

Health Effects and Regulation of Styrene (CASRN 100-42-5)

(also known as vinylbenzene, ethenylbenzene, cinnamene, or phenylethylene)

- **Styrene is the monomer used to make polystyrene and expanded polystyrene packaging.**
- **It is a known lab animal carcinogen and a possible human carcinogen.**
- **Styrene readily migrates from packaging into food and beverages.**

Industry Information. The primary California manufacturers of polystyrene food ware are Dart Container and Pactiv Corp. Styrene has been manufactured in the United States since 1938, with production increasing dramatically over the last 30 years. In 2006, the United States produced >13 billion pounds.¹ The U.S. exports >2 billion pounds of styrene annually.² The volume of imported styrene was 1.265 million pounds in 2000.³ Past and current manufacturers of styrene include BP Amoco Corp., Chevron Chemical Corp., Cos-Mar, Inc., Dow Chemical USA, Huntsman Chemical Corp., Lyondell Chemical Co., NOVA Chemicals, Inc., Sterling Chemicals, Inc., and Westlake Styrene Corp.

Uses. Styrene is used predominantly (65%) in the production of polystyrene plastics and resins, which are molded into a variety of consumer products, primarily food service ware.⁴ The Food and Drug Administration (FDA) permits styrene to be used as a direct food additive for synthetic flavoring and as an indirect additive in polyester resins, adhesives, and rubber articles (5% by weight maximum) used in food products.⁵ **The FDA permits the migration of styrene from packaging into food.** Styrene is also used in fiberglass reinforcement materials used to make boat hulls. It is also used to produce copolymers such as styrene-acrylonitrile and acrylonitrile-butadiene-styrene (used for materials such as piping, automotive components, refrigerator liners, plastic drinking glasses, and car battery enclosures), and styrene-butadiene rubber (used for such products as car tires, hoses used for industrial applications, and shoes). Styrene-butadiene latex is implemented in making carpet, coatings for paper, and as part of latex paints. Styrene copolymers are also used in liquid toner for photocopiers and printers.⁶

Human Exposure. According to the US EPA, 100% of Americans have styrene in their bodies.⁶ **The principal forms of styrene exposure for the general population include breathing indoor air contaminated with cigarette smoke or automobile exhaust, consuming food items in contact with polystyrene foam packaging and to-go containers, and drinking contaminated water. Estimated exposures for the general population range from 1 µg/person/day to >100 µg/person/day mainly from indoor inhalation and food intake.**^{7 8 9} **Styrene content in food is mainly caused by migration from polystyrene foam containers into food (higher fat content, temperature, and acidity facilitate migration) and subsequently stores in human fat tissue.**¹⁰ **Occupational exposure to styrene can be at much higher levels than in the general population and occurs particularly in polystyrene factories, the reinforced plastics industry, and boat manufacturing.**⁸

Human Health Impacts and Risks. The International Agency for Research on Cancer (IARC) has determined that styrene is a known lab animal carcinogen and a possible human carcinogen, particularly in the occupational setting, with the strongest evidence coming from reinforced plastics workers.¹¹ **Several epidemiologic studies suggest elevated rates of lymphoma,^{12 13 14} hematopoiesis, and leukemia¹⁵ in workers through inhalation.**

Acute exposure to styrene in humans results in mucous membrane (in the throat) and eye irritation, gastrointestinal effects, listlessness, and impairment of balance.¹⁶ **Chronic exposure to styrene in humans affects the central nervous system, resulting in headache, fatigue, muscle weakness, depression, hearing loss, peripheral neuropathy, and contributes to central nervous system disease incidence, especially epilepsy, particularly among workers in the reinforced plastics industry.**^{17 18 19} **Neurotoxic effects include slowed sensory nerve conduction velocity, central and peripheral nervous system decrement, slowed**

reaction time, changes in color vision, tiredness, feeling drunk, concentration problems, or balance problems.^{20 21 22} Occupational exposure to styrene has also been linked to an increased risk of hearing loss and combined exposures to noise and styrene further increase risk.²³ Little information is available on the toxicity of styrene following ingestion by humans. However, the adverse health effects of styrene ingestion are expected to be similar to those seen following inhalation.

