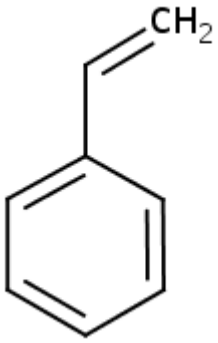
STYRENE

CASRN: 100-42-5



For more information, search the NLM HSDB database.

Human Health Effects:

Evidence for Carcinogenicity:
Evaluation: There is inadequate evidence in humans for the carcinogenicity of styrene. There is limited evidence in experimental animals for the carcinogenicity of styrene. In making the overall evaluation, the Working Group took into consideration the following supporting evidence: Styrene is metabolized to styrene-7,8-oxide, which binds covalently to DNA and shows activity in various in vitro and in vivo assays for genetic effects. The genetic and related effects of styrene are therefore associated with its oxidation, which also occurs, eg, in human whole blood cultures, where styrene induces dose related reponses of chromosomal damage at low concentrations. Styrene-7,8-oxide is detected in blood of workers exposed to styrene. Adducts in hemoglobin and DNA, DNA single strand breaks/alkali labile sites, as well as significant increases in the frequency of chromosomal damage have been found in workers exposed to styrene in the reinforced plastics industry. Positive results are associated with higher overall styrene levels and negative results with decreasing exposures to styrene. Although in human studies the role of other contaminants cannot be excluded, their occurrence is variable and their concentrations are very low in comparison with that of styrene. Overall evaluation: Styrene is possibly carcinogenic to humans (Group 2B).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. 60 297 (1994)] **PEER REVIEWED**

A4; Not classifiable as a human carcinogen. /Styrene, monomer/
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 53] **PEER REVIEWED**

Confirmed carcinogen
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Human Toxicity Excerpts:
/HUMAN EXPOSURE STUDIES/ Nine human volunteers /were exposed/ to styrene vapor at concns of 50, 100, 216, and 376 ppm for varying periods up to 7 hrs. None of the volunteers exposed at 50 ppm for 1 hr experienced any subjective symptoms or abnormal objective clinical findings. Vapor exposure at 100 ppm, however, produced mild, untoward, but transient subjective responses in half of those exposed. At 376 ppm, the majority of test subjects experienced unpleasant subjective symptoms and definite signs of neurologic impairment.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 8-9] **PEER REVIEWED**

/HUMAN EXPOSURE STUDIES/ This study evaluated the impact of different work load intensities on biological indicators of styrene exposure. Four adult Caucasian men, aged 20 to 44 years, were recruited. Groups of 2-4 volunteers were exposed to 20 ppm of styrene in an exposure chamber according to scenarios involving either aerobic, muscular, or both types of physical exercise for 3 or 7 hr. The target intensities for each 30-min exercise period-interspaced with 15 min at rest-were the following: REST, 38 watts AERO (time-weighted average intensity), 34 watts AERO/MUSC, 49 watts AERO/MUSC, and 54 watts AERO for 7 hr and 22 watts MUSC for 3 hr. End-exhaled air samples were collected at 15 time points during and after 7-hr exposures for the determination of styrene concentrations. Urine samples were collected before the start of exposure, after

the first 3 hr of exposure, and at the end of exposure for the determination of mandelic acid (MA) and phenylglyoxilic acid (PGA) concentrations. Compared with exposure at rest, styrene in alveolar air increased by a factor up to 1.7, while the sum of urinary MA and PGA increased by a factor ranging from 1.2 to 3.5, depending on the exposure scenario. Concentrations of biological indicators of styrene fluctuated with physical exertion and were correlated with the magnitude of the physical activity and pulmonary ventilation. Despite the physical exertion effect, urinary concentrations of styrene metabolites after a single-day exposure remain below the current biological exposure index value recommended by ACGIH; therefore, no additional health risk is expected. However, results shows that work load intensities must be considered in the interpretation of biological monitoring data and in the evaluation of the health risk associated with styrene exposure.
[Truchon G et al; J Occup Environ Hyg. 6(8):460-7 (2009).] **PEER REVIEWED** PubMed Abstract

/HUMAN EXPOSURE STUDIES/ ... Human volunteers /were exposed/ to styrene vapor for periods of 1-7 hr. At doses of 52 and 117 ppm subjects reported smelling a moderately strong, but not objectionable, odor of styrene upon entering the chamber. The odor diminished during the 1 or 2 hr exposure. No symptoms or objective signs of illness were reported. One of nine subjects reported nasal irritation following 20 min exposure to 216 ppm. There were no neurologic symptoms or physical findings. At 376 ppm, 2 subjects reported mild ocular irritation within 3 min and 2 more within 15 min, and all reported nasal irritation. One subject reported a burning sensation of the skin of the face. The odor decreased but remained perceptible during the exposure period. Neurologic impairments, measured by performance on a modified Romberg test, a dexterity test, and a coordination test, were noted during this exposure. One subject reported nausea, 2 reported a feeling of slight inebriation, and 2 reported headache. Clinical lab studies, including complete blood count, erythrocyte sedimentation rate, reticulocyte count, serum glutamic pyruvic transaminase (SGPT), lactic dehydrogenase (LDH), alkaline phosphatase, blood urea nitrogen, creatinine, glucose, and urinalysis, were normal and unchanged from preexposure values. To simulate a work day ... the same human volunteers /were exposed/to 99 ppm styrene for an initial 3 1/2 hr period, followed by 30 min in a uncontaminated area, then 3 1/2 hr additional exposure. Subjectively, 3 subjects reported mild eye or throat irritation within 20 min. At the end of the exposure period, the odor of styrene was barely perceptible and none of the subjects reported nausea, headache, or irritation of the eyes, nose, or throat. All reported no objection to working in this concn for an indefinite period of time. There were no objective signs of impairment of balance or coordination. Results of clinical lab studies were again normal and unchanged from preexposure values.
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992., p. 1000] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ /Exposure to/ styrene vapor /at/ ... 100 ppm in air causes mild irritation of eyes and throat in 20 min in some people. Even at 375 ppm not all people feel significant eye irritation in 15 min, but all have nasal irritation at this concn. Concn of 400 and 500 ppm more consistently cause irritation of eyes and nose, but can be tolerated.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 854] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Humans acutely exposed by inhalation to 800 ppm (3.4 mg/L) for 3 hr experience immediate eye and throat irritation, increased nasal mucous secretion, metallic taste, drowsiness, and vertigo. After test termination, slight muscular weakness, accompanied by inertia and depression are noted. /From table/
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 309] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Examined by EEG and motor and sensory neurophysiology of 31 workers exposed to >50 ppm, approx 50 ppm (the threshold limit), and <50 ppm styrene and of 17 patient judged to suffer from sequelae after long term exposure to org solvents showed similar neurophysiological changes consisting of sensory nerve responses of low amplitude and long duration, somewhat low sensory conduction velocities and incr fast activity in the central and precentral regions in the EEG in combination with normal occipital alpha activity.
[Rosen I et al; Scand J Work Environ Health 4 (Suppl 2): 184-94 (1978)] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Acute exposure to high concn of styrene may produce irritation of the mucous membranes of the upper respiratory tract, nose, and mouth, followed by symptoms of /CNS depression/, muscular contraction, and death due to respiratory center paralysis.
[NAS/NRC; The Alkyl Benzenes p.323 (1981)] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ The principal acute hazards from worker exposure to styrene are central nervous system depression and irritation of the skin, eyes, and upper respiratory tract.
[NIOSH; Criteria Document: Styrene p.15 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ "Styrene sickness" is not uncommon in industry after exposure to vapors or mists; characteristic signs and symptoms incl headache, fatigue, weakness, depression and unsteadiness or feeling of drunkenness. Many patients have exhibited abnormal electroencephalograms. ... Peripheral neuropathies (distal hypesthesia and decreased nerve conduction velocities) have been observed in chronically exposed workers. ... /There are/ no reports of hematological disturbances.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-152] **PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Long-term contact with styrene results in blistering of the skin and development of dermatitis, which is thought to result from defatting of the skin.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 277 (1994)] **PEER REVIEWED**

/CASE REPORTS/... Workers in factory producing polystyrene resins, where concn ... reached 200 ppm, revealed ... itching dermatitis in one case, and erythematous papular dermatitis of forearms in two others.
[Snyder, R. (ed.) Ethel Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume 1: Hydrocarbons. Amsterdam - New York -

Oxford: Elsevier, 1987., p. 205] **PEER REVIEWED**

/CASE REPORTS/ Splash contact with human eyes has resulted in similar superficial transient disturbance /moderate hyperemia of the conjunctiva and slight injury of the corneal epithelium/, with return to normal within 48 hr in 29/30 cases. In the exceptional case, healing took 3-10 days.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 854] **PEER REVIEWED**

/EPIDEMIOLOGY STUDIES/ /Researchers/ aimed to investigate whether styrene can affect the vibration perception threshold (VPT) and to examine the dose-effect relationship at current and past styrene exposure levels. VPT was examined using a Vibrometer (TM-31A) for 67 subjects exposed to styrene in a fiberglass reinforced plastic boat plant and 151 non-exposed subjects. /Researchers/ selected 67 age-matched controls out of the non-exposed subjects for the analyses. End shift urinary metabolites of styrene were measured for evaluation of the dose-effect relationship for the past eight years and at the time of VPT measurement. The current exposure level was expressed by the end shift urinary mandelic acid (MA) and phenylglyoxylic acid (PGA) levels. Cumulative exposure index (CEI) were calculated based on the exposure frequency and urinary MA concentrations measured for the past eight years. The VPT of the exposed group was higher than that of non-exposed group. Multiple regression analysis revealed that past maximum exposure level and age were significant factors explaining the variation of VPT. Dose-effect relationship was recognized in upper limbs but not in lower limbs among exposure groups. When the exposed group was divided into high- and low-level groups for the past maximum exposure level by the cutoff point of MA 0.83 g/g cr (equivalent to 50 ppm in air) and compared to the control group, /researchers/ found significant differences in the VPT in upper limbs, between the high-level exposed group and control group, and in lower limbs, between both of the high- and low-level exposed groups and the control group. /The authors concluded that/ if the maximum concentration of styrene exposure exceeded 50ppm in the past, effects of exposure to styrene on the VPT are likely to persist.
[Sato T et al; Neurotoxicology. 30(1):97-102 (2009).] **PEER REVIEWED** PubMed Abstract

/EPIDEMIOLOGY STUDIES/ Styrene is a basic building block for manufacturing thousands of products throughout the world. The present study aimed to (1) detect the presence of styrene and/or its metabolites in the workers in one of the Egyptian plastic factories; (2) demonstrate some common health effects of styrene exposure among the same group by some laboratory investigations and compare them with the unexposed healthy individuals; and (3) correlate the duration of styrene exposure and its level in the blood with the severity of the demonstrated health effects. This study was conducted in one of Egyptian plastic factories. The exposed group was 40 male workers, ranging in age from 18 to 33 years (23.20 +/- 4.09), working 12 h/day with 1 day off, and working without any protective equipment. A control group of 50 unexposed healthy males matched with the exposed group for age (21-35 yrs (23.40 +/- 4.05)), sex, socioeconomic status, and smoking habit is selected. Written individual consent is obtained from all participants followed by (a) a full medical and occupational history and full clinical examination; (b) ventilatory function tests: forced vital capacity (FVC), slow vital capacity, forced expiratory volume in the 1st second (FEV(1))%, FEV(1)/FVC%, peak expiratory flow, and mid-expiratory flow 25-75%; (c) analyses of beta2 microglobulin; blood styrene level; and urinary mandelic acid; and (d) cytogenetic study. The study results showed a statistically significant difference between the exposed and the control groups as regard the blood styrene level, urinary mandelic acid level, beta2 microgloblin in urine, and chromosomal study. The study also showed a statistically significant correlation between the duration of styrene exposure and ventilatory function parameters, also between the duration of styrene exposure and some detectable chromosomal aberrations...
[Helal SF et al; Toxicol Ind Health. 29(9):812-9 (2013).] **PEER REVIEWED** PubMed Abstract

/EPIDEMIOLOGY STUDIES/ Styrene is a volatile organic compound used in factories for synthesis of plastic products. The pneumotoxicity of styrene in experimental animals is known. The aim of the present study was to study the effect of styrene on lung function and oxidative stress in occupationally exposed workers in plastic factory. Thirty-four male workers, between 18 and 40 years of age, exposed to styrene for at least 8 hours a day for more than a year were studied, while 30 age- and sex-matched healthy subjects not exposed to styrene served as controls. Assessment of lung functions showed a statistically significant reduction ($p < 0.05$) in most of the lung volumes, capacities (FVC, FEV(1), VC, ERV, IRV, and IC) and flow rates (PEFR, MEF(75%), and MVV) in the study group (workers) as compared to controls. Malondialdehyde (MDA) was observed to be significantly high ($p < 0.05$) while ferric-reducing ability of plasma (FRAP) was significantly low ($p < 0.05$) in styrene-exposed subjects. Reduced glutathione (GSH) level was significantly depleted in exposed subjects as compared to control group. The mean value of serum cytochrome c in styrene-exposed subjects was found to be 1.1 ng/mL (0.89-1.89) while in control its levels were under detection limit (0.05 ng/mL). It shows that styrene inhalation by workers leads to increased level of oxidative stress, which is supposed to be the cause of lung damage.
[Sati PC et al; Hum Exp Toxicol. 30(11):1743-50 (2011).] **PEER REVIEWED** PubMed Abstract

/EPIDEMIOLOGY STUDIES/ A longitudinal study of 11 workers (aged 24-54 years) in the polyester resin boat industry in Germany assessed nerve conduction velocities in 1980 and 1983. Exposure was occupational and route was by inhalation with mean air levels of 114 + or - 38 ppm, 97 + or - 35 ppm, 92 + or - 33 ppm over 3-7 years (mean= 4 yrs). The peripheral nervous system showed no significant difference in conduction velocities between exposed and controls for ulnar and median nerves. Mean blood levels were 0.92 mg/L (+ or - 0.86) in 1980 and 0.70 mg/L (+ or - 0.33) in 1983; mean levels of mandelic acid in urine ranged from 816 to 1660 mg/g creatinine; mean levels of phenylglyoxylic acid in urine ranged from 200-342 mg/g creatinine.
[Triebig G et al; Int Arch Occup Envir Health 5 (6): 239-47 (1985)] **PEER REVIEWED**

/EPIDEMIOLOGY STUDIES/ /A 1980/ study has /examined/ men exposed to styrene used as a resin solvent in the building of fiberglass boats. Their performance was compared in behavioral tests at the beginning and end of the working day with that of a nonexposed group. Exposure was measured from diffusion buttons, blood styrene concn were measured at the end of the working day, and all urine passed between the end of work and bedtime was collected and its content of mandelic acid estimated. The exposed men were divided into high blood styrene group (>5.5 umol/L) & low styrene group (<5.4 umol/L). No convincing changes were found in most of the objective tests of performance, but those workers with high blood styrene

levels reported greater subjective feelings of physical and mental tiredness at the end of the day and had consistently slower reaction times in both the morning and the afternoon. In all 3 groups, scores in the test worsened through the day, but deterioration was greatest in the high styrene group. Even so, the results are difficult to interpret, because at a constant atmospheric concn of styrene, more will be absorbed by those undertaking the heaviest physical exercise, and it may be the effects of the exercise itself which were responsible for the findings.
[Haddad, L.M. and Winchester, J.F. Clinical Management of Poisoning and Drug Overdosage. Philadelphia, PA: W.B. Saunders Co., 1983., p. 791] **PEER REVIEWED**

/EPIDEMIOLOGY STUDIES/ A population-based case-control study of cancer comprised 3,730 histologically confirmed male cases of cancer at 11 major sites (including non-Hodgkin's lymphoma) newly diagnosed between 1979 and 1986 among residents of Montreal, Canada, aged 35-70 and ascertained in 19 major hospitals. The exposure of each subject to 293 occupational agents was evaluated by a group of chemists on the basis of jobs held, and cases of cancer at each site were compared with those in the rest of the study population, after adjustment for age, ethnic group, alcohol drinking and tobacco smoking. One percent of subjects were classified as ever having been exposed to styrene. The only significant increase in risk was seen for cancer of the rectum (odds ration, 1.7; 90% confidence interval, 0.8-3.8; six cases). A higher risk (odds ration, 4.1; 90% confidence interval, 1.4-11.8, five cases) was seen from subjects with substantial exposure to styrene (subjects with exposure to styrene at medium or high concentration and frequency and with at least five years accumulated duration of exposure, up to five years before onset of disease).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 258 (1994)] **PEER REVIEWED**

/EPIDEMIOLOGY STUDIES/ A nested case control study was conducted of gastrointestinal cancer in male workers from eight styrene-butadiene polymer manufacturing facilities in the United States and Canada to determine whether there was any association with exposures to styrene and butadiene. A study on the association between hematologic neoplasms and exposure to butadiene and styrene was reexamined using different criteria for matching and exposure. Exposure levels for each job in the industry were developed based on area and personal monitoring. The risk of lymphohematopoietic cancers was increased in the workers who had increased exposure to butadiene. Even using different methodologies such as choosing different types of controls the risk of leukemia among these workers remained high. Among the leukemia cases there was a higher than expected proportion of acute lymphocytic leukemia. Some of the odds ratios were high for butadiene and styrene associated with esophageal cancers but the findings were not statistically significant. Also not significant was a suggestive trend for increasing odds ratios with increasing butadiene exposure for colorectal cancers. When short term workers were included there was an increase in the all cause mortality, but no increase in standardized mortality ratios for cancer or circulatory diseases. Long term workers had higher risks for cancers of interest in this study than short term workers.
[Matanoski GM et al; Govt Reports Announcements & Index (GRA&I) Issue 24: (1993) NTIS/PB93-236131] **PEER REVIEWED**

/SURVEILLANCE/ Associations between occupational styrene exposures and impairment of visual functions were investigated with a view to answering three questions: (1) are the published findings for color vision deficiencies and impaired contrast sensitivity to reproduce in a new study approach, (2) if such effects exist, are they related to current or chronic exposures and (3) if effects exist, are there reductions in the effects during an exposure-free period? Workers from a boat building plant were examined in groups of current low [n = 97, mean mandelic acid (MA) + phenylglyoxylic acid (PGA) = 51 mg/g creatinine], medium (n = 115, mean = 229 mg/g creatinine) and high (n = 30, mean = 977 mg/g creatinine) level exposure to styrene. Job tenure was about 6 years. In addition, subgroups chronically exposed to low-short (n = 34, lifetime weighted mean 200 mg/g creatinine for 6 years) and high-long (n = 17, mean = 660 mg/g creatinine, 15 years) styrene levels were analyzed. The examinations were carried out during normal working days and during the company holidays. Color vision was investigated with the Lanthony desaturated panel D-15d using the color confusion index (CCI) as a relevant variable. Contrast sensitivity was investigated with the Vistech charts VCTS 6500 using frequency-related results as well as total scores as variables. Co-variance analyses with repeated measurements and multiple linear regressions were used for statistical analysis. There was no evidence of significant associations between exposure parameters and CCI. This is true for the analyses with all participants as well as for those with the subgroups with high-long versus low-short exposure. Thus, no exposure related changes in the relevant variables were found during the exposure-free period. The analyses for contrast sensitivity show similar results. The largest portions of the variances in both tests were explained by age. German as mother tongue covered a considerable portion of the CCI variances. Education, long-term alcohol use and job tenure explain only partly significant portions of the test variances exhibited. Both acute styrene exposure levels of 40 ppm (range of standard deviation up to 54 ppm) and long term exposures to 27 ppm (range of standard deviation up to 44 ppm with higher exposure levels in the past) for a period of about 15 years were not identified as causing elevated risks for the investigated parameters of color vision and contrast sensitivity. This statement contradicts the published results for styrene-related color vision deficiencies but it seems to be compatible with published results for contrast sensitivity due to styrene exposure.
[Seeber A et al; Int Arch Occup Environ Health. 82(6):757-70 (2009).] **PEER REVIEWED** PubMed Abstract

/SURVEILLANCE/ 494 workers exposed to styrene were examined. /Pre-CNS depressant/ symptoms, such as light-headedness, eye irritation, and irritation of mucous membranes were significantly more frequent in a "high" exposure group than in a "low" exposure group. A distal hypoesthesia of the legs occurred in 8.5% of the cases. The conduction velocities of both radial and peroneal nerves were less than normal in 18.8% and 16.4% of the workers, respectively. There was consistent decrement in peroneal nerve conduction velocity as the exposure to styrene exposure continued, but no such relationship was observed for radial nerve conduction velocities.
[Lilis RW et al; Environ Res 15: 133-38 (1978) as cited in NAS/NRC; The Alkyl Benzenes p.331 (1981)] **PEER REVIEWED**

/SURVEILLANCE/ Styrene is used in manufacturing fiberglass reinforced plastics: and occupational exposure was related to neurotoxicology and genotoxicity. The sum of the metabolites mandelic and phenylglyoxylic acids is the ACGIH biomarker for occupational exposure with a BEI of 400 mg/g of creatinine in end shift urine corresponding to a airborne styrene

concentration of 85 mg/cu m. There are two main molding processes, open and closed, the last more effective at controlling worker's styrene exposure. /The objectives are/ to compare the open molding process to the compression of fiber reinforced resin foils, a kind of closed molding, monitoring the styrene exposure of workers in two production sites (A and B). Environmental Monitoring was carried out by Radiello samplers and Biological Monitoring by means of the determination of MA and PGA with HPLC/MS/MS in 10 workers at Site A and 14 at Site B. The median values for styrene exposure resulted 31.1 mg/cu m for Site A and 24.4 mg/m for Site B, while the medians for the sum of the two metabolites in the end shift urine were 86.7 e 33.8 mg/g creatinine respectively. There is a significant linear correlation between personal styrene exposure and the excretion of styrene metabolites (R = 0.74). As expected the exposure markers of the workers of the two production sites resulted higher in the open process. The analytical results of both environmental and biological monitoring were all below the occupational exposure limits, confirming the efficacy of the protective devices.
[Tranfo G et al; Med Lav. 103(5):402-12 (2012).] **PEER REVIEWED** PubMed Abstract

