American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect.

LC<sub>50</sub> (Lethal Concentration<sub>50</sub>)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH IDLH -- National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL --Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

The health and regulatory values cited in this factsheet were obtained in December 1999.

<sup>a</sup> Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.

<sup>b</sup> Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.

## References

Summary created in April 1992, updated in January 2000

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14. American Conference of Governmental Industrial Hygienists (ACGIH). 1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. Cincinnati, OH. 1999.