In animal studies, mice and rats exposed to high concentrations administered through inhalation have been observed to exhibit hearing loss, changes to the lining of the nose, and liver damage.¹³ Such exposures in animals have also been linked to lesions in respiratory tracts,²⁴ lung tumors (in male and female mice), olfactory nerve damage, and liver damage.²⁵ Rat studies implementing oral administration resulted in increased liver and kidney weights and depression of growth as well as severe lung congestion at high doses.⁸ Animal in vitro studies have observed mutagenic effects in mammalian cell cultures.²¹

California State and U.S. Federal Regulations and Exposure Limits

California Office of Environmental Health Hazard Assessment (OEHHA)

DRINKING WATER: The proposed Public Health Goal (PHG), which is based solely on scientific evidence regarding public health outcomes, for styrene in drinking water is 0.5 ppb.²⁶ Note that OEHHA's PHG for styrene is much lower than the EPA's Maximum Concentration Limit for styrene of 100 ppb, which reflects technological and economic considerations.

In 2009, OEHHA proposed that styrene be listed under Proposition 65 as a known human carcinogen. The \$28 billion styrene industry launched a legal challenge in California district court. The judge ruled in favor of the plaintiffs, overruling the proposed listing as a carcinogen, on the basis of costs associated with regulating the chemical, not on the basis of the human health impact or inadequacy of the science.

US Environmental Protection Agency (EPA)

Integrated Risk Information System (IRIS)^{*27}

Reference Dose for Chronic Oral Exposure (RfD) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The (RfD) for styrene is 0.2 mg per kg of body mass per day. The Reference Concentration (RfC), the chronic inhalation exposure level, is 1 mg/m³. (0.3 ppm)

*The IRIS does not constitute enforceable legal code, but rather functions as an informational reference for regulatory agencies.

Maximum Contaminant Limit (MCL)

The enforceable standard that defines the highest level of a contaminant that is allowed in drinking water. MCLs are set as close to health-based limits (Maximum Contaminant Level Goals, or MCLGs) as feasible using the best available analytical and treatment technologies and taking cost into consideration. This limit is 100 ppb.

US Food and Drug Administration (FDA)- Title 21, Chapter I, Subchapter B—Food for Human Consumption:

Styrene concentration in bottled water is limited to 0.1 mg/L in Part 165. Styrene, styrene polymers, and styrene copolymers are approved for use as a direct food additive (as a flavoring agent and chewing gum base) in Part 172; as components of ion exchange membranes and resins for food treatment in Part 173; as components of adhesives and coatings in food packaging in Part 175; as components of paper and paperboard in contact with aqueous and fatty as well as dry foods in Part 176; in single and repeated use plastic, rubber, and textile food contact surfaces in Part 177; as indirect food additives in the production of other food-related substances in Part 178; as packaging materials for use during irradiation of prepackaged foods in Part 179; as substances used in paper and paperboard food packaging manufacturing in Part 181.

¹ SRI. 2006. Directory of chemical producers. United States of America. Menlo Park, CA: SRI Consulting, 894.

² HSDB. 2007. Styrene. Hazardous Substances Data Bank. National Library of Medicine.

<http://toxnet.nlm.nih.gov>. August 30, 2007.

³ IARC. 2006. Agents Reviewed by the IARC Monographs. Volumes 1–96. Lyon, France: International Agency for Research on Cancer. <http://monographs.iarc.fr/ENG/Classification/index.php>.

⁴ James DH, Castor WM. 2005. Styrene. In: Ullman's encyclopedia of industrial chemistry.

http://www.mrw.interscience.wiley.com/emrw/9783527306732/ueic/article/a25_329/current/pdf.

⁵ 21CFR177.1640.

⁶ The EPA National Human Adipose Tissue Survey for 1986 identified styrene residues in 100% of all samples of human fat tissue taken in 1982 in the US.. A 1988 survey published by the Foundation for Advancements in Science and Education also found styrene in human fatty tissue with a frequency of 100%.