/SURVEILLANCE/ Little evidence exists on the possible adverse effects of styrene on the central part of the auditory system. The present investigation aimed to study the possible association between styrene exposure and temporal processing abilities. Fifty-nine styrene-exposed subjects and 50 nonexposed control subjects were tested. Pure-tone audiometry (125-8000 Hz) and 3 temporal processing tests (gaps-in-noise, frequency pattern test and duration pattern test) were carried out. Significant differences between groups were found for most of the audiometric thresholds for both ears. ANCOVA analysis showed that styrene-exposed subjects had significantly poorer performances on the frequency and duration pattern tests than nonexposed subjects, when including hearing level and age as covariates. The results of the present research study suggest an association between styrene exposure and central auditory dysfunction characterized by a temporal processing disorder.
[Zamyslowska-Szmytke E et al; Audiol Neurootol. 14(5):296-302 (2009).] **PEER REVIEWED** PubMed Abstract

/SURVEILLANCE/ A study /reported in 1978/ of 345 people working in a styrene plant ... produced no evidence of optic neuropathy or other significant eye disease, despite considerable acute and chronic exposures.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 854] **PEER REVIEWED**

/SURVEILLANCE/ An elevated incidence of hematopoietic and lymphatic cancer has been reported for workers in the styrene-butadiene rubber industry. ... 10 yr mortality history of 6678 male rubber workers /were examined/. ... The age-related mortality rate due to lymphatic and hematopoietic cancer was reported to be 4.4 times higher for workers with 2 yr of experience and 5.6 times higher for workers with 5 yr of experience compared to the general population. For lymphatic leukemia, the age-adjusted mortality rate in the synthetics plant workers was 2.9 times higher for workers with 2 yr of experience and 3.7 times higher for workers with 5 yr of experience, compared to the general study population.
[McMichael AJ et al; J Occup Med 18: 178-85 (1976)] **PEER REVIEWED** PubMed Abstract

/SURVEILLANCE/ ... Effects on the liver (eg, increased serum bile acid and enhanced activity of plasma enzymes) and reproductive system (eg, decreased frequency of births and increased frequency of spontaneous abortions in female workers) have been reported.
[USEPA; Health Assessment Document: Styrene (Draft) p.3-23 (1985)] **PEER REVIEWED**

/SURVEILLANCE/ ... Ocular exams /were conducted along with evaluations of/ complete histories of 345 workers in a styrene plant. Conjunctival irritation was found in 22% of the workers and correlated with intensity of exposure to styrene.
[NTP; Executive Summary: Styrene (Draft) p.13 (1985)] **PEER REVIEWED**

/SURVEILLANCE/ One study of 50 petroleum workers who produced synthetic rubber indicated that one-half of the work force experienced gastric acidity reduction, liver detoxification, and pancreatic changes. In addition, moderate anemia, leukopenia, reticulocytosis, increased clotting time, and a rise in capillary permeability were noted. Clinical analyses indicated changes in blood protein composition and increased cholinesterase activities.
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 313] **PEER REVIEWED**

/SURVEILLANCE/ An ocular examination of 345 workers in a styrene plant revealed conjunctival irritation in 22% of the work force, but no retrobulbar neuritis and central retinal vein occlusion ... .
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 313] **PEER REVIEWED**

/SURVEILLANCE/ Cases of leukemia and lymphoma were identified among workers engaged in the production of styrene butadiene rubber, in the manufacture of styrene butadiene and in the manufacture of styrene and polystyrene. A total of 19 cases of leukemia and eight of lymphoma were reported in these studies. Exposure to benzene, butadiene, ethyl benzene and other chemicals could also have occurred in these operations.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 251 (1994)] **PEER REVIEWED**

/SURVEILLANCE/ A retrospective cohort study was conducted in two plants where styrene-butadiene rubber was produced (plants A and B in eastern Texas, USA, which included 1,662 (plant A) and 1,094 (plant B) white men who had been employed for at least 6 months (total, 53,929 person-yrs at risk). Follow-up was from 1943-1976 (plant A) and from 1950-1976 (plant B). The study was conducted after the initial finding of 2 cases of lymphatic and hematopoietic cancer at one of the plants. Environmental samples were taken only at the time of the study: mean exposures to styrene were 0.94 ppm at plant A (4 mg/cu m) and 1.99 ppm (8.5 mg/cu m) at plant B; those for 1,3-butadiene were 1.24 ppm (2.74 mg/cu m) and 13.5 ppm (30 mg/cu m), respectively. Traces of benzene were also detected in plant A. The standardized mortality ratio for all causes of death was 80 (95% confidence interval, 70-90) for workers in plant A, and 9 deaths from cancers of the lymphatic and hematopoietic tissues occurred between January 1943 and March 1976 (5.79 expected), giving a standardized mortality ratio

of 155 (95% confidence interval, 71-295). Further analysis showed that these 9 men had been employed between January 1943 and December 1945 during operation of a batch process, for which period the expected number was 4.3, giving a standardized mortality ratio of 212 (95% confidence interval,97-402). The standardized mortality ratio for leukemia was 278 (95%confidence interval, 90-648). In plant B no significant excess mortality from any cancer was found: 11 cancer deaths were observed and 21 expected; there were two deaths from neoplasms of lymphatic and hematopoietic tissues (2.6 Expected).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 252 (1994)] **PEER REVIEWED**

/SURVEILLANCE/ A study was performed/ on 622 men who had worked for at least one year in the production, polymerization and processing of styrene at a plant in the United Kingdom between 1945 and 1978. Of these, 131 men were potentially exposed to styrene in laboratories and 491 in production of styrene monomer, polymerization of styrene or manufacture of finished products. No measurements of exposure were provided, but many other chemicals were present in the working environment. Expected numbers of deaths were calculated on the basis of national rates. There were 34 deaths (43.1 Expected) among the 622 exposed workers. A significant excess of deaths from lymphoma (3 observed, 0.56 expected) was observed. An analysis of cancer registrations from this population revealed an additional case of lymphatic leukemia, giving a total of four incident cases of lymphatic and hematopoietic cancer, whereas 1.6 would have been expected from local cancer registration rates (standardized incidence ratio (SIR), 250; 67-640). Additionally, three incidents cases of laryngeal cancer were found (0.5 expected).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 254 (1994)] **PEER REVIEWED**

/SURVEILLANCE/ A historical cohort mortality study of 40,688 workers employed in 660 plants of the reinforced plastics industry and enrolled in eight subcohorts in Denmark, Finland, Italy (two), Norway, Sweden and the United Kingdom (two) /were described/. Exposure to styrene was reconstructed from job and production records, environmental measurements and, in Italy, biological monitoring. An exposure database was constructed on the basis of about 16,500 personal air samples and 18,695 measurements of styrene metabolites in urine. Styrene exposure levels decreased considerably during the study period. The data from Denmark were considered to be representative of all six countries. They showed exposures of about 200 ppm (852 mg/cu m) in the 1950s, about 100 ppm (426 mg/cu m) in the late 1960s and about 20 ppm (85 mg/cu m) in the late 1980s. The 40,688 workers accumulated 539,479 person years at risk and were followed for an average of 13 years. Workers lost to follow-up and those who emigrated constituted 3.0% of the total cohort, and in no individual cohort did the proportion exceed 8.0%; 60% of the cohort had less than two years' exposure and 9% had more than 10 years' exposure. The WHO mortality data bank was used to compute national mortality reference rates by sex, age (in five year groups) and calendar year. No excess was observed for mortality from all cases (2,196 deaths; standard mortality ratio, 96; 95% confidence interval, 92-100) or from all neoplasms (550 deaths; standard mortality ratio, 91; 83-98). The mortality rate in exposed workers for neoplasms of the lymphatic and hematopoietic tissues was not elevated (50 deaths; standard mortality ratio, 96; 95% confidence interval, 71-127) and was not associated with length of exposure. Evaluation of risk by job type also showed no significant pattern. In an analysis by country, one of the cohorts in the United Kingdom and that from Denmark had moderate increases in mortality from lymphatic and hematopoietic cancer. An increased risk for those cancers was observed in Poisson regression models for years since first exposure (p = 0.012) and for average exposure (p= 0.019) but not for cumulative exposure. Within the models there was an increasing trend in risk for lymphatic and hematopoietic cancer with average intensity of exposure culminating in an RR of 3.6 (95% confidence interval, 1.0-13) for the highest category, > 200 ppm; for more than 20 years since first employment, the RR was 4.0 (95% confidence interval, 1.3-12). Although there were no increased risks for cancers of the pancreas, kidney or esophagus, nonsignificant increase in risk at these sites were seen with time since first exposure or cumulative exposure to styrene.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 256 (1994)] **PEER REVIEWED**

/SURVEILLANCE/ 5,021 workers who had been employed in two reinforced-plastic boat-building facilities in the USA for at least one day between 1959 and 1978. On the basis of industrial hygiene surveys, 2,060 individuals were classified as having had high exposure to styrene, with means in the two facilities of 42.5 ppm and 71.7 ppm (181 and 305 mg/cu m). Of these, 48% had worked for 1 month to 1 yr and only 7% for more than 5 yr. There were 47 deaths in the high-exposure group (41.5 expected); no case of lymphatic or hematopoietic cancer was observed (approx 1 expected).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 254-5 (1994)] **PEER REVIEWED**

/SURVEILLANCE/ Central and peripheral nervous system effects have been observed in styrene-exposed workers. Nerve conduction velocities were decreased, and electroencephalographic, dopaminergic, functional and psychiatric impairments have been noted. Most effects have been seen at concentrations of about 100 ppm (433 mg/cu m) styrene, although memory and neurobehavioral disturbances were seen at 10-30 ppm (43-30 mg/cu m)and above. Other studies have shown no evidence of neurotoxicity. The hearing threshold was unchanged in workers exposed to less than 150 mg/cu m (35 ppm). In a mortality study of styrene exposed workers, an increased number of deaths attributed to symptoms, senility and ill-defined conditions was ascribed to a high local registration of these conditions in comparison with national statistics.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 276 (1994)] **PEER REVIEWED**

/SURVEILLANCE/ Mortality data have been updated for a further 12 yr for a cohort of workers in the reinforced plastics and composites industry with exposures to styrene monomer and other chemicals. The cohort consisted of 15,826 male and female

employees who were exposed to styrene for at least 6 months between 1948-1977 at 30 participating manufacturing plants in the United States. A total of 1628 deaths were reported during the extended observation period, 1948-89. Mortality from several causes showed significant increases namely, all causes, all cancers, esophageal cancer, lung cancer, cancer of the cervix, uteri, cancer of other female genital organs, hypertensive heart disease, certain non-malignant respiratory diseases, motor vehicle accidents, and homicides. When, however, mortality data were examined in terms of duration of employment, durations of styrene exposure, and cumulative styrene exposure no upward trend was detected in any of these causes of death. Most of the increases in mortality were among workers who were employed for only 6 months to a yr or who had very low cumulative exposure (<10 ppm/yr). Therefore, the increased mortality was not likely to be related to exposure to styrene. Several explanations for the increased mortality are offered, including low socioeconomic class, smoking, and lifestyle factors characteristic of short term workers. There was no increased mortality from lymphatic and hematopoietic cancers overall or from any specific hematological malignancies. In particular, no incr in mortality from non-Hodgkins lymphoma, Hodgkin's disease, multiple myeloma, or leukemia was found. Furthermore, detailed exposure response analyses did not show any relation between exposure to styrene and any of these hematological malignancies. The lack of an exposure response relation further supports the conclusion that workers in the reinforced plastics industry in this study did not experience an increased risk of lymphatic and hematopoietic cancers as a result of their exposure to styrene.
[Wong O et al; Occup Environ Med 51 (6): 386-96 (1994)] **PEER REVIEWED** PubMed Abstract Full text: PMC1127994

/SURVEILLANCE/ The effects of occupational exposures and environmental conditions on the distribution of conduction velocities (DCV) in the median nerve were studied. The cohort consisted of 10 chain saw operators, 24 workers using other vibrating tools, two lead smelter employees, 20 gun metal factory workers exposed to lead, zinc, and copper, one thallium poisoning victim, 11 painters exposed to mixed solvents, 11 persons exposed to styrene in a reinforced fiber plastic boat factory, 23 patients treated for alcoholism, and 10 patients with diabetes. The comparisons consisted of 129 healthy nonexposed persons approx matched to each group in the cohort. The DCV of the right median nerve at the second digit was measured by computerized two channel electromyography. The DCV was expressed as the proportion of active nerve fibers having conduction velocities below 10, 20, 30, 40, 50, 60, 70, 80, and 90% of the total distribution (V10, V20, V30, V40, V50, V60, V70, V80, and V90, respectively). The conventional sensory conduction velocity (SCV) of the forearm segment of the median nerve was also measured. The V10 through V90 conductance velocities and the SCV were significantly decreased in the chain saw operators. Only the V60 to V90 velocities were significantly decreased in the other vibrating tool operators. The V80 and V90 velocities were significantly decreased in the lead smelter workers. The V10 velocity was significantly decreased in the gun metal factory employees having lead and zinc exposures. The V70 to V90 velocities were significantly slowed in the thallium poisoning patient. The V60 to V90 velocities and the SCV were significantly slowed in the painters. The V80 velocity and the SCV were significantly decreased in the styrene exposed workers. The V40 to V90 velocities and the SCV were significantly decreased in the alcoholism patients. The V30 to V90 velocities were significantly decreased in the diabetics. The /results indicate/ that conduction velocities of the faster fibers of large myelinated nerve fibers are more sensitive to various occupational exposures to neurotoxic agents and environmental conditions than those of slower fibers.
[Araki S et al; Environ Res 62 (2): 325-32 (1993)] **PEER REVIEWED** PubMed Abstract

/BIOMONITORING/ Finnish studies on occupational workers /exposed to styrene/ demonstrated impairment of visuomotor accuracy and hand movements, which began at urine mandelic acid levels of 700 ug/L and became prominent at 1200 ug/L. Verbal learning skills were significantly impaired in workers with elevated urinary mandelic acid and phenylglyoxylic levels that corresponded to styrene airborne concn exceeding 25 ppm. Logical memory and visuoconstructive abilities were affected at urinary metabolite levels correlating to 50 ppm daily styrene exposures when these workers were compared with controls.
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988., p. 957] **PEER REVIEWED**

/BIOMONITORING/ (32)P-post-labeling was used to analyze for the presence of DNA adducts in 47 workers exposed to styrene in a boat manufacturing facility. Individual airborne exposures measured several times over the course of 1 year ranged from 1 to 235 mg/cu m with a mean value of 65.6 mg/cu m. Two adducts were detected in the DNA of mononuclear cells of these workers. The following levels of adducts were detected: adduct 1, range 0.6-102 x 10(-8) (mean 15.8 x 10(-8); adduct 2, range 0.1-70.9 x 10(-8) mean 14.2 x 10(-8). Significant linear relationships were found between styrene exposure and both DNA adducts (adduct 2, r = 0.330, P = 0.012; adduct 1, r = 0.244, P = 0.049). Co-chromatography experiments identified DNA adduct 1 in the exposed samples as N2-(2-hydroxy-1-phenylethyl-2-deoxyguanosine-3,5 -bisphosphate. DNA adduct 2 remains unidentified. No significant linear relationships were observed between the level of DNA adducts and sister chromatid exchanges, possibly because of the poor precision of the (32)P-post-labeling assay (the estimated coefficients of variation for adducts 1 and 2 were 2.54 and 1.96, respectively). The results demonstrate that occupational exposure to styrene results in the formation of DNA adducts in human mononuclear cells.
[Horvath E et al Carcinogenesis 15 (7): 1309-15 (1994)] **PEER REVIEWED**

/BIOMONITORING/ Monitoring occupational exposure to styrene was achieved through quantification of adducts of styrene 7,8-oxide to N-terminal valine in hemoglobin (Hb) on the basis of the enrichment of adducted globin chains by ion-exchange chromatography and gas chromatographic-mass spectrometric U analysis by the use of the N-alkyl Edman method. Application to blood samples from reinforced plastics workers exposed to styrene and from referents showed Hb adduct levels correlating with the blood styrene glycol and urinary mandelic acid concns. The blood styrene glycol and styrene 7,8-oxide levels of the exposed workers averaged 2.5 umol/L (17 subjects) and 0.09 umol/L (7 subjects), respectively. The blood styrene glycol and urinary mandelic acid content (mean 9.5 nmol/L, 17 subjects) suggested a styrene concn of about 300 mg/cu m, (75 ppm) in the workplace air. The Hb adduct levels were low (mean 28 pmol g/L), indicating rapid detoxification of styrene 7,8-oxide in humans.
[Christakopoulos A et al; Scan J Work Environ Health 19 (4): 255-63 (1993)] **PEER REVIEWED**

/BIOMONITORING/ Mandelic acid (MA) is an important metabolite of styrene. In humans, measurement of its concentration in urine provides an important assessment of the overall level of styrene exposure in workers of the reinforced plastic

manufacturing industry. The aim of /this/ study was to investigate in these workers the relationship between MA concentration and styrene exposure time and intensity as well as its dependence on work occupation. The concentration of MA in the urine samples of 35 employees was analyzed with HPLC (high performance liquid chromatography). Out of 35 workers, 11 performed laminating, 11 milling and finalizing, 6 laying-up and spraying-up, and 7 worked in background support. Urinal samples were obtained twice a day over the course of three weeks, at the beginning and the end of the work shift. /Investigators/ found a significant increase in MA concentrations during a work shift in all tested days (Wilcoxon test $p < 0.05$). Employees working in elevated atmospheric concentrations of styrene (93.77-159.88 mg/cu m) had significantly higher MA concentrations in urine compared to other groups at both the beginning and the end of the shift (Kruskal Wallis test $p < 0.001$) ($p < 0.001$). Only samples from laminating workers exceeded the biological limit of MA concentration (640 mg/L) at the end of the shift. Normalisation of MA concentration to body mass index (BMI, normal range: 21.7 +/- 3.2 kg/m2) refined differences within groups (Kruskal-Wallis analysis $p < 0.001$). The accumulation of MA at the end of the work shift for measured time period was not significant for the measured time period (Friedman analysis $p > 0.11$). /These/ results confirmed that MA is a sensitive metabolic marker of styrene exposure without cumulative effect. However, normalization of MA concentrations to BMI can improve the accuracy of styrene exposure estimates in certain groups of employees.
[Polakova M et al; Cent Eur J Public Health 20 (3): 226-32 (2012)] **PEER REVIEWED** PubMed Abstract

/BIOMONITORING/ The aim of this work was to investigate urinary analytes and hemoglobin and albumin adducts as biomarkers of exposure to airborne styrene (Sty) and styrene-(7,8)-oxide (StyOX) and to evaluate the influence of smoking habit and genetic polymorphism of metabolic enzymes GSTM1 and GSTT1 on these biomarkers. /Investigators/ obtained three or four air and urine samples from each exposed worker (eight reinforced plastics workers and 13 varnish workers), one air and urine samples from 22 control workers (automobile mechanics) and one blood sample from all subjects. Median levels of exposure to Sty and StyOX, respectively, were 18.2 mg/cu m and 133 ug/cu m for reinforced plastics workers, 3.4 mg/cu m and 12 ug/cu m for varnish workers, and <0.3 ug/cu m and <5 ug/cu m for controls. Urinary levels of styrene, mandelic acid, phenylglyoxylic acid, phenylglycine (PHG), 4-vinylphenol (VP) and mercapturic acids (M1+M2), as well as cysteinyl adducts of serum albumin (but not those of haemoglobin) were significantly associated with exposure status (controls<exposed workers). Also, levels of VP and M1+M2 were significantly affected by smoking, and levels of M1+M2 were significantly affected by GSTM1 polymorphisms. Multiple linear regression analyses of the subject-specific (logged) metabolite levels across exposed workers showed that Sty was a significant predictor for all urinary analytes while StyOX was a significant predictor of PHG only. Interestingly, the log scale regression coefficients for Sty in these models were significantly less than one for all metabolites except M1+M2. This suggests that the natural scale relationships between levels of all Sty metabolites, except M1+M2, displayed downward concavity with increasing Sty exposure, suggestive of saturable metabolism. Levels of the protein adducts were not associated with exposure to either Sty or StyOX among exposed subjects.
[Fustinoni S et al; Biomarkers 13 (6): 560-78 (2008)] **PEER REVIEWED** PubMed Abstract

/BIOMONITORING/ The aim of the work is to define occupational exposure to styrene in fiberglass manufacture; the phase of stretching styrene resins needs some manual handling and leads workers to be exposed to styrene. /The authors/ surveyed 20 workers in two companies manufacturing fiberglass, checking environmental levels and urinary concentrations of mandelic acid (MA), and phenylglyoxylic acid (PGA). Workers completed a questionnaire collecting their medical history. Environmental monitoring showed some styrene concentrations higher than the threshold limit value-time-weighted average. Biological monitoring confirmed these findings and four workers had levels of urinary PGA and MA concentrations higher than the Biological Exposure Indices of the American Conference of Governmental Industrial Hygienists. ...
[Papaleo B et al; J Occup Environ Med 53 (11): 1273-8 (2011)] **PEER REVIEWED** PubMed Abstract

/BIOMONITORING/ Many natural substances and drugs have long been known to cause goiter or thyroid dysfunction. More recently, several environmental pollutants, such as pesticides and industrial compounds, have been investigated for their thyroid-disrupting activity and related adverse effects on human health. The aim of this study was to evaluate the effects of styrene on the thyroid axis in occupationally exposed workers. Thirty-eight exposed (E) and 123 nonexposed (NE) male workers (controls) were assessed. Serum concentrations of thyrotropin (TSH; basal and after thyrotropin-releasing hormone [TRH] administration.), free thyroxine (FT(4)), free triiodothyronine (FT(3)), anti-thyroglobulin, thyroid peroxidase antibody, and calcitonin were measured. Thyroid ultrasound examination was also performed. In E workers, urinary creatinine, mandelic acid (MA), and phenylglyoxylic acid (PGA) were also measured. No significant differences between E and NE workers were demonstrated, as far as thyroid volume, nodularity, serum thyroid antibodies, and calcitonin were analyzed. However, in the E group a positive correlation between duration of exposure and thyroid volume was detected. After exclusion of subjects with nodular or autoimmune thyroid diseases, serum concentrations of FT(4), FT(3), and TSH did not differ between the two groups. In E workers there was a positive correlation between the urinary concentrations of styrene metabolites (MA plus PGA) and FT(4) or FT(4)/FT(3) ratio ($p < 0.05$; $r = 0.45$ and $p < 0.005$; $r = 0.61$, respectively), while no correlation was observed between urinary concentrations of MA plus PGA and serum TSH (either basal and stimulated). /The authors concluded that/ chronic exposure to styrene is not associated with an increase in nodular or autoimmune thyroid diseases. However, styrene could interfere with peripheral metabolism of thyroid hormones by inhibiting T(4) to T(3) conversion. Whether this is a direct effect on iodothyronine deiodinases or a consequence of a general distress, such as in nonthyroidal illnesses, remains to be established. Further studies in a larger population of exposed workers are needed to confirm these preliminary observations.
[Santini F et al; Thyroid 18 (10): 1065-9 (2008)] **PEER REVIEWED** PubMed Abstract

