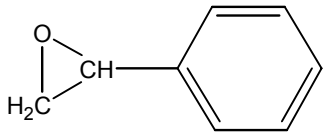
**STYRENE-7,8-OXIDE**
**CAS No. 96-09-3**
First listed in the *Tenth Report on Carcinogens*




## CARCINOGENICITY

Styrene-7,8-oxide (1,2-epoxyethylbenzene) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors at multiple tissue sites in multiple species of experimental animals. Styrene-7,8-oxide (SO) given by oral intubation induced high incidences of both benign and malignant tumors of the forestomach in both male and female rats (three strains) and mice (one strain) (IARC 1994) and, in one study, tumors of the liver in male mice (Lijinsky 1986).

No adequate human studies of the relationship between exposure to SO and human cancer have been reported.

## OTHER INFORMATION RELATING TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

SO is genotoxic in a variety of test systems, including prokaryotic, plant, eukaryotic, and mammalian (including human) *in vitro* and *in vivo* systems. SO induces mutations in bacteria, yeast, insects, and cultured mammalian cells, including mutations at the *hprt* locus in Chinese hamster V79 cells and human T lymphocytes. It induces chromosome damage (chromosomal aberrations or sister chromatid exchange) in Chinese hamster V79 cells, Chinese hamster ovary cells, mouse bone marrow cells *in vivo*, and cultured human lymphocytes. DNA strand breaks occur after SO exposure of cultured primary animal hepatocytes, human embryonal cells, and human lymphocytes and in lymphocytes, liver, and kidney cells in mice (IARC 1994). SO-DNA adducts have been found in several organs in mice and in cultured mammalian cells exposed to SO (Cantoreggi and Lutz 1993). A study of workers in a boat-making facility where styrene concentrations ranged from 1 to 235 mg/m$^3$ (mean of 65.6 mg/m$^3$, or 13.3 ppm) found elevated levels of SO-DNA adducts in mononuclear cells (Huff 1984, McConnell and Swenberg 1993). DNA adducts in rodents and humans appear to be similar.

SO given orally to rabbits, rats, and mice is absorbed and broken down rapidly in the acid environment of the stomach and excreted almost completely in the urine. SO can be metabolized by epoxide hydrolase to form the glycol or by glutathione S-transferase to glutathione conjugates. Styrene glycol is further metabolized to mandelic, phenylglyoxylic, and hippuric acids, which are excreted in urine (IARC 1976, 1994).

Workers exposed to SO vapors excreted large amounts of mandelic acid and phenylglyoxylic acid, both known metabolites of SO, in their urine. DNA and albumin adducts were found in the blood of plastics workers exposed to SO (Fustinoni et al. 1998). Low levels of covalent binding of SO to DNA were observed in the stomachs of rats given SO orally (Cantoreggi and Lutz 1993).

No available data would suggest that mechanisms thought to account for the observed genotoxic effects and tumor induction by SO in experimental animals would not also operate in humans.

## PROPERTIES

SO is a colorless to straw-colored liquid with a pleasant odor. It is a corrosive chemical that reacts vigorously with compounds having a labile hydrogen (including water) in the presence of catalysts such as acids, bases, and certain salts. It releases heat when it polymerizes (HSDB 2000). It is slightly soluble in water and soluble in alcohol, ether, benzene, acetone, methanol, carbon tetrachloride, and heptane (IARC 1994).

## USE

SO is used primarily in the production of styrene glycol and its derivatives. It also is used as a reactive diluent for epoxy resins and as a chemical intermediate for cosmetics, surface coatings, and agricultural and biological chemicals. SO has been used as raw material for the production of phenylethyl alcohol, which is used in perfumes, and for treatment of fibers and textiles (HSDB 2000).

## PRODUCTION

The U.S. International Trade Commission (U.S. ITC 1994) has no data on domestic SO production. The Hazardous Substances Data Bank identified one U.S. manufacturer of SO. SO was listed by the U.S. Environmental Protection Agency (EPA) as a high production volume chemical in 1990, indicating that annual production exceeded 1 million lb, but not in 1994 (EPA 1990, 1994).

## EXPOSURE

The general population may be exposed to SO by contact with contaminated air or water; however, according to EPA's Toxic Release Inventory, annual environmental releases of SO from industrial facilities have been less than 100 lb since 1994 (TRI 2001). No data quantifying exposure were found.

Philo *et al*. (1997) analyzed various plastics and resins in the United Kingdom to determine whether SO could migrate to food. They found SO in items that came into contact with food, including 9 base resins and 16 samples of polystyrene articles. Concentrations of SO in typical polystyrene materials were low, ranging from undetectable (< 0.5 mg/kg) to 3 mg/kg. Assuming that SO will migrate in the same pattern as the styrene monomer, estimates of migration to food range from 0.002 to 0.15 μg/kg.

Occupational exposure to SO occurs most often to workers in the fabricated rubber products, paints, and allied products industry (HSDB 2000). The National Occupational Exposure Survey (NIOSH 1990) estimated that 457 employees potentially were exposed to SO in the United States between 1981 and 1983, of which 59% potentially were exposed to SO and 41% to materials containing SO. SO can form in air at low levels (< 1 $mg/m^3$, or < 203 ppb) when styrene reacts with oxygen or

hydroperoxides (used to initiate the curing of reinforced plastics) (Yeowell-O'Connell *et al*. 1997).

Occupational exposure to SO is primarily indirect via exposure to styrene. The National Occupational Exposure Survey (NIOSH 1990) estimated that 108,000 workers, including 39,400 women, potentially were exposed to styrene between 1982 and 1983.

In personal exposure samples taken at a U.S. boat manufacturing company, the average concentration of SO in air was 0.14 $mg/m^3$ (28.5 ppb) for 19 workers who also were heavily exposed to styrene, at a mean concentration of 64 $mg/m^3$ (IARC 1994).

Nylander-French *et al*. (1999) studied levels of SO exposure and factors contributing to SO exposure in workers who manufactured reinforced plastics. From laboratory experiments, they hypothesized that SO formed either by breakdown of polymeric styrene peroxide radicals resulting from the copolymerization of styrene and oxygen, by epoxidation of the styrene monomer, or by reaction of styrene with volatile organic peroxides used in curing reinforced plastics. However, no measurements in manufacturing plants have confirmed these speculations. Overall, as styrene exposure increases, so does SO exposure, but this correlation was significant only among hand laminators, the workers who were exposed to the highest levels of styrene and SO. Resin use also was an important factor in predicting SO exposure, but the amount of resin was not important. This study shows that factors other than styrene exposure affect SO exposure.

## REGULATIONS

The U.S. EPA regulates SO under the Clean Air Act as a volatile hazardous air pollutant and under the Comprehensive Environmental Response, Compensation, and Liability Act and the Superfund Amendments and Reauthorization Act. SO has a reportable quantity of 100 pounds (45.4 kg).

SO is regulated by the U.S. Food and Drug Administration for use as a coating for certain containers.

The Occupational Safety and Health Administration regulates styrene oxide under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 164.

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