⁷ ATSDR. 1992. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Styrene. U.S. Department of Health and Human Services, Public Health Service.

⁸ Health Canada (1993). Priority substances list assessment report-styrene.

⁹ EU. Risk assessment report-styrene-part I-environment.

http://ecb.jrc.it/documents/existing-chemicals/risk_assessment/report/styrenereport034.pdf.

¹⁰ U.S. EPA (1994). Styrene Fact Sheet. U.S. Environmental Protection Agency, Pollution Prevention and Toxics. EPA749-F-95-019. November 1994.

¹¹ IARC (1994). Styrene. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Some Industrial Chemicals. Vol. 60:235-320.

¹² Hodgson J (1985). Mortality of styrene production, polymerization and processing workers at a site in northwest England. Scandinavian Journal of Work, Environment & Health, 11(5), 347-352.

¹³ Barale R (1991). The Genetic Toxicology of Styrene and Styrene Oxide. Mutation Research, Vol. 257, No. 2, pages 107-126.

¹⁴ Bond G (1992). Mortality among workers engaged in the development or manufacture of styrene-based products--an update. Scandinavian Journal of Work, Environment & Health, 18(3), 145-54.

-
- ¹⁵ Kolstad H A, Lynge E, Olsen J, Breum N (1994). Incidence of lymphohematopoietic malignancies among styrene-exposed workers of the reinforced plastics industry. *Scandinavian Journal of Work, Environment & Health*, 20, 272-278.
- ¹⁶ OEHHA (1999). Styrene. Determination of acute reference exposure levels for airborne toxicants. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. March 1999, pp. C296-C305.
- ¹⁷ OEHHA (2001). Styrene. Chronic Toxicity Summary. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html.
- ¹⁸ Welp E, Kogevinas M, Andersen A, Bellander T, Biocca M, Coggon D, Esteve J (1996). Exposure to Styrene and Mortality from Nervous System Diseases and Mental Disorders. *American Journal of Epidemiology* Vol. 144, No. 7: 623-633
- ¹⁹ Viaene M (2001). Neurobehavioural changes and persistence of complaints in workers exposed to styrene in a polyester boat building plant: influence of exposure characteristics and microsomal epoxide hydrolase phenotype. *Occupational and Environmental Medicine*, 58, 103-112
- ²⁰ Pahwa R (1993). A Critical Review of the Neurotoxicity of Styrene in Humans. *Veterinary and Human Toxicology*, Vol. 35, No. 6, pages 516-520.
- ²¹ Arlien-Soborg P (1992). Styrene. Solvent Neurotoxicity. CRC Press. Boca Raton, Florida, pp. 129-53.
- ²² Viaene M (2001). Neurobehavioural changes and persistence of complaints in workers exposed to styrene in a polyester boat building plant: influence of exposure characteristics and microsomal epoxide hydrolase phenotype. *Occupational and Environmental Medicine*, 58, 103-112
- ²³ Sliwinska-Kowalska M, Zamyslowska-Szmytko E, Szymczak W, Kotylo P, Fiszler M, Dudarewicz A et al (2003). Ototoxic effects of occupational exposure to styrene and co-exposure to styrene and noise. *J Occup Environ Med* 45:15–24.
- ²⁴ Cruzan G, Cushman JR, Andrews LS, Granville GC, Johnson KA, Bevan C, Hardy CJ, Coombs DW, Mullins PA, Brown WR (2001). Chronic toxicity/oncogenicity study of styrene in CD-1 mice by inhalation exposure for 104 weeks. *J Appl Toxicol* 21:185-98.
- ²⁵ Conti B (1988). Long-Term Carcinogenicity Bioassays on Styrene Administered by Inhalation, Ingestion and Injection and Styrene Oxide Administered by Ingestion in Sprague-Dawley Rats, and para-Methylstyrene Administered by Ingestion in Sprague-Dawley Rats and Swiss Mice. *Annals of the New York Academy of Sciences*, 534, 203-34.
- ²⁶ <http://oehha.ca.gov/water/phg/phg053008.html>
- ²⁷ <http://www.epa.gov/iris/subst/0104.htm>