/BIOMONITORING/ Urine samples from humans occupationally exposed to styrene, with mandelic acid levels ranging from 400 to 1145 mg/g creatinine and from 68 to 400mg/g creatinine for high and low exposure group, respectively, were analyzed for N3 adenine DNA adducts, namely, 3-(2-hydroxy-1-phenylethyl)adenine (N3 alpha A) and 3-(2-hydroxy-2-phenylethyl)adenine (N3 beta A). A sensitive LC-ESI-MSMS method was developed with the limit of quantification of 1 pg/mL for both analytes. Peaks corresponding to N3 alpha A and/or N3 beta A were found in seven of nine end-of-shift samples of the high exposure group and in six of 19 end-of-shift samples of the low exposure group. Concentration of N3 alpha A+N3 beta A amounted to 2.8+/-1.6 pg/mL (mean+/-S.D.; n=9) and 1.8+/-1.3 pg/mL (mean+/-S.D.; n=19) in the high and low exposure group,

respectively. Of other 10 samples taken the next morning after exposure, two contained low but quantifiable concentrations of N3 alpha A and none contained N3 beta A. However, interfering peaks were detected also in some control urine samples. Out of 22 controls, six and two samples contained peaks co-eluting with N3 alpha A and N3 beta A, respectively. Therefore, the method used was found insufficiently specific to be applicable for biological monitoring. Comparing the excretion of N3 alpha A+N3 beta A to that reported previously in mice it can be estimated that at the same absorbed dose, humans excreted not more than 1/30 of the amount of adenine adducts excreted by mice. As a consequence, the damage to DNA caused by styrene 7,8-oxide (SO), a reactive metabolite of styrene, appears to be much lower in humans than in mice.
[Mikes P et al; Toxicol Lett 197 (3): 183-7 (2010)] **PEER REVIEWED** PubMed Abstract

/BIOMONITORING/ The CYP2E1 has been identified as the main cytochrome P450 isoform involved in human styrene metabolism. CYP2E1 presents polymorphism in humans and the different genotypes may, at least partly, be related to the different levels of individual expression of enzyme activity. /Investigators/ studied whether the genetic polymorphisms and phenotype of CYP2E1 modulate the level of urinary styrene metabolites and if they can be used for assessing risks of occupational exposure to styrene. A population of 49 male workers exposed to styrene (average level 362.7mg/cu m) and a control group were selected. Samples of urine, blood and buccal swab were taken to determine the urinary biological indicators (phenylglyoxylic acid and mandelic acid), to quantify mRNA of CYP2E1 in blood using RT-PCR and to analyze different polymorphisms of enzyme CYP2E1 from buccal swab. /Investigators/ found decreased expression of mRNA of the enzyme, as well as decreased excretion of the styrene metabolites in individuals carrying the CYP2E1*5B heterozygote allele (cl/c2) with respect to the wild-type homozygote (c1/c1), which indicates a reduction in the inducibility of the enzyme in the presence of this polymorphism. The results show that the combined effect of both the CYP2E1 phenotype, measured by the expression of the specific mRNA in blood samples, and the CYP2E1*5B allele genotype, may explain the variability of urinary excretion of the styrene metabolites.
[Prieto-Castello MJ et al; Toxicol Lett 192 (1): 34-9 (2010)] **PEER REVIEWED** PubMed Abstract

/ENDOCRINE MODULATION/ In this study /the authors/ examined estrogenic activity of styrene oligomers after metabolic activation by rat liver microsomes. Trans-1,2-diphenylcyclobutane (TCB), cis-1,2-diphenylcyclobutane (CCB), 1,3-diphenylpropane, 2,4-diphenyl-1-butene, 2,4,6-triphenyl-1-hexene, and 1-alpha-phenyl-4ss-(1 -phenylethyl)tetralin were negative in the yeast estrogen screening assay and estrogen reporter assay using estrogen-responsive human breast cancer cell line MCF-7. However, TCB exhibited estrogenic activity after incubation with liver microsomes of phenobarbital-treated rats in the presence of reduced nicotinamide adenine dinucleotide phosphate (NADPH). Minor activity was observed when liver microsomes of untreated or 3-methylcholanthrene-treated rats were used instead of those from phenobarbital-treated rats. CCB, 1,3-diphenylpropane, and 2,4-diphenyl-1-butene also exhibited estrogenic activity after metabolic activation by liver microsomes, but the activity was lower than that of TCB. 2,4,6-Triphenyl-1-hexene and 1-alpha-phenyl-4ss-(1 -phenylethyl)tetralin did not show estrogenic activity after such incubation. When TCB was incubated with liver microsomes of phenobarbital-treated rats in the presence of NADPH, three metabolites were detected by high-performance liquid chromatography (HPLC). One metabolite isolated by HPLC exhibited a significant estrogenic activity. The active metabolite was identified as trans-1-(4-hydroxyphenyl)-2-phenylcyclobutane by mass and nuclear magnetic resonance spectral analysis. These results suggest that the estrogenic activity of TCB was caused by the formation of the 4-hydroxylated metabolite.
[Kitamura S et al; Environ Health Perspect 111 (3): 329-34 (2003)] **PEER REVIEWED** PubMed Abstract Full text: PMC1241390

/ENDOCRINE MODULATION/ Recently, several substances from among the huge numbers of chemicals used by mankind have been implicated as instigators of disrupted endocrine function and related human health problems. Polystyrene (PS) is one of the most frequently used resins in the world, and the styrene oligomer dissolved out from PS has been designated as a potential trigger of estrogen-like activity in the Wingspread Declaration and the Japan Environment Agency's SPEED98 [JEA (Japan Environment Agency) Strategic Problem on Environmental Endocrine Disruptors 98.... In order to assess the endocrine disrupting effect of styrene oligomers, /investigators/ tested one styrene monomer (SM), three styrene dimers (SDs) and seven styrene trimers (STs), newly isolated from optical isomers, known to dissolve in small amounts from cup noodle containers made of polystyrene by the estrogen receptor binding assay, luciferase reporter gene assay, and human breast cancer cell MCF-7 proliferation assay. In all three tests, none of the SM, SDs and STs showed any significant activity. Accordingly, the authors concluded that these substances have no estrogenic activity.
[Ohno K et al; Food Chem Toxicol 39 (12): 1233-41 (2001)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ The present study aimed to evaluate the effects of styrene exposure at levels below the recommended standards of the Threshold Limit Value (TLV-TWA(8)) of 20 ppm (ACGIH, 2004) in reinforced-fiberglass plastics workers. Study subjects comprised 50 exposed workers and 40 control subjects. The exposed workers were stratified by styrene exposure levels, i.e. group I (<10 ppm, <42.20 mg/cu m), group II (10-20 ppm, 42.20-84.40 mg/cu m), and group III (>20 ppm, >84.40 mg/cu m). The mean styrene exposure levels of exposed workers were significantly higher than those of the control workers. Biomarkers of exposure to styrene, including blood styrene and the urinary metabolites, mandelic acid (MA) and phenylglyoxylic acid (PGA), were significantly increased with increasing levels of styrene exposure, but were not detected in the control group. DNA damage, such as DNA strand breaks, 8-hydroxydeoxyguanosine (8-OHdG), and DNA repair capacity, were used as biomarkers of early biological effects. DNA strand breaks and 8-OHdG/10(5)dG levels in peripheral leukocytes of exposed groups were significantly higher compared to the control group ($P<0.05$). In addition, DNA repair capacity, determined by the cytogenetic challenge assay, was lower in all exposed groups when compared to the control group ($P<0.05$). The expression of CYP2E1, which is involved in styrene metabolism, in all styrene exposed groups, was higher than that of the control group at a statistically significant level ($P<0.05$). Levels of expression of the DNA repair genes hOGG1 and XRCC1 were significantly higher in all exposed groups than in the control group ($P<0.05$). In addition to styrene contamination in ambient air, a trace amount of benzene was also found but, the correlation between benzene exposure and DNA damage or DNA repair capacity was not statistically significant. The results obtained from this study indicate an increase in genotoxic effects and thus health risk from occupational styrene exposure, even at levels below the recommended TLV-TWA(8) of 20 ppm.
[Wongvijitsuk S et al; Int J Hyg Environ Health. 214(2):127-37 (2011).] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ The present study comprised a biomonitoring study in 95 workers occupationally exposed to styrene and 98 unexposed controls, employing an integrated approach involving biomarkers of exposure, effect, and susceptibility. Airborne styrene was evaluated at workplace, and urinary styrene metabolites, mandelic acid (MA), phenylglyoxylic acid (PGA), vinylphenols (VPTs) and phenylhydroxyethylmercapturic acids (PHEMAs), were measured as biomarkers of internal dose. Cytogenetic alterations were evaluated by analysing the frequency of chromosomal aberrations (CAs) and micronucleated binucleated cells (MNBN) in peripheral blood lymphocytes. The micronucleus assay was coupled with centromeric fluorescence in situ hybridization to distinguish micronuclei (MN) arising from chromosomal breakage (C- MN) from those harboring whole chromosomes (C+ MN). The possible influence of genetic polymorphisms of xenobiotic-metabolizing enzymes involved in styrene biotransformation (EPHX1, GSTT1, GSTM1, GSTP1) and NAT2 on the cytogenetic endpoints was investigated. The exposed workers showed a significantly higher frequency of MNBN (13.8 +/- 0.5% versus 9.2 +/- 0.4%; P<0.001) compared to control subjects. The effect appeared to concern both C- and C+ MN. A positive correlation was seen between the frequency of C+ MN and urinary level of MA+PGA (P<0.05) and VPTs (P<0.001). Chromosome-type CAs positively correlated with airborne styrene level and VPTs (P<0.05), whereas chromatid-type CAs correlated with PHEMAs (P<0.05). Workers bearing GSTM1 null genotype showed lowered levels of PHEMAs (P<0.001). The GSTT1 null genotype was associated with increased MNBN frequencies in the exposed workers (P<0.05) and the fast activity EPHX genotype with a moderate decrease in both MNBN and CAs in the controls. Our results suggest that occupational exposure to styrene has genotoxic effects that are potentiated by the GSTT1 gene deletion. These observations may have relevance considering the risk of lymphatic and hematopoietic malignancies tentatively associated with styrene exposure.
[Migliore L et al; Pharmacogenet Genomics 16 (2): 87-99 (2006)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ 10 Men aged 20-41 yr and exposed occupationally to styrene showed incr in rate of chromosomal aberrations in cultured lymphocytes from peripheral blood (11-26% compared with 3% or less among 5 non-exposed controls). In addn to an increase in chromosomal type breaks, decondensation of chromatin and incr numbers of micronuclei and nuclear bridges were also observed.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 244 (1979)] **PEER REVIEWED**

/GENOTOXICITY/ A longitudinal investigation of styrene exposure was conducted among 48 workers employed at a reinforced plastic boat manufacturing facility. 8-hr time-weighted average (TWA) exposures to styrene and concentrations of styrene in the breath were determined for each individual on 7 randomly chosen days during 1 year. Peripheral blood lymphocytes from each subject were analyzed for sister chromatid exchanges (SCEs) 2 times and micronuclei (MN) 4 times during this period. Individual mean SCEs ranged from 4.7 to 9.5 SCEs per cell with a population mean of 6.4 +/- 0.2 SCEs per cell. SCEs were found to be significantly increased with an overall observed increase of 11.7% related to increasing exposure to styrene (mean air concentration 64.2 mg/cu m +/- 71.5; range 0.88-235 mg/cu m) and with cigarette smoking. Examination of the relative contribution of each variable to regression of SCEs showed that smoking contributed about 62% and styrene exposure contributed about 25% of the total variability. Intra-individual lymphocyte MN frequencies did not vary significantly over time nor was a gradient toward increased MN observed with styrene exposure. However, significant inter-individual differences in MN frequencies were observed. Females had significantly higher MN frequencies than did males; MN were also increased with age. This study ... illustrates the ability to separately quantify the relative contribution of each of two variables--smoking and styrene exposure--to an increase in SCEs in lymphocytes of an exposed human population.
[Yager JW et al; Mutat Res 319 (3): 155-65 (1993)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ /Researchers/ studied the relationship between DNA damage, DNA repair rates and messenger RNA (mRNA) expression levels of cell cycle genes TP53, p21(CDKN1A), BCL2 and BAX in a group of 71 styrene-exposed workers and 51 control individuals. The exposure was assessed by measuring the concentration of styrene at workplace and in blood. Parameters of DNA damage [measured as single-strand breaks (SSBs) and endonuclease III-sensitive sites], gamma-irradiation-specific DNA repair rates and mRNA levels of studied genes were analyzed in peripheral blood lymphocytes. The workers were divided into low (<50 mg/cu m) and high (>50 mg/cu m) styrene exposure groups. /Researchers/ found negative correlations between mRNA expression of TP53, BCL2, BAX and styrene exposure (P < 0.001 for all parameters). In contrast, p21(CDKN1A) mRNA expression significantly increased with increasing styrene exposure (P = 0.001). SSBs and endonuclease III-sensitive sites increased with increasing mRNA levels of TP53 (P < 0.001 for both) and BCL2 (P = 0.038, P = 0.002, respectively), whereas the same parameters decreased with increasing mRNA levels of p21(CDKN1A) (P < 0.001, P = 0.007, respectively). gamma-Irradiation-specific DNA repair rates increased with p21(CDKN1A) mRNA levels up to the low exposure level (P = 0.044). Our study suggests a possible relationship between styrene exposure, DNA damage and transcript levels of key cell cycle genes.
[Hanova M et al; Carcinogenesis 32 (1): 4-9 (2011)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ Occupational exposure to styrene was studied in 34 workers employed in the production of fiberglass-reinforced plastic sheets and compared to 29 unexposed healthy controls. /Investigators/ evaluated genotoxic effects induced by occupational styrene exposure in lymphocytes by alkaline version of the comet assay to detect single-strand breaks (SSBs), DNA oxidation products (formamido pyrimidine glycosilase (Fpg)- and endonuclease (Endo III)-sensitive sites) and DNA repair kinetics studies, as well as the neutral version of comet assay for DNA double-strand breaks (DSBs). An innovative aspect of this study was the use of immuno-comet assay, a new technique that recognizes DSBs with specific antibody by DAPI/FITC method. The battery of parameters included markers of external and internal exposure. Exposed workers showed significant high levels of SSBs (p<0.0001) and DSBs (p<0.0001) in neutral- and immuno-comet assay. A drastic decrease in DNA repair activity as compared to controls was observed (180 min vs. 35 min). Styrene workplace concentration significantly correlated with alkaline comet parameters (TM, p=0.013; TI, p=0.008), in negative with TL (p=0.022), and with DNA-base oxidation (TM Endo III, p=0.048 and TI Endo III, p=0.028). There was a significant negative correlation between urinary metabolites (MA+PGA) and TM Endo III (p=0.032) and TI Endo III (p=0.017).

[Fracasso ME et al; Toxicol Lett 185 (1): 9-15 (2009)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ Styrene is a commercially important chemical widely used in the manufacture of synthetic rubber, resins, polyesters and plastics. The highest levels of human exposure to styrene occur during the production of reinforced plastic products. The objective of this work was to evaluate both DNA and cytogenetic damage in styrene-exposed workers, analyzing only non-smoker individuals. Environmental levels of styrene and urinary concentrations of mandelic and phenylglyoxylic acids were determined, and genetic damage was studied by means of micronucleus (MN) test, sister chromatid exchanges (SCEs) and comet assay. Fifty-two fiberglass-reinforced plastics workers and 54 controls took part in the study. The mean air concentration of styrene in the breathing zone of workers exceeded the threshold limit value, and 24 workers exceeded the biological exposure index. A strong and significant correlation was found between styrene environmental concentrations and urinary metabolites. Higher SCE rate (P<0.01) was observed in exposed workers than in controls. Besides, significant correlations were obtained for SCE rate with both environmental and internal exposure parameters (r=0.496, P<0.01 and r=0.511, P<0.01, respectively). Results from MN test and comet assay showed slight and non-significant increases related to the exposure. /These/ data seem to support previous studies reporting genotoxicity associated with occupational exposure to styrene, excluding the confounding influence of smoking, although caution must be taken in the interpretation of these results since the significance of an increase in SCE rate is still unclear.
[Teixeira JP et al; Mutagenesis 25 (6): 617-21 (2010)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ Decreased levels of single-strand breaks in DNA (SSBs), reflecting DNA damage, have previously been observed with increased styrene exposure in contrast to a dose-dependent increase in the base-excision repair capacity. To clarify further the above aspects, /researchers/ have investigated the associations between SSBs, micronuclei, DNA repair capacity and mRNA expression in XRCC1, hOGG1 and XPC genes on 71 styrene-exposed and 51 control individuals. Styrene concentrations at workplace and in blood characterized occupational exposure. The workers were divided into low (below 50 mg/cu m) and high (above 50 mg/cu m)) styrene exposure groups. DNA damage and DNA repair capacity were analyzed in peripheral blood lymphocytes by Comet assay. The mRNA expression levels were determined by qPCR. A significant negative correlation was observed between SSBs and styrene concentration at workplace (R=-0.38, p=0.001); SSBs were also significantly higher in men (p=0.001). The capacity to repair irradiation-induced DNA damage was the highest in the low exposure group (1.34+/-1.00 SSB/10+9 Da), followed by high exposure group (0.72+/-0.81 SSB/10+9 Da) and controls (0.65+/-0.82 SSB/10+9 Da). The mRNA expression levels of XRCC1, hOGG1 and XPC negatively correlated with styrene concentrations in blood and at workplace (p<0.001) and positively with SSBs (p<0.001). Micronuclei were not affected by styrene exposure, but were higher in older persons and in women (p<0.001). In this study, /researchers/ did not confirm previous findings on an increased DNA repair response to styrene-induced genotoxicity. However, negative correlations of SSBs and mRNA expression levels of XRCC1, hOGG1 and XPC with styrene exposure warrant further highly-targeted study.
[Hanova M et al; Toxicol Appl Pharmacol 248 (3): 194-200 (2010)] **PEER REVIEWED** PubMed Abstract

/ALTERNATIVE and IN VITRO TESTS/ Styrene is a volatile organic compound that is widely used as an intermediate in many industrial settings. There are known adverse health effects at environmentally significant concentrations, but little is known about the molecular effect of exposure to styrene at sub-acute toxic concentrations. /Investigators/ exposed human lung epithelial cells, at a wide range of concentrations (1 mg/cu m-10 g/cu m), to styrene and analyzed the effects on the proteome level by 2-DE, where 1380 proteins spots were detected and 266 were identified unambiguously by MS. A set of 16 protein spots were found to be significantly altered due to exposure to styrene at environmentally significant concentrations of 1-10 mg/cu m (0.2-2.3 ppm). Among these, superoxide dismutase as well as biliverdin reductase A could be correlated with the molecular pathway of oxidative stress, while eukaryotic translation initiation factor 5A-1, ezrin, lamin B2 and voltage-dependent anion channel 2 have been reported to be involved in apoptosis. Treatment with styrene also caused the formation of styrene oxide-protein adducts, specifically for thioredoxin reductase 1. These results underline the relevance of oxidative stress as a primary molecular response mechanism of lung epithelial cells to styrene exposure at indoor-relevant concentrations.
[Morbt N et al; Proteomics 9 (21): 4920-33 (2009)] **PEER REVIEWED** PubMed Abstract Full text: PMC3463241

/OTHER TOXICITY INFORMATION/ Associations between occupational styrene exposure and cognitive as well as psychomotor functions were investigated with a view to answering three questions: (1) are the published results for neurobehavioral impairment reproducible, (2) if such effects exist, are they related to current or to chronic exposure and (3) if effects exist, are there reductions in the effects during an exposure-free period. Workers from a boat-building plant, some of whom were laminators, were investigated in groups of low (n = 83, mean mandelic acid MA + phenylglyoxylic acid PGA = 53 mg/g creatinine), medium (n = 101, 230 mg/g creat.) and high (n = 29, 928 mg/g creat.) levels of exposure to styrene. The mean job tenure was about 6 years. In addition, subgroups chronically exposed to low-short (n = 30, lifetime weighted average exposure mean 184 mg/g creat. for 6 years) and high-long (n = 16, 693 mg/g creat., 15 years) styrene levels were analyzed. The examinations were carried out during normal working days and during the company holidays. A symptom questionnaire and the tests Benton visual retention, symbol digit substitution and digit span for cognitive functions as well as choice reaction, aiming, peg board, tapping, and steadiness for psychomotor functions were administered. Co-variance analyzes with repeated measurements and linear regressions were used for statistical analysis. Co-factors were education, age, job tenure, long-term alcohol consumption, and German as mother tongue. In some cases also the activity as a laminator was considered. Symptoms were not related to exposure. The tests for cognitive functions generally revealed (all variance analyses) no exposure-related associations. Only the linear regressions of Benton test results showed significant correlation with parameters of chronic exposure which was still evident as a tendency in the work-free and exposure-free period. Most tests for psychomotor functions also revealed no relationships with exposure. However, the peg board test results showed significant correlations with chronic exposure which disappeared during holidays. The activity as a laminator--considered in addition to exposure parameters--was significant as a factor to explain the variability of psychomotor variables. /The authors concluded that/ acute exposures to up to 40 ppm styrene and long-term exposures to about 27 ppm averaged over a period of 15 years were not identified as being associated with an elevated risk of developing impaired cognitive and psychomotor functions or

increased symptom levels with the tests applied. This statement must be qualified by two exceptions: performances in the Benton test and in a finger dexterity test were associated with parameters of long-term exposure as a dose-response relationship, but not with current exposure.
[Seeber A et al; Int Arch Occup Environ Health 82 (8): 969-84 (2009)] **PEER REVIEWED** PubMed Abstract

/OTHER TOXICITY INFORMATION/ Products having high irritancy to the human eye are formed when styrene is photo-oxidized with ozone and nitrogen dioxide as in formation of smog. Also, a potent lacrimator has been formed when styrene wastes became mixed with bromine or chlorine wastes and reacted under the influence of sunlight.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 854] **PEER REVIEWED**

Skin, Eye and Respiratory Irritations:
Acute exposure to high concn of styrene may produce irritation of the mucous membranes of the upper respiratory tract, nose and mouth.
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.71 (1981)] **PEER REVIEWED**

HAZARD WARNING: Primary irritant to mucosal surfaces at vapor concn above 200 ppm, but pungent odor usually gives adequate warning.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-152] **PEER REVIEWED**

Irritating to skin ...
[Commission of the European Communities. Legislation on Dangerous Substances - Classification and Labelling in the European Communities. Vol. II. London and Trotman Ltd., 1989., p. 224] **PEER REVIEWED**

Exposure to concn of styrene above 200 ppm causes irritation of the eyes and upper respiratory tract.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

At high concns (higher than 100 ppm), styrene is a respiratory and mucous membrane irritant. Skin contact may result in the development of primary irritant dermatitis.
[Young, L.Y., M.A. Koda-Kimble (eds.). Applied Therapeutics. The Clinical Use of Drugs. 6th ed. Vancouver, WA., Applied Therapeutics, Inc. 1995., p. 594] **PEER REVIEWED**

The principal acute hazards from worker exposure to styrene /is/ ... irritation of the skin, eyes, and upper respiratory tract.
[NIOSH; Criteria Document: Styrene p.15 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

Medical Surveillance:
Initial Medical Screening: Employees should be screened for history of certain medical conditions which might place the employee at increased risk from styrene exposure. /These are/ central nervous system disorders ... chronic respiratory disease ... skin disease ... kidney disease ... /and/ liver disease.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 1] **PEER REVIEWED**

Expectant mothers and women with ovulation and menstrual disorders should /be protected from working conditions/ exposing them to /styrene & ethylbenzene/ compounds.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983., p. 2115] **PEER REVIEWED**

Urinary mandelic acid excretion indicates exposure.
[Dart, R.C. (ed). Medical Toxicology. Third Edition, Lippincott Williams & Wilkins. Philadelphia, PA. 2004., p. 1330] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning ... /cytogenetic and/or other/ tests that might become useful or mandatory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 23] **PEER REVIEWED**

The results of this study suggest that exposure to styrene below the current Swedish permissible exposure limit of 20 ppm induces neurotoxic effects expressed as an increased number of neuropsychiatric symptoms. Twenty men exposed to styrene at a plastics factory participated. The reference group included 20 non-exposed men matched for age, working schedule and physical work load. Exposure to styrene during one workday was assessed by personal air monitoring and biological monitoring. To evaluate the physical work load the pulse (heart) rate was measured. One week before the study each man completed a neuropsychiatric symptom questionnaire containing 16 items. Also 17 questions regarding acute symptoms of local irritation and symptoms of the central nervous system were presented after the psychometric tests were performed. The tests were simple reaction time, color, word vigilance and symbol digit. A follow up with regard to the symptoms among the exposed men was done after their summer vacation about two to five weeks after their last exposure. The mean eight hour time weighted average (TWA) concentration of styrene in air measured by passive dosimetry was 8.6 ppm (range 0.04-50.4 ppm). The exposed men had significantly more symptoms than the referents although there were no significant differences for the psychometric tests. At the follow up the exposed men reported fewer symptoms. This study indicates that symptoms are earlier indicators of adverse effects than complex tests and underlines the importance of regular follow up of people exposed to styrene. ...

[Edling C et al; Br J Indust Med 50 (9): 843-50 (1993)] **PEER REVIEWED**

Urinary styrene excretion in workers occupationally exposed to styrene was studied ln 214 persons, 100 women and 114 men, mean age 28.1 years, employed at ten Italian fiberglass reinforced plastics factories. Breathing zone samples were collected and analyzed for styrene. Half and full shift urine samples were collected and analyzed for styrene and its metabolites mandelic acid and phenylglyoxylic acid. Blood samples were collected and analyzed for styrene. Preliminary separate analysis of male and female workers revealed no differences between the two groups. Eight hour time weighted average styrene exposures ranged from 23 to 7397 uMol/cu m, mean 843.8 uMol/cu m. The mean styrene exposure was about 33% of the ACGIH standard, 2044.931 uMol/cu m. The geometric mean urine styrene concentrations measured after the morning and afternoon half shifts were 480.58 and 605.38 nanomoles/l, respectively. The mean urinary mandelic acid concentration measured after the afternoon half shift was 9.73 moles/l. The mean urinary PGA concentration measured after the afternoon shift was 13.031 mol/l. Mean urinary excretion of styrene was significantly correlated with breathing zone styrene concentrations, correlation coefficient 0.88 and with mandelic acid and PGA excretion, correlation coefficients 0.82 and 0.78, respectively. Urinary styrene excretion and blood styrene concentrations were well correlated, correlation coefficient 0.86. ... Urinary styrene excretion is a good marker for monitoring exposure to styrene.
[Gobba F et al; Scand J Work Environ Health 19 (3): 175-82 (1993)] **PEER REVIEWED** PubMed Abstract

Biological monitoring of styrene exposure among workers in the reinforced plastics industry is widely implemented in the region of Emilia Romagna, Italy. More than 18,000 urine samples measurements of the main metabolites of styrene, mandelic acid and phenylglyoxylic acid were retrieved for the period 1978-1990, and 4689 values of mandelic acid in postshift urine samples were analyzed for various variables thought to influence styrene exposure. The job performed was found to be the most important predictor of styrene exposure. Hand laminators had the highest exposure (mean mandelic acid 682 mg/g creatinine); spray laminators showed lower values (404 mg/g) while levels in semiautomatic process operators (243 mg/g) were only slightly higher than in nonprocess workers (186 mg/g). The use of ventilation resulted in lower exposure, but differences in average values were not particularly wide. Exposure decreased weakly during the study period in all work categories but the percentage of measurements exceeding the current biological limit value (900 mg/g creatinine, 1300 mg/l corrected for density) is still very high (20% of measurements among hand laminators in 1990). These results /suggest/ that the control measures implemented are only partially effective for the prevention of styrene exposure.
[Galassi C et al; Int Arch Occup Environ Health 65 (2): 89-95 (1993)] **PEER REVIEWED** PubMed Abstract

Blood & urine styrene & urine mandelic acid & phenylglycoxylic acid concns as markers of occupational styrene exposure were examined. Breathing zone samples were collected during a shift during the middle of the work week from 39 males, 21 to 56 yr old employed at a fiber reinforced boat manufacturing factory in Singapore & were analyzed for styrene. End of shift exhaled breath samples were collected, blood & urine samples were collected at the end of the shift, & urine samples were collected the next morning. The breathing zone & breath styrene concns ranged from 0.2-32.3 & 0.1-2.3 ppm respectively. The geometric mean styrene concns were 10.36 & 0.50 ppm respectively. The end of shift blood & urine styrene concns ranged from O-1.4 mg/l & 8-83.2 ug/l respectively. The corresponding geometric mean styrene concns were 0.19 mg/l & 26.3 ug/l. The end of shift & morning after urine mandelic acid concns varied from 12-544 & 1-69 mg/g creatinine respectively. The corresponding geometric mean concns were 109.84 & 4.6 mg/g. The end of shift & morning after urine phenylglycoxylic acid concns ranged from 5-248 & 0.5-150 mg/l creatinine respectively. The geometric mean concns were 77.49 & 29.57 mg/l respectively. End of shift breath & blood styrene concns were well correlated with the breathing zone styrene concns. End of shift styrene concns were poorly correlated with breathing zone styrene concns. The breathing zone styrene concns were well correlated with the end of shift urine mandelic acid, phenylglycoxylic acid plus phenylglycoxylic acid concns. When the morning after urine concns were used the correlations became weaker. ...
[Ong CN et al; Amer J Indust Med 25 (5): 719-30 (1994)] **PEER REVIEWED**

The assessment of styrene exposure can be accomplished through measurement of styrene. It has been recommended that venous blood samples be collected in vacutainers containing EDTA as anticoagulant, and that the vacutainers be filled completely to avoid loss of styrene into the vapor phase above the blood. In addition, contact of the sample with rubber and plastic materials must be prevented, due to absorption of styrene. Whole Blood Reference Ranges: Normal - none detected; Exposed - BEI (sampling time is end of shift, measured as styrene in venous blood), 0.55 mg/l. BEI (sampling time is prior to next shift, measured as styrene in venous blood), 0.02 mg/l.; Toxic - Not established.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1089] **PEER REVIEWED**

Serum or Plasma Reference Ranges: Normal - None detected; Exposed - Not established; Toxic - Not established.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1089] **PEER REVIEWED**

Renal Function Tests /include/ ... Urine Albumin ... Urinary Beta-2-Microglobulin and/or Retinal Binding Protein (RBP) ... Urinary Alpha and Pi Isoenzymes of Glutathione S-Transferase ... Urinary Enzyme N-Acetylglucosaminidase ... /and/ Routine Urinalysis.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1090] **PEER REVIEWED**

Respiratory Symptom Questionnaires: Questionnaires published by the American Thoracic Society (ATS) and the British Medical Research Council have proven useful for identifying people with chronic bronchitis. Certain pulmonary function tests such as the FEV1 have been found to be better predictors of chronic airflow obstruction.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1091] **PEER REVIEWED**

Chest Radiography: Chest radiographs are widely used to assess pulmonary diesase. They are useful for detecting early lung

early lung cancer in asymptomatic people, and especially for detecting of peripheral tumors such as adenocarcinomas. However, even though OSHA mandates this test for exposure to some toxicants such as asbestos, experts' views on the risk-to-benefit ratio in detection of pulmonary disease conflict, so routine annual chest x-rays are not recommended for all people.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1091] **PEER REVIEWED**

Pulmonary Function Tests: The tests that have been found to be practical for population monitoring include: Spirometry and expiratory flow-volume curves; Determination of lung volumes; Diffusing capacity for carbon monoxide; Single-breath nitrogen washout; Inhalation challenge tests; Serial measurements of peak expiratory flow; Exercise testing.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1092] **PEER REVIEWED**

The assessment of styrene exposure can be accomplished through measurement of the metabolites, mandelic acid or phenylglyoxylic acid. ... In addition, assessment of exposure has been reported by measuring unchanged styrene in urine. Measurement of styrene in urine was found to be a reliable indicator of styrene exposure if the exposure was recent. Measurement of mandelic acid is the most widely used and documented test, followed by measurement of phenylglyoxylic acid. Both tests are useful for assessing styrene exposure; however, phenylglyoxylic acid does not appear to be as stable as mandelic acid, and has been shown to be prone to decomp when stored at room temperature. Stability of the urine sample prior to analysis can be increased by refrigeration of the sample. Urine Reference Ranges: Normal - None detected; Exposed - BEI (sampling time is end of shift, measured as the metabolite, mandelic acid), 800 mg/g creatinine. BEI (sampling time is prior to next shift, measured as the metabolite, mandelic acid), 300 mg/g creatinine. BEI (sampling time is end of shift, measured as the metabolite, phenylglyoxylic acid), 240 mg/g creatinine. BEI (sampling time is prior to next shift, measured as the metabolite, phenylglyoxylic acid), 100 mg/g creatinine. BAT (sampling time is end of exposure or end of shift, measured as the metabolite, mandelic acid), 400 mg/L. BAT (sampling time is end of exposure or end of shift, measured as the metabolites, mandelic acid plus phenylglyoxylic acid), 600 mg/L. Urinary levels of styrene ranging from 0.7 to 4.1 ug/L were found in workers exposed to air concns of 16-61 mg/cu m (4-14 ppm).; Toxic - Central nervous depression induced by styrene has been correlated with urinary mandelic acid levels of 800 mg/L, and measurable decrements in psychomotor performance have been associated with mandelic acid concns >1200 mg/L.
[Ryan, R.P., C.E. Terry, S.S. Leffingwell (eds.) Toxicology Desk Reference 5th ed. Volumes 1-2. Taylor & Francis Philadelphia, PA. 2000, p. 1090] **PEER REVIEWED**

Populations at Special Risk:
In general, fair-skinned individuals appear to be less resistant than dark-skinned persons to the defatting and dehydrating action of styrene.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994., p. 1356] **PEER REVIEWED**

... Effects on the liver (eg, increased serum bile acid and enhanced activity of plasma enzymes) and reproductive system (eg, decreased frequency of births and increased frequency of spontaneous abortions in female workers) have been reported.
[USEPA; Health Assessment Document: Styrene (Draft) p.3-23 (1985)] **PEER REVIEWED**

Probable Routes of Human Exposure:
NIOSH (NOES Survey 1981-1983) has statistically estimated that 333,212 workers (86,902 of these are female) are potentially exposed to styrene in the US(1). Occupational exposure to styrene may occur through inhalation and dermal contact with this compound at workplaces where styrene is produced or used(SRC). Occupational exposure to styrene can be classified according to the types of operations in which it is present(2). In polystyrene manufacture, occupational chemical exposure is mainly styrene(2). The styrene concns found in polystyrene production are generally <21 mg/cu m (5 ppm); through occasional value of 210 mg/cu m (50 ppm) or more have been reported(2). In reinforced plastics applications, where styrene is a solvent-reactant for copolymerization, styrene is also the major air contaminant(2). Concentrations of styrene found during the production of reinforced plastics were generally much higher than those found in the polystyrene production plants, with peak concns as high as 6,300 mg/cu m (1,500 ppm)(2). The full-shift time-weighted avg (TWA) styrene exposures associated with styrene monomer and copolymer production are generally less than 10 ppm(3). Avg styrene exposures in reinforced plastics/composites plants can range from 40-100 ppm, with individual TWA and short-term exposures as high as 150-300 ppm and 1000-1500 ppm, respectively(3). Workers manufacturing boats and yachts, truck parts, tubs and showers and tanks and pipes that use reinforced plastics may be substantially exposed to styrene(4,5). Workers using certain polyester resins may be exposed to styrene(6,7), and the measured TWA ranged from 3.93-45.96 ppb(7). In the Finnish reinforced plastic industry, workers might be exposed to up to 3 g styrene per day(8). In non-production departments of pulp, paper, and paper product mills, the occupational exposure to styrene was 9.9 ppm for maintenance, construction and cleaning workers(9).
[(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available from, as of Mar 12, 2014: http://www.cdc.gov/noes/ (2) WHO; Environ Health Criteria 26 (Styrene). Geneva, Switzerland: WHO (1983) (3) Santodonato J et al; Monograph on Human Exposure to Chemicals in the Workplace: Styrene p 3-1 to 3-12 Bethesda, MD: National Cancer Institute NO1-CP-26002-03 (1985) (4) LeMasters GE et al; Am Ind Hyg Assoc J 46: 434-41 (1985) (5) Anderson KE; Diss Abstr Int B 47: 979 (1986) (6) Malek RF et al; Am Ind Hyg Asoc J 47: 524-29 (1986) (7) Bartolucci GB et al; Appl Ind Hyg 1: 125-31 (1986) (8) Hemminki K, Vianio H; Human exposure to potentially carcinogenic compounds. IARC Sci Pub1 59: 37-45 (1984) (9) Teschke K et al; Am Ind Hyg Assoc J 60: 73-83 (1999)] **PEER REVIEWED**

In Norway between 1972-1996, the average concentration of styrene in air during boat production, small items production, car body production, and other occupational environments were about 60, 40, 50 and 15 ppm, respectively(1)
[(1) Lenvik K et al; Appl Occup Environ Hygiene 14: 165-70 (1999)] **PEER REVIEWED**

Monitoring data indicate that the general population may be exposed to styrene via ingestion of food which has been packaged in polystyrene, by ingestion of contaminated finished drinking water, by inhalation of air contaminated by industrial sources, auto exhaust, or incineration emission, and by inhalation of smoke from cigarettes(1). Exposure to styrene may occur during the use of miscellaneous products containing styrene such as floor waxes and polishes, paints, adhesives, putty, metal cleaners, autobody fillers, and varnishes(2). Concn of styrene was 26-71 ppb in the indoor air of high-rise apartments(3).
[(1) IARC; IARC; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 60: 248-9 (1994) (2) NIOSH; Criteria Document: Styrene. DHEW Pub. NIOSH 83-119 p.18 (1983) (3) Tanaka T, Kogai 19: 121-28 (1984)] **PEER REVIEWED**

... Exposure to styrene may occur during the use of miscellaneous products containing styrene such as floor waxes and polishes, paints, adhesives, putty, metal cleaners, autobody fillers, and varnishes.
[NIOSH; Criteria Document: Stryene p.18 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

At fabrication facilities, workers may be exposed to unreacted monomer or monomer as a thermal degradation product.
[Hoff A et al; Scand J Work Environ Health 8 (Suppl 2): 1-60 (1982) as cited in NTP; Executive Summary: Styrene (Draft) p.6 (1985)] **PEER REVIEWED**

Body Burden:
Styrene was one of 110 chemicals monitored in blood and urine samples of 321 firefighters that responded to the Sept 11, 2001 World Trade Center collapse and 47 firefighters that were used as a control group(1). Styrene was determined to not be statistically different for these groups(1). Styrene was detected at a mean concentration of 0.06 ng/L in the blood of 43 children (3-6 year olds) living in the Phillips neighborhood of Minneapolis, MN; samples were collected Jan 2000 to Apr 2002(2). As part of the School Health Initiative: Environment, Learning, Disease study, 134 children (6-10 years old) from the Minneapolis, MN area donated blood samples for styrene analysis; 89.6% of 103 samples, 92.3% of 108 samples, 56.8% of 54 samples and 98.9% of 88 samples collected Feb 2000, May 2000, Feb 2001 and May 2001, respectively, contained measurable amounts of styrene(3).
[(1) Edelman P et al; Environ Health Perspect 111: 1906-11 (2003) (2) Sexton K et al; Environ Health Perspect 114: 453-9 (2005) (3) Sexton K et al; Environ Health Perspect 113: 342-9 (2005)] **PEER REVIEWED**

Personal air concentrations of styrene for 46 students from Philip Randolph Academy in Harlem, New York City were 1.01 and 1.68 ug/cu m in the winter and summer, respectively(1).
[(1) Kinney PL et al; Environ Health Perspect 110: 539-46 (2002)] **PEER REVIEWED**

A study done in 2000 on the exposure of school children in the inner city of Minneapolis, MN to volatile organic compounds found the following atmospheric values for styrene(1):

Sample Location/Type	% Detections winter	% Detections Summer	Median Concn (ug/cu m)
Outdoor	0	0	0.0
School	31.3	39.7	0.1
Home	91.9	91.9	0.8
Personal	93.5	85.2	0.5

[(1) Adgate JL et al; Environ Health Perspect 112: 1386-92 (2004)] **PEER REVIEWED**

Styrene was detected, but not quantified in 8 of 8 human breast milk samples from USA women in 4 cities(1). Six of 250 patients with suspected volatile organics exposure-related symptoms showed significantly elevated levels of styrene in blood(2). Concentration of styrene ranged from none detected to 1.9 ppb with a mean value of 0.6 ppb(2). A National Human Adipose Tissue Survey (NHATS) by EPA during the fiscal year 1982 detected styrene in wet adipose tissue with a frequency of 100% at a concentration range 8-350 ppb(3). Styrene, determined in the blood of 108 normal subjects from Italy was identified in 102 blood samples, with a mean concentration of 217 ng/L(4). Blood concentrations of styrene in a reference group of a nonoccupationally exposed US population averaged 0.074 ppb (number of samples = 657)(5). Urinary styrene was determined in 48 subjects, all blood donors living in urban areas, with a mean of 262 ng/L(4). Styrene has been identified in exhaled breath at mean concentrations of 0.7-1.6 ug/cu m(6).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-28 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanely JS; Broad Scan Analysis of Human Adipose Tissue Vol 1. Executive Summary. Washington, DC: USEPA-560/5-86-035 p. 22 (1986) (4) Brugnone F et al; Med Lav 85: 370-89 (1994) (5) Ashley DL et al; Clin Chem 40: 1401-4 (1994) (6) WHO; Environ Health Criteria 26 (Styrene). Geneva, Switzerland: WHO (1983)] **PEER REVIEWED**

The concentrations of styrene in the blood of service station attendants, street vendors, and office workers in Mexico City (in 1996) were 0.031 ug/L (range, 0.022-0.045 ug/L), 0.041 ug/L (range, 0.025-0.18 ug/L), and 0.025 ug/L (range, 0.022-0.049 ug/L), respectively, at the beginning of their shifts(1); post shift concentrations of styrene in blood were 0.027 ug/L (range, 0.020-0.093 ug/L), 0.031 ug/L (range, 0.022-0.073 ug/L), and 0.024 ug/L (range, 0.022-0.027 ug/L), respectively(1). The concentration of styrene in the urine and blood of reinforced plastics workers in Italy was 546.62 nmol/L (mean) and 5.65 nmol/L, respectively(2).
[(1) Romieu I et al; Environ Health Perspect 107: 511-5 (1999) (2) Gobba F et al; Scand J Work Environ Health 19: 175-82 (1993)] **PEER REVIEWED**

Blood Concentrations: Three volunteers exposed to styrene at an air concentration of approximately 50 ppm for 1 hour developed blood styrene concentrations of 0.2-0.7 mg/L; exposure to approximately 100 ppm for 8 hours produced maximal blood concentrations of 0.9-1.4 mg/L.
[Stewart RD et al; Arch Environ Health 16: 656-62 (1968) as cited in Baselt RC; Biological Monitoring Methods for Industrial Chemicals p. 238 (1980)] **PEER REVIEWED**

Blood styrene was measured by a gas chromatography-mass spectrometry method in 81 normal people and in 76 workers exposed to styrene. In the normal subjects, styrene was also tested in alveolar and environmental air. Styrene was found in nearly all (95%) blood samples. Average styrene levels in the normal subjects were 221 ng/L in blood, 3 ng/L in alveolar air, and 6 ng in environmental air. Styrene levels did not differ significantly between smokers and nonsmokers, 95% of the values being below 512 ng/L in blood, 7 ng/L in alveolar air, and 15 ng/L ln environmental air. In workers with an average exposure to styrene of 204 ug/L at the end of the workshift, mean blood styrene concentration was 1211 ug/L. In blood samples collected at the end of the Thursday shift styrene levels were significantly higher (1590 ug/L) than those found at the end of the Monday shift (1068 ug/L). A similar difference was found in samples taken the morning after exposure (60 and 119 micrograms/L respectively). Significant correlations between blood and environmental styrene were found both at the end of the shift and the morning after exposure (r = 0.61 and 0.41 respectively). In workers occupationally exposed to styrene 16 hr after the end of the workshift blood styrene (94 ug/L) was significantly higher than that found in the normal subjects (0.22 ug/L). The half life of blood styrene was 3.9 hr.
[Brugnone F et al; Int Arch Occup Environ Health 65 (2): 125-30 (1993)] **PEER REVIEWED** PubMed Abstract

A longitudinal study of 11 workers (aged 24-54 years) in the polyester resin boat industry in Germany assessed nerve conduction velocities in 1980 and 1983. Exposure was occupational and route was by inhalation with mean air levels of 114 ppm, 97 ppm, 92 ppm over 3-7 years (mean = 4 yrs). The peripheral nervous system showed no significant difference in conduction velocities between exposed and controls for ulnar and median nerves. Mean blood levels were 0.92 mg/L in 1980 and 0.70 mg/L in 1983; mean levels of mandelic acid in urine ranged from 816 to 1660 mg/g creatinine; mean levels of phenylglyoxylic acid in urine ranged from 200-342 mg/g creatinine.
[Triebig G et al; Int Arch Occup Envir Health 5 (6): 239-47 (1985)] **PEER REVIEWED**

Average Daily Intake:
Worst-case exposure estimates for styrene of 0-0.5 ug/day from drinking water, 30 ug/day from food, and 65 mg/day from air were calculated by EPA(1); these estimates are based on the highest levels estimated or monitored and, therefore, reflect the highest potential exposure rather than typical exposure for the general population(1). The following nominal daily respiratory intakes of styrene have been estimated(1): worker in reinforced plastics industry, 2 g; worker in styrene polymerization, 100 mg; living within 1 km of a production unit, 600 ug; breathing polluted urban air, 400 ug; breathing typical urban air, 6 ug; breathing indoor air, 6-1000 ug; drinking polluted water, 2 ug; cigarette smoke (20 cigarettes per day), 400-960 ug(2). In a Boston Exposure Assessment in Microenvironments, time weighted average intake of styrene from air for 55 people living and working in the Boston area averaged 0.64 ug/cu m(3).
[(1) USEPA; Drinking water criteria document for styrene. Final draft. Cincinnati, OH: US EPA, Office of Health and Environmental Assessment. ECAO-CIN-409 (1988) (2) IARC; Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 60: 248 (1994) (3) Dodson RE et al; Environ Sci Technol 41: 8498-505 (2007)] **PEER REVIEWED**

The estimated daily intake of styrene by Canadians from various media were reported. Units for all values are ug/kg body weight/day. For the two categories 12-19 yrs and 20-70 yrs, cigarette smoking daily intakes were reported as 3.51 and 2.86 ug/kg body weight/day, respectively(1).

Estimated intake (ug/kg bw per day)

Population	Ambient Air	Indoor Air	Drinking Water	Food
0-6 months	0.004-0.11	0.07	0.005-0.03	<0.58
7 months-4 yrs	0.006-0.15	0.09	0.003-0.02	<0.53
5-11 yrs	0.007-0.17	0.10	0.002-0.008	<0.30
12-19 yrs	0.006-0.14	0.09	0.001-0.006	<0.15
20-70 yrs	0.005-0.13	0.08	0.001-0.005	<0.11

[(1) Newhook R, Caldwell I; Butadiene and Styrene: Assessment of Health Hazards (Publ 127). Lyon, France: IARC, pp. 27-33 (1993)] **PEER REVIEWED**

Human exposure to styrene was calculated in the general German population based on exposure concentration in food and air(1).

Intake via:	Time frame	ug/person	ug/kg
Food	Daily	0.2-1.2	0.003-0.017
Food	Annually	80-450	1.1-6.5
Inhalation	Daily	18-54	0.3-0.8

Inhalation	Annually	6600-19,700	94.3-281

[(1) Tang W et al; Toxicology 144: 39-50 (2000)] **PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

EMT Copyright Disclaimer:

The following Overview, *** STYRENE ***, is relevant for this HSDB record chemical.

Life Support:

o This overview assumes that basic life support measures have been instituted.

Clinical Effects:

0.2.1 SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

A) WITH POISONING/EXPOSURE

1) Styrene may be irritating to the eyes, skin, and mucous membranes. It can be ototoxic, nephrotoxic and hepatotoxic, and is a CNS depressant. Signs and symptoms of exposure may include nausea, fatigue, headache, loss of coordination, muscle weakness, a feeling of drunkenness, dizziness, and unconsciousness.

2) "Styrene sickness" with nausea, vomiting, and a sensation of drunkenness occurs with inhalation exposure.

3) Liver damage may occur with substantial chronic exposure (over 5 years).

4) Peripheral neuropathy and pulmonary edema may occur. Prolonged or repeated exposure may lead to defatting dermatitis. Fetotoxicity has been observed in experimental animals and genotoxicity has been observed in vitro.

5) ACUTE: Central nervous system depression can occur in serious acute exposures. Following chronic exposure, styrene can disrupt amino acid transport across the blood-brain barrier. Effects of styrene on the nervous system include CNS depression and peripheral neuropathy.

6) Irritation of the respiratory tract and occupational asthma may occur following acute exposure. Pulmonary edema has been reported in animals. Ongoing exposure to styrene can result in irritation or even obstructive lung disease.

0.2.3 VITAL SIGNS

0.2.3.1 ACUTE EXPOSURE

A) WITH POISONING/EXPOSURE

1) FEVER: Following the accidental contamination of a drinking-water tank in two buildings, 46 of 93 residents exposed to high styrene concentrations (up to 905 mcg/L) experienced symptoms. Three (4%) residents experienced fever (Arnedo-Pena et al, 2003).

0.2.20 REPRODUCTIVE HAZARDS

A) There are several studies suggestive of potential reproductive effects in humans. Styrene has also been extensively studied for possible reproductive effects in experimental animals.

0.2.21 CARCINOGENICITY

0.2.21.1 IARC CATEGORY

A) IARC Carcinogenicity Ratings for CAS100-42-5 (International Agency for Research on Cancer (IARC), 2016; International Agency for Research on Cancer, 2015; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010a; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2008; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2007; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2006; IARC, 2004):

1) IARC Classification

a) Listed as: Styrene

b) Carcinogen Rating: 2B

1) The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans. This category is used for agents, mixtures and exposure circumstances for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in humans but there is sufficient evidence of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is inadequate evidence of carcinogenicity in humans but limited evidence of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

0.2.21.2 HUMAN OVERVIEW

A) Styrene is generally considered as metabolically toxic due to its metabolic conversion to styrene epoxide (Lewis, 1998).

0.2.21.3 ANIMAL OVERVIEW

A) Negative results were reported for rat carcinogenesis studies.

Laboratory:

A) Patients with acute exposure should have baseline liver and renal function tests, urinalysis, complete blood count, and amylase and lipase levels. Monitor arterial blood gases and chest x-ray if significant respiratory tract irritation occurs.

Treatment Overview:

0.4.2 ORAL EXPOSURE

A) AVOID INDUCED EMESIS. Gastric lavage is of questionable safety, and should be done only with caution.

B) DILUTION: If no respiratory compromise is present, administer milk or water as soon as possible after ingestion. Dilution may only be helpful if performed in the first seconds to minutes after ingestion. The ideal amount is unknown; no more than 8 ounces (240 mL) in adults and 4 ounces (120 mL) in children is recommended to minimize the risk of vomiting.

C) ACTIVATED CHARCOAL: Administer charcoal as a slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.

0.4.3 INHALATION EXPOSURE

A) INHALATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer oxygen and assist ventilation as required. Treat bronchospasm with an inhaled beta2-adrenergic agonist. Consider systemic corticosteroids in patients with significant bronchospasm.

B) Administer 100% humidified supplemental oxygen with assisted ventilation as required. Central nervous system depression may make airway management including endotracheal intubation mandatory.

C) ACUTE LUNG INJURY: Maintain ventilation and oxygenation and evaluate with frequent arterial blood gases and/or pulse oximetry monitoring. Early use of PEEP and mechanical ventilation may be needed.

0.4.4 EYE EXPOSURE

A) DECONTAMINATION: Remove contact lenses and irrigate exposed eyes with copious amounts of room temperature 0.9% saline or water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, the patient should be seen in a healthcare facility.

B) A thorough ophthalmic examination should be done if visual symptoms are present.

0.4.5 DERMAL EXPOSURE

A) OVERVIEW

1) DECONTAMINATION: Remove contaminated clothing and jewelry and place them in plastic bags. Wash exposed areas with soap and water for 10 to 15 minutes with gentle sponging to avoid skin breakdown. A physician may need to examine the area if irritation or pain persists (Burgess et al, 1999).

Range of Toxicity:

A) Styrene airborne concentrations of 10,000 parts per million are dangerous to life within 20 to 30 minutes. Concentrations of 2500 ppm are dangerous to life within 8 hours.

[Rumack BH POISINDEX(R) Information System Micromedex, Inc., Englewood, CO, 2017; CCIS Volume 172, edition expires May, 2017. Hall AH & Rumack BH (Eds): TOMES(R) Information System Micromedex, Inc., Englewood, CO, 2017; CCIS Volume 172, edition expires May, 2017.] **PEER REVIEWED**

Antidote and Emergency Treatment:

Immediate first aid: Ensure that adequate decontamination has been carried out. If patient is not breathing, start artificial respiration, preferably with a demand-valve resuscitator, bag-valve-mask device, or pocket mask, as trained. Perform CPR as necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep patient quiet and maintain normal body temperature. Obtain medical attention. /Aromatic hydrocarbons and related compounds/

[Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 209] **PEER REVIEWED**

Basic treatment: Establish a patent airway (oropharyngeal or nasopharyngeal airway, if needed). Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . Anticipate seizures and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with 0.9% saline (NS) during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 mL/kg up to 200 mL of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Aromatic hydrocarbons and related compounds/
[Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 209-10] **PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious, has severe pulmonary edema, or is in severe respiratory distress. Consider drug therapy for pulmonary edema ... . Positive-pressure ventilation techniques with a bag valve mask device may be beneficial. Consider drug therapy for pulmonary edema ... . Consider administering a beta agonist such as albuterol for severe bronchospasm ... . Monitor cardiac rhythm and treat arrhythmias if necessary ... Start IV administration of D5W /SRP: "To keep open", minimal flow rate/. Use 0.9% saline (NS) or lactated Ringer's (LR) if signs of hypovolemia are present. For hypotension with signs of hypovolemia, administer fluid cautiously. Watch for signs of fluid overload ... .Treat seizures with diazepam or lorazepam ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Aromatic hydrocarbons and related compounds/
[Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 210] **PEER REVIEWED**

Animal Toxicity Studies:

Evidence for Carcinogenicity:
Evaluation: There is inadequate evidence in humans for the carcinogenicity of styrene. There is limited evidence in experimental animals for the carcinogenicity of styrene. In making the overall evaluation, the Working Group took into consideration the following supporting evidence: Styrene is metabolized to styrene-7,8-oxide, which binds covalently to DNA and shows activity in various in vitro and in vivo assays for genetic effects. The genetic and related effects of styrene are therefore associated with its oxidation, which also occurs, eg, in human whole blood cultures, where styrene induces dose related reponses of chromosomal damage at low concentrations. Styrene-7,8-oxide is detected in blood of workers exposed to styrene. Adducts in hemoglobin and DNA, DNA single strand breaks/alkali labile sites, as well as significant increases in the frequency of chromosomal damage have been found in workers exposed to styrene in the reinforced plastics industry. Positive results are associated with higher overall styrene levels and negative results with decreasing exposures to styrene. Although in human studies the role of other contaminants cannot be excluded, their occurrence is variable and their concentrations are very low in comparison with that of styrene. Overall evaluation: Styrene is possibly carcinogenic to humans (Group 2B).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. 60 297 (1994)] **PEER REVIEWED**

A4; Not classifiable as a human carcinogen. /Styrene, monomer/
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 53] **PEER REVIEWED**

Confirmed carcinogen
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Non-Human Toxicity Excerpts:
/LABORATORY ANIMALS: Acute Exposure/ Administration of a single high dose of styrene (878 mg/kg, ip in corn oil) to young male rats produced significant elevations in the activities of serum transaminase: 230, 209, and 71% increases in the activity of serum glutamic-oxaloacetic transaminase (SGOT) and 163, 437, and 227% of serum glutamic-pyruvic transaminase (SGPT) at 2, 6, and 24 hr, respectively. These results demonstrated that styrene could produce acute hepatic injury in young rats. Urinary nonprotein sulfhydryl contents and mandelic acid, phenylglyoxylic acid, and hippuric acid were all increased. /Srp: toxicity due to unreacted styrene/
[Chakrabarti S, et al; J Toxicol Environ Health (4): 599-607 (1981)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ ... Rats and guinea pigs inhaling concn of styrene ranging from 1,300-10,000 ppm experienced increased eye and nose irritation with increased concns. General weakness and unsteadiness were observed after 12-30 hr of exposure to 1,300 ppm. Exposure to 2,500 ppm resulted in weakness, stupor, lack of coordination, loss of equilibrium, tremors, and unconsciousness after 10-12 hr. All rats and guinea pigs died within 21 and 14 hr, respectively. At 5,000 ppm, there were immediate effects on the CNS and the animals became unconscious within 1 hr. At exposures of 10,000 ppm, all animals died within 3 hr. Between 2 and 4 wk after exposure, the surviving animals were autopsied. The most prominent organ lesions, which were found in the lung, were characterized by congestion, hemorrhage, and edema. There were also some parenchymatous changes in the liver and kidneys.
[NAS/NRC; The Alkyl Benzenes p.323 (1981)] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Styrene is known to be hepatotoxic and pneumotoxic in rodents, and these adverse effects are related to its metabolism. Mice deficient in the enzymes responsible for both the activation and detoxification of styrene are useful in examining this relationship more closely. In the current study, mice deficient in glutathione S-transferase P1P2(-/-) (GST(-/-)) were compared with wild-type mice. Similar changes in serum sorbitol dehydrogenase, as an indicator of hepatotoxicity, and bronchioalveolar levels of protein, cells, and lactate dehydrogenase, as indicators of pneumotoxicity, were observed after styrene administration. Glutathione depletion followed a similar pattern. The administration of the toxic metabolite, styrene oxide, which is a direct substrate for glutathione metabolism, and 4-vinylphenol, which is a minor metabolite but is more potent than either styrene oxide, yielded results similar to those of styrene / dose administered iv, and hepato- and pneumotoxicity measurements were made 24 hours after administration, and GSH measurements were made 3 hours after administration/. The results indicate that either other isoforms of glutathione S-transferase are more important than the P1P2 form in styrene detoxification or that this pathway contributes in only a minor way to styrene detoxification, compared to other pathways.
[Carlson GP; Drug Chem Toxicol 34 (4): 440-4 (2011)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ After placing two drops of liquid styrene in the right eyes of an unspecified number of rabbits, ocular injury was manifested by moderate conjunctival irritation, inflammation, slight swelling of the eyelids, and slight transient corneal injury.
[USEPA; Health Assessment Document: Styrene (Draft) p.3-9 (1985)] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Rats and guinea pigs that inhaled 10,000 ppm styrene became comatose within minutes and died after 30 to 60 minutes of exposure. Animals exposed at 2500 ppm showed weakness and stupor, followed by incoordination, tremor, and coma; death followed within 8 hours. A 50% reduction in respiratory rate occurred in mice that inhaled 160 ppm for 3 minutes; mice that inhaled 250 ppm for two 6-hr periods or 500 ppm for a single 6-hr period developed severe centrilobular hepatic coagilative necrosis. Mice inhaling 125 ppm styrene, 6 hrs/day for 4 days developed incr liver wt.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 2] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Acute exposure of animals to styrene causes irritation of the skin and respiratory tract, and central nervous system effects. Liquid styrene is a skin irritant which, on direct contact, causes erythema. ... Single exposures of rats and guinea pigs to 1300 ppm (5633 mg/cu m) styrene resulted in central nervous system effects, including weakness and unsteadiness. After exposure to 2500 ppm (10.8 g/cu m) styrene for 10 hr, both rats and guinea pigs lost consciousness; exposure to 5,000-10,000 ppm (21.7-43.3 g/cu m) resulted in unconsciousness and death. The principal pathological findings in these animals were severe pulmonary irritation, congestion, oedema, hemorrhage and leukocytic infiltration.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 277 (1994)] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Many solvents have been implicated in central nervous disorders and some of them are known to produce hearing loss, probably mediated by damage to cochlear hair cells. Hearing loss was studied by recording the brainstem auditory evoked response (BAER) in male Long Evans rats exposed 8 hr/day for 5 days to mixtures of styrene, and trichloroethylene. Dose groups included air or solvent pairs (styrene, trichloroethylene) following concns (ppm): (0:3000, (250:2250), (500:1500), (750:750) and (1000:0). Decreased BAER amplitude, indicative of hearing loss, was correlated with blood levels of total solvent. The effects were as predicted by a linear dose-addition model, indicating neither synergistic nor antagonistic interactions at the concns studied.
[Rebert CS et al; Govt Reports Announcements & Index (GRA&I), Issue 22: (1993) NTIS/PB93-229573] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Inhalation toxicity studies were conducted to evaluate mouse strain differences in the susceptibility to styrene vapors. Male and female B6C3Fl, C57BL/6, Swiss, and DBA/2 mice (18 wk old) were exposed to 0, 125, 250 or 500 ppm styrene 6 hr/day for 4 days (20/sex/dose). Histopathological changes and changes in liver weights were evaluated as a measure of hepatotoxicity. Styrene uptake and styrene-7,8-oxide formation were estimated by measuring levels of styrene and styrene-7,8-oxide in blood. An estimate of styrene-7,8-oxide detoxification by conjugation with GSH was obtained by measuring hepatic GSH depletion. In general mortality increased liver weights and hepatocellular necrosis were observed in the 250 and 500 ppm dose groups for all strains and both sexes. Considerable sex and strain differences were observed. Mortality increased liver weights and hepatocellular necrosis were greatest in B6C3Fl and C57BL/6 mice in the 250 ppm dose group and in males; hepatotoxicity was similar in both strains. Swiss mice exhibited dose dependent increases in mortality liver weights and in hepatocellular necrosis with only slight sex differences at early time points. Hepatotoxicity in DBA/2 B6C3Fl and C57BL/6 strains was greater at 250 than 500 ppm; however toxicity was less severe in DBA/2 than in other strains based on absence of mortality In either sex and less extensive liver necrosis at both 250 and 500 ppm. Blood styrene and SO levels did not correlate well with strain differences in toxicity. The relative toxicity (mortality and hepatotoxicity) was B6C3Fl >Swiss >DBA/2; however relative blood styrene and styrene-7,8-oxide levels were B6C3Fl >DBA/2 >Swiss. Hepatic GSH depletion (B6C3Fl\DBA/2 >Swiss) correlated with blood SO levels as expected. These results demonstrate significant biologic variability in the susceptibility of mouse strains to styrene toxicity. These differences are presumably due to strain and sex differences in styrene-7,8-oxide metab; however toxicity did not correlate well with blood styrene-7,8-oxide levels, suggesting that other metabolites may contribute to styrene toxicity in mice.
[Morgan DL et al; Fundam Appl Toxicol 21 (3): 326-33 (1993)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ ... In initial short term styrene inhalation studies, toxicity was significantly greater in male B6C3Fl mice than in females suggesting that males may metabolize styrene more extensively and/or may be less able to detoxify reactive metabolites. In addn a nonlinear dose response was observed where toxicity and mortality were greater in mice exposed to 250 ppm than in those exposed to 500 ppm. These studies were conducted to investigate potential

mechanisms for sex differences and the nonlinear dose-response in styrene toxicity by evaluating the effects of repeated styrene exposure on styrene oxide production, hepatic GSH availability and hepatotoxicity in male and female B6C3F1 mice. Mice (36/sex/dose) were exposed to 0, 125, 250 or 500 ppm styrene 6 hr/day for up to 3 days. Styrene exposure caused increased mortality and hepatotoxicity (centrilobular necrosis) increased serum liver enzymes in males and females after 1 or 2 exposures to 250 and 500 ppm. Hepatic GSH levels were decreased in a dose-dependent manner in males and females. After one exposure, GSH levels in males rebounded above controls in all dose groups. After 3 exposures to 125 or 250 ppm males appeared to maintain GSH levels; GSH was still decreased in the 500 ppm group. GSH levels in females were decreased after each exposure in all dose groups to lower levels than in males and did not rebound above controls. Male mice had significantly greater blood styrene levels than females after one exposure to 500 ppm; however there were no significant sex differences in blood styrene after subsequent exposures. Levels of SO in blood were not significantly greater in male mice than females within a dose group and did not change significantly with repeated styrene exposures for 3 days. Blood styrene and SO levels were significantly higher at 500 ppm than at 250 ppm indicating that styrene uptake and metab are greater at 500 ppm than at 250 ppm. The higher incidence of mortality in male mice and the nonlinear dose response to styrene cannot be explained by gender or dose related differences in hepatotoxicity, GSH depletion or blood styrene or styrene-7,8-oxide levels.
[Morgan DL et al; Fundam Appl Toxicol 21 (3): 317-25 (1993)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ ... /Results of expt designed to show action of benzene and its alkylated derivative/ on skin of rabbits ... /showed/ moderate irritation (moderate erythema) for styrene, with slight necrosis (thin layer of dead tissue being eliminated by exfoliation) when there was repeated contact with pure monomer.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968., p. 159] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Exposure /of animals/ to 5000 ppm ... produces irritation of eyes and nose, followed by central nervous disturbance manifested by tremors, incoordination, loss of equilibrium, and finally unconsciousness.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965., p. 100] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Acute deaths /of animals/ ... are due to injury of CNS and delayed deaths to pneumonia following initial lung irritation; lung shows congestion, hemorrhage, edema and exudation. Kidney and liver also show congestion.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965., p. 101] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Increased serum alanine amino transferase activity and histological examination indicated that styrene in intraperitoneal doses of 2-3 g/kg body weight caused hepatic necrosis in hamsters. The acute lethality was increased by pretreatment with phenobarbital.
[Parkki MG; Scand J Work Environ Health 4 (Suppl 2): 53-9 (1978) as cited in NAS/NRC; The Alkyl Benzenes p.324 (1981)] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ IP administration of styrene in doses of 150 to 1,000 mg/kg body weight to mice, rats, hamsters, and guinea pigs caused a depression of the hepatic nonprotein sulfhydryl content. Mice were the most sensitive, and rats the most resistant.
[Vainio H, Makinen A; Res Commun Chem Pathol Pharmacol 17: 115-24 (1977) as cited in NAS/NRC; The Alkyl Benzenes p.326 (1981)] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Vapors of ... styrene in concn over 2 mg/cu m may cause acute poisoning in laboratory animals, the initial symptoms being irritation of mucous membranes ... are followed by ... /CNS depression/, cramps and death due to respiratory center paralysis. The main pathological findings are edema of the brain and lung, epithelial necrosis of the renal tubules and hepatic dystrophy.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983., p. 2114] **PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ A single exposure of rats to styrene significantly increased the specific binding of (3)H-spiroperidol to striatal membranes at doses of 200 and 400 mg/kg. The repeated admin of the same doses of styrene for 90 days significantly increased the specific binding of (3)H-spiroperidol to striatal membranes 24 hr after the last dose. Styrene exposure had no significant effect on body wt and striatal wt of rats. The increase in binding may be due to alterations in the affinity of receptor sites or increase in the number of dopamine receptors.
[Agrawal AK et al; Bull Environ Contam Toxicol 29 (4): 400-3 (1982)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Styrene in the rabbit eye caused moderate conjunctival irritation and slight, transient corneal injury. Nystagmus was demonstrated in rabbits, and during styrene exposure the directions of the rotatory nystagmus reversed.
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 308] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ The relationship between outer hair cell (OHC) loss and cochlear sensitivity is still unclear, because in many animal models there exist surviving but dysfunctional OHCs and also injured/dead inner hair cells (IHC). Styrene is an ototoxic agent, which targets and destroys OHCs starting from the third row to the second and first rows depending on the exposure level. The remaining cells may be less affected. In this experiment, rats were exposed to styrene by gavage at different doses (200-800 mg/kg/day) for varying periods (5 days/week for 3-12 weeks). An interesting finding was that the cochlear sensitivity was not affected in a few rats with all OHCs in the third row being destroyed by styrene. A further loss of OHCs was usually accompanied with a linear input/output (I/O) function of cochlear compound action potentials (CAP), indicating the loss of cochlear amplification. However, normal CAP amplitudes at the highest stimulation level of 90 dB SPL were often observed when all OHCs were destroyed, indicating normal function of the remaining IHCs. The OHC-loss/hearing-loss relation appeared to be a sigmoid-type function. Initially, styrene-induced OHC

losses (<33%) did not result in a significant threshold shift. Then CAP threshold shift increased dramatically with OHC loss from 33% to 66%. Then, CAP threshold changed less with OHC loss. The data suggest a tri-modal relationship between OHC loss and cochlear amplification. That is, under the condition that all surviving OHCs are ideally functioning, the cochlear amplifier is not affected until 33% of OHCs are absent, then the gain of the amplifier decreases proportionally with the OHC loss, and at last the amplifier may fail completely when more than 67% of OHCs are lost.
[Chen GD et al; Hear Res 243 (1-2): 28-34 (2008)] **PEER REVIEWED** PubMed Abstract Full text: PMC5309704

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Presbycusis, or age-related hearing loss is a growing problem as the general population ages. In this longitudinal study, the influence of noise or styrene exposure on presbycusis was investigated in Brown Norway rats. Animals were exposed at 6 months of age, either to a band noise centered at 8 kHz at a Lex, 8hr = 85 dB (86.2 dB SPL for 6 h), or to 300 ppm of styrene for 6 hr per day, five days per week, for four weeks. Cubic distortion product otoacoustic emissions (2f1-f2 DPOAEs) were used to test the capacity of the auditory receptor over the lifespan of the animals. 2f1-f2DPOAE measurements are easy to implement and efficiently track the age-related deterioration of mid- and high-frequencies. They are good indicators of temporary auditory threshold shift, especially with a level of primaries close to 60 dB SPL. Post-exposure hearing defects are best identified using moderate, rather than high, levels of primaries. Like many aging humans, aging rats lose sensitivity to high-frequencies faster than to medium-frequencies. Although the results obtained with the styrene exposure were not entirely conclusive, histopathological data showed the presbycusis process to be enhanced. Noise-exposed rats exhibit a loss of spiral ganglion cells from 12 months and a 7 dB drop in 2f1-f2DPOAEs at 24 months, indicating that even moderate-intensity noise can accelerate the presbycusis process. Even though the results obtained with the styrene exposure are less conclusive, the histopathological data show an enhancement of the presbycusis process.
[Campo P et al; Hear Res 280 (1-2): 122-32 (2011)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Exposure to styrene causes hearing loss and hair cell death in the middle frequency region in the cochlea. The current study was designed to examine the cell death pathways and the protective effect of L-NAC against styrene-induced cochlear injuries. Seventeen rats were exposed to styrene by gavage at 400 mg/kg 5 days per week for 3 weeks. Nine of the styrene-treated rats received L-NAC by intraperitoneal injection (325 mg/kg), and the remaining eight rats received saline injections as controls. The styrene-induced hearing loss was assessed by auditory brainstem responses (ABRs). Apoptotic, necrotic, and missing hair cells were quantified using combined methods, including nuclear staining with propidium iodide, F-actin staining with FITC-phalloidin, and the TUNEL assay. The styrene exposure caused a threshold shift of 15+/-4.3 dB. Both apoptosis and necrosis were involved in the pathogenesis of the cochlear lesion, but apoptosis appeared to be the major cell death pathway leading to the styrene ototoxicity. Treatment with L-NAC reduced the number of missing and dying outer hair cells (OHCs) and reduced the styrene-induced hearing loss. /The authors concluded that/ styrene exposure causes hair cell death through both apoptotic and necrotic pathways and treatment with N-acetyl-L-cysteine (L-NAC) reduces styrene ototoxicity.
[Yang WP et al; Acta Otolaryngol 129 (10): 1036-43 (2009)] **PEER REVIEWED** PubMed Abstract Full text: PMC4517195

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Styrene exposure is highest among workers in the reinforced plastics industry with exposure seen for 5 consecutive days during the work week. Styrene is both hepatotoxic and pneumotoxic in mice, in addition to causing lung tumors. Human epidemiological studies are inconclusive as to the carcinogenicity of styrene so it is important to understand the mechanism responsible for styrene tumors in mice. Previous studies showed significant decreases in CC10 protein for 5 days following a single dose of the active metabolite R-styrene oxide (R-SO), yet little change in the bax/bcl-2 protein ratio was seen until 10 days following styrene or R-SO administration. Styrene or R-SO was given to CD-1 mice for 5 consecutive days. Mice were euthanized 24 hr, 10 days or 30 days following the last dose, and CC10, bax and bcl-2 mRNA and protein levels were determined in isolated Clara cells. CC10 mRNA levels were decreased at 24 hr for both styrene and R-SO. R-SO decreased CC10 protein levels up to 10 days following the last dose. Increases in the bax/bcl-2 mRNA and protein ratio were seen 24 hr following R-SO administration. Styrene did not significantly increase the bax/bcl-2 mRNA ratio until 10 days after treatment, with the bax/bcl-2 protein ratio increased at both 10 days and 30 days. It is likely that oxidative stress is involved in the toxicity caused by styrene and that minimal apoptosis may be involved. Chronically decreased CC10 levels may lead to increases in oxidative stress in Clara cells, the main target for styrene toxicity in the lung, and may be an early indicator for lung carcinogenesis in mice.
[Harvilchuck JA et al; Toxicology 259 (3): 149-52 (2009)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ When male rats were exposed by inhalation to 1.3 g/cu m (300 ppm) styrene in air for 2-11 wk for 6 hr/day on 5 days/wk, incr in frequency of chromosomal aberrations in bone-marrow cells (8-12% in exposed group, 1-6% in controls) was observed in 9 and 11 wk.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 241 (1979)] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ In rats, aryl hydrocarbon hydroxylase and aniline hydroxylase activities were significantly enhanced at high doses of styrene (450 and 900 mg/kg, orally for 7 consecutive days). A significant lowering of glutathione content accompanied with the inhibition of glutathione-s-transferase activity was also noticed at the highest dose of styrene (900 mg/kg).
[Das M et al; Drug Chem Toxicol 4 (3): 219-27 (1981)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Following repeated, high (1000-2000 mg/kg) oral doses for 28 days, the cause of death was the pronounced irritation of the rat esophagus and stomach.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 2] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Overt hepatotoxicity (hepatocyte degeneration and coagulative

necrosis) developed in mice only when liver glutathione levels had been depleted by repeated exposures at 200 ppm styrene (6 hrs/day, 5 days/wk for up to 2 wks).
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 2] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ The respiratory toxicity of styrene /was investigated/ in rats. Epithelial changes occurred in the nose and trachea of animals exposed to 800 ppm (3466 mg/cu m) styrene for 4 hr/day for 8 wks. The changes included vacuolation of epithelial cells, nuclear pyknosis and exfoliation of epithelial cells. Changes in the nasal mucosa occurred at exposure levels of 30 ppm (130 mg/cu m). Morphological damage was more severe in the upper than in the lower respiratory tract.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 277 (1994)] **PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Induction of cellular proliferation in the forestomach by styrene-7,8-oxide and butylated hydroxyanisole was studied in rats to determine if cell proliferation played a role in the forestomach carcinogenicity of styrene-7,8-oxide and whether the mechanism was similar to that of butylated hydroxyanisole a nongenotoxic forestomach carcinogen. Male F344 rats were gavaged with 0, 137, 275 or 550 mg/kg styrene-7,8-oxide 3 days/wk for 4 weeks. Other rats were administered 0, 0.5, 1 or 2% BHA in their diet for 4 weeks. The rats were implanted subcutaneously with osmotic minipumps delivering 5-bromo-2-deoxyuridine (BrdU) 24 hr before the end of the experiment after which they were sacrificed and the forestomachs removed. Sections of the forestomachs were examined for histopathological changes. The extent of cell proliferation was determined by measuring uptake of BrdU into the cellular DNA in these regions. Labeling indices were computed. A marginal increase in the thickness of the squamous epithelium and a slight increase in keratinization of the forestomach was seen in styrene-7,8-oxide treated rats. BHA induced a dose dependent increase in the number and severity of hyperplastic lesions in the squamous epithelium and hyperkeratinization. These lesions were more pronounced in the midregion and prefundic region. Styrene-7,8-oxide and BHA induced significant increases in labeling indices in all forestomach regions. The increases in labeling indices were similar in all forestomach regions in styrene-7,8-oxide treated rats. In BHA treated rats the increases were more pronounced in the prefundic region. ...
[Cantoreggi S et al; Cancer Res 53 (15): 3505-8 (1993)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ A single undiluted application of styrene to a rabbit's ear caused no appreciable reaction, but 20 such applications over 4 wk produced moderate irritation with blistering and hair loss. Prolonged dermal exposure under a bandage produced marked irritation and slight necrosis. Installation of undiluted styrene into the inferior conjunctival sac of a rabbit produced moderate conjunctival irritation slight transient corneal injury.
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992., p. 1000] **PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Styrene is lung tumorigenic in mice but not in rats. Styrene and its alkene-oxidized metabolite styrene oxide (SO) were not lung toxic in CYP2F2(-/-) (knockout) mice, indicating styrene-induced mouse lung tumors are mediated through mouse-specific CYP2F2-generated ring-oxidized metabolite(s) in lung bronchioles. The human relevance of the CYP2F MOA was assessed by insertion of a human CYP2F1, 2A13, 2B6 transgene into CYP2F2(-/-) mice; CYP2F1 expression and activity were confirmed in the transgenic (TG) mice. No evidence of cytotoxicity or increased cell proliferation (BrdU labeling) was seen in TG mice treated with either styrene or SO (200 mg/kg/day ip for 5 days). In contrast to styrene and SO, 4HS (105 mg/kg/day ip for 5 days) increased BrdU labeling 5-10-fold in WT mice, <3-fold increase in KO mice and 2-4-fold in TG mice. The limited response of 4HS in KO and TG mice may result from intrinsic toxicity or from further metabolism; regardless of the mode of action (MOA), these findings indicate that the CYP2F-mediated tumorigenic MOA in WT mice is not operative for styrene, SO, or for 4HS putatively derived from metabolism of styrene by CYP2F1 in humans, and thus S-induced mouse lung tumors are unlikely to be relevant to human risk.
[Cruzan G et al; Regul Toxicol Pharmacol 66 (1): 24-9 (2013)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ /Styrene was administered/ to beagle hounds by stomach tube at 200, 400, or 600 mg/kg/day for up to 561 days. Erythrocyte Heinz bodies were found in males dosed with 400 and 600 mg/kg/day, and sporadically in females admin 200 mg/kg/day. Other changes found occasionally were decreased packed cell volume, erythrocyte counts, erythrocyte sedimentation rate, and hemoglobin levels; an increased incidence of anisocytosis and hypochromia of erythrocytes, hemosiderin in reticuloendothelial cells of the liver; and an increased number of hepatocellular intranuclear acidophilic crystalline inclusions. Other blood elements examined were not affected by the admin of styrene at these doses. The blood changes were readily reversed after the admin of styrene was stopped.
[NIOSH; Criteria Document: Styrene p.95 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Administration of 125-200 ppm in drinking water of rats over a 2 yr period showed no deleterious health or reproductive effects.
[Beliles RP et al; Fundam Appl Toxicol 5 (5): 855-68 (1985)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ When beagle dogs were given 200, 400, or 600 mg/kg/day by oral gavage for 560 days, dogs given the two highest doses developed dyscrasias, evidenced by increased numbers of intraerythrocytic Heinz bodies, decreased packed cell volume, and reductions in hemoglobin and erythrocyte counts. No evidence for hematologic toxicity could be seen in dogs given 200 mg/kg/day.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 3] **PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Styrene was admin to rats by inhalation, ingestion and injection. Styrene oxide was admin to rats by ingestion. para-Methylstyrene was admin to rats and mice by ingestion. Styrene exposure produced a higher incidence of total malignant tumors in the group exposed at 100 ppm by inhalation. This was not

due to the increase of any specific type of tumor. A higher incidence of total benign and malignant mammary tumors and malignant mammary tumors was reported in the females of all groups exposed to styrene through inhalation. The incidence of malignant mammary tumors was treatment related. Lower incidence of total benign and malignant tumors and of total mammary tumors was noted in rats treated by ingestion at the highest dose level as a consequence of increased mortality. A dose related increase in total and malignant tumors was noted in groups treated with styrene oxide primarily due to forestomach neoplasias. In the forestomach, styrene oxide produced squamous cell carcinomas, papillomas, and acanthomas and precursor lesions. para-Methylstyrene was not shown to be carcinogenic.
[Conti B et al; Ann NY Acad Sci 534: 203-34 (1988)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ ... no convincing evidence for the carcinogenicity of the compound was obtained in Fischer 344 rats or B6C3F1 mice of either sex.
[Bioassay of Styrene for Possible Carcinogenicity (1979) Technical Rpt Series No. 185 DHEW Pub No. (NIH) 79-1741, U.S. Department of Health Education and Welfare, National Cancer Institute, Bethesda, MD 20014] **PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Twenty-nine pregnant O20 mice were each given single treatment of 1350 mg/kg body wt styrene (99% pure) dissolved in olive oil by stomach tube on 17th day of gestation. A control group of pregnant animals received olive oil alone. Neonatal mortality of the offspring was 43% compared with 22% in those of olive-oil treated controls. The same amt of styrene was then admin weekly by stomach tube to 49 male and 39 female progeny from weaning up to 16 wk of age, at which time the treatment was stopped because of high mortality (64% alive at 20 wk). Expt was terminated at 100 wk when all animals had died. No differences in tumor incidences were found between mothers treated with styrene and those given olive oil. In progeny, which received weekly treatments, lung tumors (adenomas and adenocarcinomas) were found in 20/23 males and 32/32 females, compared with 8/19 and 14/21 olive-oil treated controls ($p< 0.01$, $p< 0.01$) and 34/53 and 25/47 untreated controls ($p< 0.05$, $p< 0.001$). No differences in tumor incidences at sites other than lung were seen in the progeny, as compared with styrene-treated or olive-oil or untreated controls (ponomarkov and tomatis, 1979) from 9th wk onwards, incr activity of lysosomal acid proteinase in brain was detected.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 238 (1979)] **PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ A group of 21 pregnant BDIV rats received a single administration of 1,350 mg/kg body weight styrene (purity, 99%) in olive oil by gastric intubation on day 17 of gestation. A control group of 10 pregnant rats received olive oil alone. There was a slight treatment-related increase in neonatal mortality. Groups of 73 male and 71 female progeny of dams that received styrene were administered 500 mg/kg body weight styrene in olive oil by gastric intubation weekly from weaning up to 120 weeks. Control groups of 36 male and 39 female rats received olive oil alone. The experiment was terminated at 120 weeks. There was no treatment-related effect on body weight or survival. At the time of observation of the first tumor, 32 control and 54 treated male progeny and 35 control and 68 treated female progeny were still alive. Stomach tumors occurred in three female rats (adenoma, fibrosarcoma, carcinosarcoma) administered styrene and in one female rat (fibrosarcoma) in the control group. Non-neoplastic stomach lesions (morphology and incidence unspecified) were reported in rats administered styrene. There was no significant treatment-related increase in tumor incidence at any site.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 263 (1994)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Doses of styrene ranging from 46-90 mg/kg/egg injected into yolk sac of fresh, fertile chicken eggs had no toxic effect. When injected on 4th day of incubation, it had LD50 of 40 umol/embryo; malformations were found in up to 20% of treated embryos, depending on dose and time of injection. Doses of 1.5 to 5 g/cu m (350-1100 ppm) inhaled by rats during ... pregnancy had embryotoxic effect.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 240 (1979)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Pregnant Sprague-Dawley rats and New Zealand white rabbits inhaled 0, 300 or 600 ppm styrene for 7 hr/day from days 6-15 (rats) and 6-18 (rabbits) of gestation. Addnl groups of rats were given styrene by gavage at dose levels of 0, 90 or 150 mg/kg twice daily (0, 180 or 300 mg/kg/day, respectively) from days 6-15 of gestation. Embryotoxicity and fetotoxicity were not evident in rats or rabbits inhaling styrene or in rats given the cmpd orally. No teratogenic effect was detected in either species inhaling styrene or in rats given styrene by gavage.
[Murray FJ et al; Toxicol 11 (4): 335-44 (1978)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ When COBS (SD) BR rats were given commercial grade styrene (98.9%, stabilized with t-butyl catechol) at 0, 125, or 250 ppm in their drinking water for three generations, no treatment related changes in reproduction could be detected.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 3] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ A group of 15 pregnant C57B1 mice received a single administration of 300 mg/kg body weight styrene (purity, 99%) in olive oil by gastric intubation on day 17 of gestation. A control group of five pregnancy mice received olive oil only . There was no treatment-related effect on neonatal mortality. Groups of 27 male and 27 female progeny of dams that received styrene were administered 300 mg/kg body weight styrene in olive oil by gastric intubation once a week from weaning up to 120 weeks. Control groups of 12 male and 13 female mice received olive oil alone. The experiment was terminated at 120 weeks. There was no treatment-related effect on body weight or survival. At the time of observation of the first tumor, 12 male controls and 24 treated male progeny, 13 female controls

and 24 treated progeny, and 10 control and 5 treated dams were still alive. There was no treatment-related difference in the incidences of tumors at any site in dams or progeny.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 263 (1994)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ The effect of orally administered styrene at dose levels of 250 or 400 mg/kg body weight daily from day 6-15 of gestation on embryo/fetus of rats was studied. Styrene treatment 400 mg/kg body weight resulted in decr of maternal body weight, increased fetal resorptions, decreased fetal weight and no such affects were observed at low dose level. No teratogenic effect was detected in rats exposed to any dose level of styrene.
[Srivastava S et al; J Environ Biol 11 (1): 73-7 (1990)] **PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ The effect of in utero exposure to styrene 200 or 400 mg/kg/day orally was studied on mixed function oxidase activities cytochrome P450 and glutathione contents and on the glutathione-S-transferase activity in rat fetal liver. Activities of aminopyrine-N-demethylase, aniline hydroxylase, aryl hydrocarbon hydroxylase and the cytochrome P450 contents were significantly decreased in the fetal liver. A significant decr in the glutathione contents and the glutathione-S-transferase activity was also observed in the liver of the fetuses of styrene exposed animals. The current data show that prenatal exposure to styrene could adversely affect the developing biotransformation process.
[Srivastava S et al; Drug Chem Toxicol 15 (3): 233-44 (1992)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Styrene was evaluated for the reproductive effects of pregnant rats and the neurochemical effects in the offspring of rats exposed during gestation. Pregnant Wistar rats were exposed to 0, 50 or 300 ppm styrene for 6 hr/day during days 7 to 21 of gestation. No significant differences in the number of offspring delivered were observed between the exposed and control groups. Body weights at 1 day of age of the offspring whose mothers were exposed to styrene were significantly lower than those of the control group. Although there were neither statistically significant differences of protein contents nor brain weights among styrene-exposed and their control offsprings of rats analyses of neurotransmitter studies showed dose-dependent decreases of neuroamines especially 5-HT (serotonin) and its metabolite 5HIAA (5-hydroxyindoleacetic acid) in the newborn offspring of styrene exposed rats. The results suggest that gestational exposure to styrene at these concentrations does not produce apparent reproductive toxicity but affects the body weight of pups and causes lowering of the neurotransmitter levels in the brain.
[Kishi R et al; Toxicol Lett 63 (2): 141-6 (1992)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ In the present study, the embryotoxicity of toluene, xylene, benzene, styrene and its metabolite styrene oxide was evaluated using the in vitro culture of postimplantation rat embryos. Possible interactions between toluene, xylene and benzene were also studied using mixtures of these solvents. The results of the study showed that toluene, xylene, benzene and styrene all have a concn dependent embryotoxic effect on the developing rat embryo in vitro. Styrene was embryotoxic at a lower concn (1.00 umol/mL) than benzene (1.56 umol/mL) toluene (2.25 umol/mL) or xylene (1.89 umol/mL). The metabolite of styrene, styrene oxide was embryotoxic at a concn (0.038 umol/mL) more than 20 times < the parent compound. There was no evidence of a synergistic interaction between toluene, xylene and benzene in causing embryotoxicity; the solvents interacted in an additive manner. The embryos were exposed to the solvents for 40 hr of the organogenic period. When the levels of solvents found to be embryotoxic in the present study are compared to blood levels in the human following industrial exposure or solvent abuse it appears unlikely that the threshold blood levels for embryotoxicity would be exceeded in the workplace. ...
[Brown-Woodman PD et al; Reprod Toxicol 8 (2): 121-35 (1994)] **PEER REVIEWED** PubMed Abstract

/LABORATORY ANIMALS: Neurotoxicity/ Exposure to the industrial solvent, styrene, induces locomotor and cognitive dysfunction in rats, and parkinsonian-like manifestations in man. The antipsychotic, haloperidol (HP), well known to induce striatal toxicity in man and animals, and styrene share a common metabolic pathway yielding p-fluoro phenylglyoxylic acid and phenylglyoxylic acid (PGA), respectively. Using an exposure period of 30 days and the vacous chewing movement (VCM) model as an expression of striatal-motor toxicity, /investigators/ found that incremental PGA dosing (220-400 mg/kg) significantly increased VCMs up to day 25, but decreased to control levels shortly after reaching maximum dose. However, a diminishing dose of PGA (400-200 mg/kg) did not evoke an immediate worsening of VCMs but precipitated a significant increase in VCMs following dosage reduction to 200 mg/kg on day 22. PGA exposure, therefore, compromises striatal-motor function that is especially sensitive to changes in exposure dose. Longer alternating dose exposure studies are needed to establish whether motor dysfunction is progressive in severity or longevity. These findings are of significance for the environmental toxicology of styrene in the chemical industry.
[Terre'Blanche G et al; Neurotox Res 20 (1): 97-101 (2011)] **PEER REVIEWED** PubMed Abstract Full text: PMC3089729

/LABORATORY ANIMALS: Neurotoxicity/ Occupational exposure to styrene monomer has been associated with cognitive dysfunction in humans, and changes in dopaminergic function have been suggested to underlie effects of repeated exposure to styrene monomer in animals. The study was designed to determine whether styrene and/or dopaminergic drugs affect working and reference memory in animals. Male Long Evans rats were administered styrene by gavage at 4.5 - 6.5 months of age and subsequently trained to perform an appetitive operant task which allowed daily quantification of working memory (accuracy of spatial delayed nonmatching-to-position) reference memory accuracy of visual discrimination perseverative responding (position bias) and motor function (choice lever press latencies and nosepoke inter-response times during delay). Styrene alone did not affect acquisition or any measure of performance on this task. ...
[Bushnell PJ et al; Effects of Dopaminergic Drugs on Working and Reference Memory in Rats. Govt Reports Announcements & Index (GRA&I) 24: (1993)] **PEER REVIEWED**

/ENDOCRINE MODULATION/ Subchronic oral exposure to styrene in rodents (25 or 50 mg/kg/day in mice; 160 or 320 mg/kg/day in rats and guinea pigs, 5 days/week) for 4 weeks resulted in moderate congestion of pancreatic lobules, focal

inflammatory reactions around islets (in mice) and altered serum insulin level while blood glucose levels remained unaffected. Increased beta cell degranulation together with characteristic neoformation of islets were predominantly seen in pancreas of guinea pigs.
[Khanna S et al; Indian J of Expl Biology; 32:68-71 (1994)] **PEER REVIEWED**

/ENDOCRINE MODULATION/ The endocrine-disrupting effects of styrene dimers (SD: NSD-01, -08 and -09) and styrene trimers (ST: NST -01, -03 and -12), which migrated from polystyrene (PS) containers into instant food, were investigated together with styrene monomer (SM) using in vitro and in vivo assays. In the estrogen (ER) and androgen receptor (AR) binding assay, SM, SD and ST showed no binding activity at concentration of 10(-10)-10(-5) mol/l. In order to evaluate the estrogenic activity in vivo, the uterotrophic assay was conducted. When prepubertal and ovariectomized adult rats were dosed with SM, SD and ST for 3 days by subcutaneous injection, these compounds did not induce significant increase in uterine weight. Additionally, to evaluate anti-androgen activity in vivo, the Hershberger assay for anti-androgenic activity in the presence of testosterone treatment was conducted. When castrated, testosterone-treated immature male rats were dosed SM, SD and ST for 7 days by oral gavage, these compounds did not induce a decrease in the seminal vesicle, ventral prostate and levator ani plus bulbocavernosus muscle weights. To evaluate the effects on hormones other than sex hormones, the thyroid hormone receptor (TR) binding assay and rat serum prolactin (PRL) was conducted. In the TR binding assay, SM, SD and ST showed no binding activity at a concentration of 10(-5) mol/l. When ovariectomized rats were dosed with SM, SD and ST for 3 days by sc injection, the results showed there was no change in rat serum PRL. From the above these results, we concluded that SM, SD and ST exhibit no apparent estrogenic, androgenic, anti-androgenic and thyroid activity.
[Date K et al; Food Chem Toxicol 40 (1): 65-75 (2002)] **PEER REVIEWED** PubMed Abstract

/ENDOCRINE MODULATION/ In this study, three of the representative EDCs, 17beta-estradiol, bisphenol A, and styrene, were employed to find their mode of toxic actions in Escherichia coli. To accomplish this, four different stress response genes, recA, katG, fabA, and grpE genes, were used as a representative for DNA, oxidative, membrane, or protein damage, respectively. The expression levels of these four genes were quantified using a real-time RT-PCR after challenge with three different EDCs individually. Bisphenol A and styrene caused high-level expression of recA and katG genes, respectively, whereas 17beta-estradiol made no significant changes in expression of any of those genes. These results lead to the classification of the mode of toxic actions of EDCs on E. coli.
[Kim YS et al; J Microbiol Biotechnol 17 (8): 1390-3 (2007)] **PEER REVIEWED** PubMed Abstract

/ENDOCRINE MODULATION/ /The authors/ have investigated whether chronic exposure to styrene could inflict persistent effects on the binding characteristics of dopamine D-2 agonist binding sites in rat neostriatal membranes. Styrene exposure (1000 ppm, 6 months, 16 hr/d overnight, and left without exposure for another 5 months) caused a marked increase (+160%) in the IC50 value of dopamine without significantly affecting the total amount of specifically bound ((3)H)raclopride. The specific ((3)H)raclopride binding in membranes from subcortical limbic areas was too low to yield acceptable displacement curves. These data indicate that chronic exposure to styrene can induce a persistent decrease in affinity of the neostriatal dopamine D-2 agonist binding sites, possibly mediated by membrane perturbations.
[Von Euler G, Bjornaes S ; Toxicol Lett (AMST); 54 (1): 101-106 (1990)] **PEER REVIEWED**

/ENDOCRINE MODULATION/ Styrene trimers migrate from polystyrene food container into foods. /The authors/ evaluated the estrogenic activity of styrene trimers such as 2,4,6-triphenyl-1-hexene (ST-1), 1a-phenyl-4a-(1'-phenylethyl)tetralin (ST-2), 1a-phenyl-4e-(1'-phenylethyl)tetralin(ST-3), 1e-phenyl-4a-(1'-phenylethyl)tetralin (ST-4), and 1e-phenyl-4e-(1'-phenylethyl)tetralin (ST-5) using the reporter-gene assay with MVLN cells stably expressing the estrogen-stimulated reporter gene, and it was confirmed that ST-1, ST-3, and ST-4 had estrogen-like activity. On the other hand, ST-2 and ST-5 had anti-estrogen-like activity. /The authors/ examined the estrogenic activity in vivo of ST-1, ST-3, and ST-4. The styrene trimers were administered to pregnant rats, and the effects on the offspring were examined. ST-1, ST-3, or ST-4 (0, 10, 100, 1000 ug/kg bw/day) were subcutaneously injected into pregnant rats from gestational Day 11 through 17, and the male offspring were sacrificed on postnatal days (PND) 101-103. In the ST-4 treatment groups, the relative anogenital distance on PND 3 was significantly shortened. The relative testis weight was remarkably decreased in all styrene trimer treatment groups. Relative weights of the prostate and epididymides significantly decreased in the ST-4 treatment groups. The relative brain weight was markedly reduced in the ST-3 and ST-4 treatment groups. A significant decrease of the Sertoli cell count was observed in the ST-1 and ST-4 treatment groups. The serum follicle stimulating hormone level was remarkably reduced in all styrene trimer treatment groups. The luteinizing hormone level was significantly decreased and the testosterone level increased in the ST-1 and ST-4 groups. These results suggest that prenatal exposure to estrogenic styrene trimers at low levels obstructed genital organ development, and disrupted the endocrine systems of male rat offspring.
[Ohyama K et al; Exp Biol Med (Maywood) 232 (2): 301-8 (2007)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ Recent spills in European waters have released polycyclic aromatic hydrocarbons, important components of heavy fuel oil, and the hydrocarbon styrene. Heavy fuel oil and styrene are classified as potentially genotoxic and carcinogenic. ... Transcription of genes involved in cancer development in the liver of juvenile turbots and in the digestive gland of mussels exposed to heavy fuel oil and to styrene and after a recovery period /was investigated/. In turbot, oil produced a significant up-regulation of p53 and gadd45alpha after 14 days exposure. cyclin G1 was up-regulated after 7 days treatment with styrene. In mussels, ras was down-regulated in both treatments after the recovery periods. No mutations in ras hotspots were detected in exposed mussels. gadd45alpha was up-regulated after the recovery period of the styrene experiment. Overall, transcriptional responses differed in mussels compared to turbot. Turbot responded to hydrocarbon exposure by triggering cell cycle arrest (p53) and DNA repair (gadd45alpha).
[Ruiz P et al; Ecotoxicology 21 (3): 820-31 (2012)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ Styrene induced reverse mutations in Salmonella typhimurium TA1535 and TA100 in presence of 9000 x G supernatant of liver of rats pretreated with clophen C or aroclor 1254; it was not mutagenic to TA1537, TA1538 or TA98. Styrene was not mutagenic in spot test with various strains of Salmonella typhimurium without metabolic activation. It did not

induce forward mutations in ... schizosaccharomyces pombe, even in the presence of mouse-liver microsomes. In host-mediated assay, using male swiss albino mice, 1000 mg/kg styrene incr gene conversion frequency in Saccharomyces cerevisiae strain D4.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 241 (1979)] **PEER REVIEWED**

/GENOTOXICITY/ The cytogenetic alterations in leukocytes and the increased risk for leukemia, lymphoma, or all lymphohematopoietic cancer observed in workers occupationally exposed to styrene have been associated with its hepatic metabolisation into styrene-7,8-oxide, an epoxide which can induce DNA damages. However, it has been observed that styrene-7,8-oxide was also found in the atmosphere of reinforced plastic industries where large amounts of styrene are used. Since the main route of exposure to these compounds is inhalation, in order to gain new insights regarding their systemic genotoxicity, Fisher 344 male rats were exposed in full-body inhalation chambers, 6 hr/day, 5 days/week for 4 weeks to styrene-7,8-oxide (25, 50, and 75 ppm) or styrene (75, 300, and 1000 ppm). Then, the induction of micronuclei in circulating reticulocytes and DNA strand breaks in leukocytes using the comet assay was studied at the end of the 3rd and 20th days of exposure. /These/ results showed that neither styrene nor styrene-7,8-oxide induced a significant increase of the micronucleus frequency in reticulocytes or DNA strand breaks in white blood cells. However, in the presence of the formamidopyridine DNA glycosylase, an enzyme able to recognize and excise DNA at the level of some oxidized DNA bases, a significant increase of DNA damages was observed at the end of the 3rd day of treatment in leukocytes from rats exposed to styrene but not to styrene-7,8-oxide. This experimental design helped to gather new information regarding the systemic genotoxicity of these two chemicals and may be valuable for the risk assessment associated with an occupational exposure to these molecules.
[Gate L et al; Toxicol Lett 211 (3): 211-9 (2012)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ Styrene induces various cytogenetic effects in onion root-tip cells in vivo, and it shows strong c-mitotic effect. In allium cepa, styrene is slightly more toxic than styrene oxide. Styrene glycol, a further metabolite of styrene oxide, does not cause mitotic inhibition.
[Linnainmaa K et al; Mutat Res 58 (2-3): 277-86 (1978)] **PEER REVIEWED** PubMed Abstract

/GENOTOXICITY/ 1-Vinylbenzene 3,4-oxide, a putative intermediate in the metabolism of styrene to 4-vinylphenol, was synthesized and examined for its obligatory intermediacy to the phenol, its physical properties, and mutagenicity toward Salmonella typhimurium TA98 & TA100. 1-Vinylbenzene 3,4-oxide had a potent mutagenicity toward TA100 but not the TA98 strain. /1-Vinylbenzene 3,4-oxide/
[Watabe T et al; Mutat Res 93 (1): 45-56 (1982)] **PEER REVIEWED** PubMed Abstract

/ALTERNATIVE and IN VITRO TESTS/ Styrene, widely used in manufacturing, has both acute and chronic effects in humans. In mice, styrene is both hepato- and pneumo-toxic and causes lung tumors. The primary site for styrene metabolism and its effects in mouse lung is the Clara cell, which secretes Clara cell 10kDa protein (CC10) and surfactant protein A (SPA). Both play important roles in host defenses and inflammation prevention. The mode of action for styrene-induced lung tumor formation has yet to be elicited, yet one possibility relates to oxidative stress and decreased CC10 levels. CC10 mRNA and protein expression were measured in isolated Clara cells 3, 12, and 24 hr following in vivo administration of styrene (600 mg/kg ip) or its metabolites [R-, S-, racemic styrene oxide (SO) (300 mg/kg ip), 4-vinylphenol (100 mg/kg ip)]. The largest decreases in CC10 mRNA expression were seen with R-SO and racemic SO at 24h. To determine if rebound effects would be seen, CC10 mRNA and protein expression were determined 48, 120, and 240 hr following styrene and R-SO administration. The CC10 protein level did not reach its lowest point to correlate with mRNA expression until 120 hr after R-SO administration. Styrene exposure caused a significant decrease in CC10 protein after 24 hr, rebounding through 240 hr. SPA protein expression showed little change from control levels, indicating a more specific effect on CC10 in the Clara cell by styrene and its metabolites. These studies demonstrate that acute changes in lung CC10 protein and mRNA expression do occur following in vivo treatment with styrene and its metabolites. These changes may be early indicators for a potential mechanism for lung tumor formation in mice as it relates to oxidative stress and the possibility deserves further study.
[Harvilchuck JA et al; Toxicol Lett 183 (1-3): 28-35 (2008)] **PEER REVIEWED** PubMed Abstract

/ALTERNATIVE and IN VITRO TESTS/ ...Human exposure to styrene occurs mainly in the reinforced plastics industry, particularly in developing countries. Styrene has been found to be hepatotoxic and pneumotoxic in humans and animals. The biochemical mechanisms of styrene-induced toxicities remain unknown. Albumin and hemoglobin adduction derived from styrene oxide, a major reactive metabolite of styrene, has been reported in blood samples obtained from styrene-exposed workers. The objectives of the current study focused on cellular protein covalent binding of styrene metabolite and its correlation with cytotoxicity induced by styrene. /Investigators/ found that radioactivity was bound to cellular proteins obtained from mouse airway trees after incubation with (14)C-styrene. Microsomal incubation studies showed that the observed protein covalent binding required the metabolic activation of styrene. The observed radioactivity binding in protein samples obtained from the cultured airways and microsomal incubations was significantly suppressed by co-incubation with disulfiram, a CYP2E1 inhibitor, although disulfiram apparently did not show a protective effect against the cytotoxicity of styrene. A 2-fold increase in radioactivity bound to cellular proteins was detected in cells stably transfected with CYP2E1 compared to the wild-type cells after (14)C-styrene exposure. With the polyclonal antibody developed... /investigators/ detected cellular protein adduction derived from styrene oxide at cysteinyl residues in cells treated with styrene. Competitive immunoblot studies confirmed the modification of cysteine residues by styrene oxide. Cell culture studies showed that the styrene-induced protein modification and cell death increased with the increasing concentration of styrene exposure. In conclusion, /the authors/ detected cellular protein covalent modification by styrene oxide in microsomal incubations, cultured cells, and mouse airways after exposure to styrene and found a good correlation between styrene-induced cytotoxicity and styrene oxide-derived cellular protein adduction.
[Wieslander G et al; Int Arch Occup Environ Health 83 (5): 585-91 (2010)] **PEER REVIEWED** PubMed Abstract Full text: PMC3463232

/ALTERNATIVE and IN VITRO TESTS/ The aims of our studies were to examine the developmental effects of styrene oxide the toxic metabolite of styrene using different in vitro developmental toxicity test systems. In experiments performed with primary embryo cells in culture (micromass system) a 50% reduction of cell differentiation and survival was found to occur at styrene oxide concentratlons (ug/mL) of 18.6 and 4.4 respectively for CNS cells and 7.2 and 28.2 ug/mL for limb bud (LB) cells. The differences in concentrations of styrene oxide affecting cell viability versus differentiation for CNS suggests that inhibition of differentiation by styrene oxide is a reflection of styrene oxide cytotoxicity. The results also indicated a selective sensitivity of mesenchymal cells to styrene oxide in the differentiation process. In a separate series of studies the post implantation whole embryo culture (WEC) system was used to examine the embryotoxic effects of styrene oxide. Endpoints of developmental toxicity monitored in these studies included embryolethality, malformation, growth retardation and changes in macromolecular cell components following styrene oxide exposures. Styrene oxide induced a dose dependent increase in embryolethality and embryo malformation at concentratlons that were comparable to effective concentrations in the micromass culture system. Styrene oxide exposure also caused a dose dependent reduction in somite number, crown rump length and embryonic DNA and protein content. These findings suggest quantitative comparability between two in vitro developmental toxicity systems. /Styrene oxide/
[Gregotti C et al; Toxicologist 12 (1): 333 (1992)] **PEER REVIEWED**

/IMMUNOTOXICITY/ The aim of this study was to evaluate the expression of a panel of genes involved in toxicology in response to styrene exposure at levels below the occupational standard setting. Workers in a fiber glass boat industry were evaluated for a panel of stress- and toxicity-related genes and associated with biochemical parameters related to hepatic injury. Urinary styrene metabolites (MA+PGA) of subjects and environmental sampling data collected for air at workplace were used to estimate styrene exposure. Expression array analysis revealed massive upregulation of genes encoding stress-responsive proteins (HSPA1L, EGR1, IL-6, IL-1beta, TNSF10 and TNFalpha) in the styrene-exposed group; the levels of cytokines released were further confirmed in serum. The exposed workers were then stratified by styrene exposure levels. EGR1 gene upregulation paralleled the expression and transcriptional protein levels of IL-6, TNSF10 and TNFalpha in styrene exposed workers, even at low level. The activation of the EGR1 pathway observed at low-styrene exposure was associated with a slight increase of hepatic markers found in highly exposed subjects, even though they were within normal range. The ALT and AST levels were not affected by alcohol consumption, and positively correlated with urinary styrene metabolites as evaluated by multiple regression analysis. /The authors concluded that/ the pro-inflammatory cytokines IL-6 and TNFalpha are the primary mediators of processes involved in the hepatic injury response and regeneration. Here, /the authors/ show that styrene induced stress responsive genes involved in cytoprotection and cytotoxicity at low-exposure, that proceed to a mild subclinical hepatic toxicity at high-styrene exposure.
[Strafella E et al; PLoS One. 8(9): e75401 (2013)] **PEER REVIEWED** PubMed Abstract Full text: PMC3781025

Ecotoxicity Excerpts:
/AQUATIC SPECIES/ The endocrine disruptor activity of styrene in humans and other vertebrates appears to be negligible. However, offspring numbers were reduced in Ceriodaphnia dubia bred in polystyrene cups. Styrene dimers and trimers were found to be eluted from the polystyrene cups by hexane and methanol with gas chromatography-mass spectrometry. Styrene dimers and trimers at concentrations of 0.04-1.7 ug/L affected C. dubia fertility (25% reduction after seven days), suggesting that styrenes have the potential to impair crustacean populations in the aquatic environment. /Styrenes/
[Tatarazako N et al; Chemosphere 48 (6): 597-601 (2002)] **PEER REVIEWED** PubMed Abstract

/AQUATIC SPECIES/ Two strains of bluegreen algae, bacteria, and protozoa /were utilized/ in the cell multiplication inhibition test. In this test, the onset of the inhibition of cell multiplication (toxicity threshold) under the influence of styrene is determined. The test cultures are kept under standardized laboratory conditions for a period of 8 days. The toxicity thresholds for styrene to the bluegreen algae Microcystis aeruginosa and Scenedesmus quadricauda were 67 mg/L and greater than 200 mg/L, respectively.
[Bringmann G, Kuehn R; Water Res 14 (3): 231-41 (1980)] **PEER REVIEWED**

/AQUATIC SPECIES/ The swimming activity of the amphipod, Pontoporeia affinis, was stimulated by styrene at concentrations between 2.3 and 23 mg/L. Higher styrene levels (35 and 46 mg/L) caused amphipods to cease swimming for several days, then resume greater than normal activity.
[USEPA; Health and Environmental Effects Profile for Styrene (Final Draft) p.56 (1984) ECAO-CIN-P103] **PEER REVIEWED**

National Toxicology Program Studies:
A bioassay for the possible carcinogenicity of styrene was conducted using Fischer 344 rats and B6C3F1 mice. Styrene was admin by gavage to groups of 50 male and 50 female animals of each species. Forty rats of each sex and twenty mice of each sex were placed on test as vehicle controls. The high, medium, and low dosages of styrene admin to rats were, respectively, 2,000, 1,000, and 500 mg/kg. The high and low dosages admin to mice were 300 and 150 mg/kg, respectively. The cmpd was admin for 78 wk to high and medium dose rats, for 103 wk to low dose rats, and for 78 wk to mice. The period of cmpd admin was followed by an observation period of 27 wk for high and medium dose rats, 1 wk for low dose rats, and 13 wk for mice. Mortality among male and female high dose rats was significantly higher than that among their respective vehicle controls. In response to this elevated and early mortality, an additional dosed group of each sex was included in the chronic bioassay. No significant positive association was apparent between dosage and mortality among any other dosed rat groups. For mice, there was a significant positive association between mortality and the dosages of styrene administered to males, but not to females. Adequate numbers of animals in all groups, except for the high dose male and female rats, survived sufficiently long to be at risk from late developing tumors. ... It is concluded that, under the conditions of this bioassay, no convincing evidence for the carcinogenicity of the compound was obtained in Fischer 344 rats or B6C3F1 mice of either sex.
[Bioassay of Styrene for Possible Carcinogenicity (1979) Technical Rpt Series No. 185 DHEW Pub No. (NIH) 79-1741, U.S. Department of Health Education and Welfare, National Cancer Institute, Bethesda, MD 20014] **PEER REVIEWED**

Non-Human Toxicity Values:

LC50 Mice 4940 ppm (2 hr exposure)
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 2] **PEER REVIEWED**

LC50 Rats 2770 ppm (4 hr exposure).
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 2] **PEER REVIEWED**

LD50 Rat oral, male and female 5000 mg/kg
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 2] **PEER REVIEWED**

LD50 Rat oral 1 g/kg
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 1057] **PEER REVIEWED**

LD50 Rat ip 898 mg/kg
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

LC50 Rat inhalation 24 g/cu m/4 hr
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

LD50 Mouse oral 316 mg/kg
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Ecotoxicity Values:

LC50: Species: Artemia salina (Brine shrimp) nauplii; Conditions: saltwater, static, 24 deg C; Concentration: 68000 ug/L for 24 hr /formulation/
[Price KS et al; J Water Pollut Control Fed 46 (1): 63-77 (1974) as cited in the ECOTOX database. Available from, as of March 26, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50: Species: Artemia salina (Brine shrimp) nauplii; Conditions: saltwater, static, 24 deg C; Concentration: 52000 ug/L for 48 hr /formulation/
[Price KS et al; J Water Pollut Control Fed 46 (1): 63-77 (1974) as cited in the ECOTOX database. Available from, as of March 26, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Carassius auratus (goldfish) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 64740 ug/L for 96 hr (95% confidence interval: 57170-75480 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of March 26, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Poecilia reticulata (Guppy) age 6 month, length 1.9-2.5 cm, weight 0.1-0.2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 74830 ug/L for 96 hr (95% confidence interval: 58750-95320 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of March 26, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Cyprinodon variegatus (sheepshead minnow); Conditions: /static bioassay/, ambient salinity from 10-30 parts per trillion and temp from 25-31 deg C; Concentration: 9.1 mg/L for 96 hr
[Heitmuller PT et al; Bull Environ Contam Toxicol 27 (5): 596-604 (1981)] **PEER REVIEWED** PubMed Abstract

LD50; Species: Carassius auratus (goldfish); Concentration: 26 mg/L for 24 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983., p. 1057] **PEER REVIEWED**

EC50; Species: Pseudokirchneriella subcapitata (Green Algae) 1X10+4 cells/mL; Conditions: freshwater, static, 24-25 deg C, pH 7.6-9.4; Concentration: 3900 ug/L for 24 hr (95% confidence interval: 220-66000 ug/L); Effect: decreased population abundance /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

EC50; Species: Pseudokirchneriella subcapitata (Green Algae) 1X10+4 cells/mL; Conditions: freshwater, static, 24-25 deg C, pH 7.6-9.4; Concentration: 560 ug/L for 48 hr (95% confidence interval: 50-6000 ug/L); Effect: decreased population abundance /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

EC50; Species: Pseudokirchneriella subcapitata (Green Algae) 1X10+4 cells/mL; Conditions: freshwater, static, 24-25 deg C,

pH 7.6-9.4; Concentration: 1400 ug/L for 72 hr (95% confidence interval: 460-4300 ug/L); Effect: decreased population abundance /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

EC50; Species: Pseudokirchneriella subcapitata (Green Algae) 1X10+4 cells/mL; Conditions: freshwater, static, 24-25 deg C, pH 7.6-9.4; Concentration: 720 ug/L for 96 hr (95% confidence interval: 150-3200 ug/L); Effect: decreased population abundance /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Daphnia magna (Water Flea) age < or =24 hr; Conditions: freshwater, flow through, 20-21 deg C, pH 7.5-8.0, hardness 170-180 mg/L CaCO3, alkalinity 110-120 mg/L CaCO3, dissolved oxygen 5.8-8.4 mg/L; Concentration: 5000 ug/L for 24 hr (95% confidence interval: 3300-7400 ug/L) /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Daphnia magna (Water Flea) age < or =24 hr; Conditions: freshwater, flow through, 20-21 deg C, pH 7.5-8.0, hardness 170-180 mg/L CaCO3, alkalinity 110-120 mg/L CaCO3, dissolved oxygen 5.8-8.4 mg/L; Concentration: 4700 ug/L for 48 hr (95% confidence interval: 3300-7400 ug/L) /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Daphnia magna (Water Flea) age < or =24 hr; Conditions: freshwater, static, 20-22 deg C, pH 7.6-7.7; Concentration: 255000 ug/L for 24 hr /formulation/
[Bringmann G, Kuhn R; Z Wasser-Abwasser-Forsch 10 (5): 161-166 (1977) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Daphnia magna (Water Flea) age < or =24 hr; Conditions: freshwater, static, 22 deg C, pH 7.4-9.4, dissolved oxygen 6.5-9.1 mg/L; Concentration: 27000 ug/L for 24 hr (95% confidence interval: 20000-35000 ug/L) /> or =80% purity/
[LeBlanc GA; Bull Environ Contam Toxicol 24 (5): 684-691 (1980) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Daphnia magna (Water Flea) age < or =24 hr; Conditions: freshwater, static, 22 deg C, pH 7.4-9.4, dissolved oxygen 6.5-9.1 mg/L; Concentration: 23000 ug/L for 48 hr (95% confidence interval: 18000-29000 ug/L) /> or =80% purity/
[LeBlanc GA; Bull Environ Contam Toxicol 24 (5): 684-691 (1980) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Lepomis macrochirus (Bluegill) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 25050 ug/L for 24 hr (95% confidence interval: 19030-33530 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Lepomis macrochirus (Bluegill) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 25050 ug/L for 48 hr (95% confidence interval: 19030-33530 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Lepomis macrochirus (Bluegill) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 25050 ug/L for 96 hr (95% confidence interval: 19030-33530 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 37 (29-46) mm; Conditions: freshwater, flow through, 22 deg C, pH 6.9-7.2, hardness 35-36 mg/L CaCO3, alkalinity 21-23 mg/L CaCO3, dissolved oxygen 7.4-9.3 mg/L; Concentration: 12000 ug/L for 24 hr (95% confidence interval: 11000-14000 ug/L) /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 37 (29-46) mm; Conditions: freshwater, flow through, 22 deg C, pH 6.9-7.2, hardness 35-36 mg/L CaCO3, alkalinity 21-23 mg/L CaCO3, dissolved oxygen 7.4-9.3 mg/L; Concentration: 11000 ug/L for 72 hr (95% confidence interval: 10000-13000 ug/L) /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 37 (29-46) mm; Conditions: freshwater, flow through, 22 deg C, pH 6.9-7.2, hardness 35-36 mg/L CaCO3, alkalinity 21-23 mg/L CaCO3, dissolved oxygen 7.4-9.3 mg/L; Concentration: 10000 ug/L for 96 hr (95% confidence interval: 9000-12000 ug/L) /99.929% purity/
[Cushman JR et al; Ecotoxicol Environ Saf 37: 173-180 (1997) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25

deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 56730 ug/L for 24 hr (95% confidence interval: 47670-67830 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 8.2, hardness 360 mg/L CaCO3, alkalinity 300 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 62810 ug/L for 24 hr (95% confidence interval: 54990-73690 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 53580 ug/L for 48 hr (95% confidence interval: 43040-71210 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 8.2, hardness 360 mg/L CaCO3, alkalinity 300 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 62810 ug/L for 48 hr (95% confidence interval: 54990-73690 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 7.5, hardness 20 mg/L CaCO3, alkalinity 18 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 46410 ug/L for 96 hr (95% confidence interval: 37110-59540 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Pimephales promelas (Fathead Minnow) length 3.8-6.4 cm, weight 1-2 g; Conditions: freshwater, static, 25 deg C, pH 8.2, hardness 360 mg/L CaCO3, alkalinity 300 mg/L CaCO3, dissolved oxygen 7.8 mg/L; Concentration: 59300 ug/L for 96 hr (95% confidence interval: 50870-70340 ug/L) /formulation/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38 (9): 1419-1429 (1966) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Oncorhynchus mykiss (Rainbow Trout); Conditions: freshwater, static; Concentration: 0.0633 mM for 96 hr /formulation/
[Castano A et al; Chemosphere 32 (11): 2141-2157 (1996) as cited in the ECOTOX database. Available from, as of February 20, 2014: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

Ongoing Test Status:
The following link will take the user to the National Toxicology Program (NTP) Test Agent Search Results page, which tabulates all of the "Standard Toxicology & Carcinogenesis Studies", "Developmental Studies", and "Genetic Toxicity Studies" performed with this chemical. Clicking on the "Testing Status" link will take the user to the status (i.e., in review, in progress, in preparation, on test, completed, etc.) and results of all the studies that the NTP has done on this chemical.
[Available from, as of February 24, 2014: http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=100-42-5

TSCA Test Submissions:
Chronic toxicity and oncogenicity were evaluated in groups of male and female Sprague-Dawley rats (96/sex/group) receiving whole body exposures to monomeric styrene vapor at nominal concentrations of 0, 600 or 1200ppm (due to overt toxicity, concentration changed to 1000ppm) in a dynamic air flow chamber. At each concentration, groups of male and female rats (7-8 weeks of age) were exposed for 6 hours per day, 5 days per week, for 18.3 months (males) and 20.7 months (females). A high incidence of chronic murine pneumonia was evident in the controls and high dose males, which complicated mortality analysis for male rats. No statistically significant differences were evident between treated females and controls for mortality. Mean body weights of all treated males and high dose females were lower throughout part or all the study period. At six and twelve month sacrifices, statistically significant decreases were evident for absolute kidney weights and absolute liver weights in treated males. At the six month sacrifice and at termination of the study, high dose females showed a significant increase in mean absolute liver weights. Histopathologic examination of the lung of high dose females in the later part of the study revealed a significant increase in the incidence of alveolar histiocytosis. The incidences of leukemia-lymphosarcoma are as follows: control males -1/85, control females -1/85, 600ppm males -5/86, 600ppm females -6/85, 1000ppm males -1/84 and 1000ppm females -6/85.
[Dow Health and Environmental Research: Two-Year Chronic Inhalation Toxicity and Carcinogenicity Study on Monomeric Styrene in Rats, Final Report, (1978), EPA Document No FYI-AX-0478-0028, Fiche No OTS0000028-0] **UNREVIEWED**

Styrene (CAS #100-42-5) was evaluated for effect on the lung tissue of male CD-1 mice (10/group). Styrene in corn oil was administered orally at 10, 100, and 200 mg/kg daily for 5 days. A control group of 10 mice were given corn oil only. Three days prior to sacrifice, all animals were fitted with an osmotic pump containing 200 ul 5-bromo-2'-deoxyuridine (15 mg/ml in 0.9% saline). Bodyweight gains and clinical signs were comparable to controls. Three mice at the 200 mg/kg dose exhibited focal crowding in the terminal bronchioles. There were dose dependent increases in cell replication in the terminal bronchioles at the 100 and 200 mg/kg dose levels. The no-effect level was 100 mg/kg for morphological change, and for both

morphological damages and cell replication, was 10 mg/kg.
[Styrene Information & Research Ctr, Inc; The Effects of Styrene on Mouse Lung Following Oral Dosing; 06/21/99; EPA Doc No. 88990000252; Fiche No. OTS0559780] **UNREVIEWED**

Styrene (CAS #100-42-5) was evaluated for chronic toxicity and carcinogenicity in CD-1 mice (70/sex/exposure group) receiving whole-body inhalation exposures for 6 hours a day, 5 days a week at concentrations of 0, 20, 40, 80, and 160 ppm. Bodyweight gain at 13 weeks was significantly less than controls in mice receiving 40, 80, and 160 ppm, but especially in males receiving 80 ppm styrene and both sexes at the 160 ppm exposure level. Food consumption was reduced in mice of both sexes at 160 ppm and in males at 80 ppm during the first 13 weeks. These two effects persisted throughout the study and were considered treatment-related. There were no treatment-related differences observed in the ophthalmological, hematological, blood chemical, urinalysis, and organ weight parameters measured at intervals. Blood levels of styrene oxide and styrene monomer increased with exposure. Macroscopic examination at terminal sacrifice (97 weeks for females; 104 weeks for males) showed statistically significant (using Fischer's Exact Test) increases in incidence of pulmonary bronchiolar-alveolar adenomas in males receiving 40, 80, or 160 ppm and females receiving 20, 40, or 160 ppm styrene. Females receiving 160 ppm also had significant increases in bronchiolar-alveolar carcinomas. This effect showed no clear dose-relationship. Non-neoplastic lesions were found in the lungs of all mice receiving styrene including decreased eosinophilia of the epithelial cells in th terminal bronchioles, and bronchiolar epithelial hyperplasia. These effects increased in incidence with increased time and/or exposure concentration. Treatment-related changes were also observed in the nasal passages of mice of both sexes in all groups, including respiratory metaplasia and degeneration or necrosis of the olfactory epithelium, and changes to the Bowman's gland.
[Styrene Information & Research Ctr, Inc; Styrene- 104 Week Repeat Dose Inhalation Combined Toxicity/Carcinogenicity Study in Mice- Vol I; 05/28/98; EPA Doc No. 89-980000259; Fiche No. OTS0558579-2] **UNREVIEWED**

The effect that inhibition of cytochrome P-450 has on the toxicity and increased cell replication caused by exposure to inhaled styrene was investigated. Preliminary studies were conducted to determine the minimum number of exposures to styrene required to induce significant increases in bronchiolar cell replication as well as to select a suitable in vivo cytochrome P-450 inhibitor. Male Cd-1 mice (10/group) were exposed to 0, 40, and 160 ppm styrene, 6 hours/day, for 3 days. Twenty four hours before the first exposure and immediately after each exposure, half the mice in each group were given a single oral dose of 200 mg/kg 5- phenyl-1-pentyne in corn oil (10 ml/kg) while the remainder were given corn oil alone. Immediately after the first exposure, all mice were fitted with 5-bromo-2- deoxyuridine (BrdU) minipumps. In the absence of the cytochrome P-450 inhibitor, there was an increase in the labeling index of bronchiolar epithelium in mice exposed to both 40 and 160 ppm styrene. Control mice receiving cytochrome P-450 inhibitor in the absence of styrene also showed a slight increase in cell replication. However, mice exposed to styrene and receiving 5-phenyl-1-pentyne showed no increase in the labeling index over those mice receiving inhibitor alone.
[Styrene Information & Research Ctr, Inc; The Role of Cytochrome P-450 in Styrene Induced Cell Division in the Mouse Lung; 06/21/99; EPA Doc No. FYI-OTSL-0100-1369; Fiche No. OTS0001369] **UNREVIEWED**

A comparison of the metabolism of styrene (CAS #100-42-5) to R- and S-styrene oxide in mouse, rat, and human nasal tissues was made in vitro. Respiratory and olfactory nasal tissues, and liver tissues were removed separately from 40 Sprague-Dawley male rats and 100 CD-1 male mice, pooled according to tissue type, and S9 and microsomal fractions were collected from each group. Only one of nine human nasal tissue samples (4 females, 3 males, and 2 unknown donors) had sufficient quantity for preparation of a microsomal fraction; S9 fractions were prepared from the remaining eight. Human CYP2E1 was expressed and purified from E. coli. The metabolism of styrene to styrene oxide as well as the ratio of R to S enantiomers were determined using tissue fractions. Styrene and styrene oxide were extracted from the incubations with hexane and the ratio of R and S enantiomeric isomers was determined for each sample: 3:1 for all nasal tissues as well as a similar ratio found for mouse liver, while rat liver showed 0.72:1. Purified CYP2E1 produced a ratio of 0.48 R to S isomer. The rates of styrene metabolism in rat and mouse olfactory microsomes were comparable, as well as the rates for rat and mouse respiratory fractions. Mouse liver showed half the metabolism rate of mouse olfactory, while rat liver showed an even lower rate. Evidence of styrene metabolism could not be detected in any of the human nasal tissue fractions (limit of detection = 0.04 nmol/min/mg protein). The above procedures measuring the metabolism of styrene in rat and mouse nasal tissues and purified CYP2E1 protein (40 pmol (0.1 mg)), were then repeated in the presence of the cytochrome P-450 inhibitors chlorzoxazone (0.1-1.0 mM), 8-methoxypsoralen (0.005-1.0 mM), coumarin (0.005-1.0 mM), and 5-phenyl-1-pentyne (0.005-1.0 mM), which were added in 5 ul DMSO at the beginning of the experiments. All the inhibitors reduced the styrene metabolism rate, with 5-phenyl-1-pentyne being the most effective. Antibodies to cytochromes P-4502E1 and 2F2 showed that both enzymes are heavily expressed in both rat and mouse nasal tissues with the greatest concentrations being found in the olfactory regions. The expression of CYP2F2 was generally greater than CYP2E1. An in vivo metabolism and covalent binding study supported the above results. The authors conclude that the high rate of metabolism of styrene to styrene oxide in rodent nasal tissue is due to high concentrations of cytochromes P-4502E1 and P-4502F2. Of these two, CYP2F2 is believed to result in the preferential formation of the more toxic R isomer. Assays of the metabolism of styrene in human nasal tissue suggests that the nasal toxicity seen in the rodent is unlikely to occur in humans.
[Styrene Information & Research Ctr; The Metabolism of Styrene by Rat, Mouse, and Human Nasal Cytochrome P-450's; EPA Doc No. FYI-OTSL-0100-1369; Fiche No. OTS0001369] **UNREVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:
New metabolites of styrene, three isomeric vinylphenylmercapturic acids (2-, 3-, and 4-VPMA), were recently identified by LC-ESI-MS in the urine of mice. In this study, 4-VPMA together with traces of 2- and 3-VPMA were found also in the urine of hand-lamination workers, which were exposed to styrene vapors at concentrations ranging from 23 to 244mg/cu m.

Concentrations of 4-VPMA in these end-of-shift samples were 4.59+/-3.64ng/mL (mean+/-S.D.; n=10), those found next morning after the work-shift were 2.14+/-2.07ng/mL (mean+/-S.D.; n=10). Strong correlation (R=0.959) was found in the next-morning samples between concentrations of 4-VPMA and phenylglyoxylic acid, whereas correlations found between 4-VPMA and mandelic acid in both end-of-shift and next-morning samples were much weaker. The excretion of 4-VPMA accounted for only about 3.5 x 10(-4)% of the absorbed dose of styrene. Despite very low metabolic yield, formation of VPMAs clearly indicates occurrence and extent of styrene ring oxidation considered to be a toxicologically relevant metabolic pathway.
[Linhart I et al; Toxicol Lett. 213(2):260-5 (2012).] **PEER REVIEWED** PubMed Abstract

Human P450 2A13 is the most efficient enzyme for catalyzing the metabolism of nicotine and metabolic activation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). It is conceivable that P450 2A13 also metabolizes chemicals in air pollutants because this enzyme is highly expressed in the respiratory tract. In this study, /the authors/ investigated the possibility that P450 2A13 can metabolize naphthalene, styrene, and toluene, which are included in air pollutants as well as tobacco smoke, although they were known to be metabolized by P450 1A2 or 2E1. /They/ found that P450 2A13 catalyzed 1- and 2-naphthol formations from naphthalene with higher intrinsic clearances (kcat/ Km) (3.1- and 2.2-fold, respectively) than P450 1A2 and also more efficiently catalyzed the styrene 7,8-oxide formation from styrene and the benzylalcohol formation from toluene than P450 2E1. The overlapping substrate specificity of P450 2A13 with P450 2E1 was supported by the finding that P450 2A13 catalyzed chlorzoxazone 6-hydroxylation (8-fold higher value of kcat/ Km) and p-nitrophenol 2-hydroxylation (19-fold higher value of kcat/ Km), which are marker activities of P450 2E1. Thus, /the authors/ found that P450 2A13 metabolizes diverse environmental chemicals and has overlapping substrate specificities of P450 1A2 and 2E1, suggesting that P450 2A13 plays important roles in the local metabolism of environmental chemicals in the respiratory tract related to toxicity or carcinogenicity.
[Fukami T et al; Chem Res Toxicol. 21(3):720-5 (2008).] **PEER REVIEWED** PubMed Abstract

The current study was aimed at examining the role of cytochrome P450 (CYP450) activation and the electrophile-sensitive transient receptor potential ankyrin 1 receptor (TRPA1) in mediating the sensory irritation response to styrene and naphthalene. Toward this end, the sensory irritation to these vapors was measured in female C57Bl/6J mice during 15-min exposure via plethysmographic measurement of the duration of braking at the onset of each expiration. The sensory irritation response to 75 ppm styrene and 7 ppm naphthalene was diminished threefold or more in animals pretreated with the CYP450 inhibitor metyrapone, providing evidence of the role of metabolic activation in the response to these vapors. The sensory irritation response to styrene (75 ppm) and naphthalene (7.6 ppm) was virtually absent in TRPA1-/- knockout mice, indicating the critical role of this receptor in mediating the response. Thus, these results support the hypothesis that styrene and naphthalene vapors initiate the sensory irritation response through TRPA1 detection of their CYP450 metabolites.
[Lanosa MJ et al; Toxicol Sci. 115(2):589-95 (2010).] **PEER REVIEWED** PubMed Abstract Full text: PMC2948824

The CYP2E1 has been identified as the main cytochrome P450 isoform involved in human styrene metabolism. CYP2E1 presents polymorphism in humans and the different genotypes may, at least partly, be related to the different levels of individual expression of enzyme activity. /Investigators/ studied whether the genetic polymorphisms and phenotype of CYP2E1 modulate the level of urinary styrene metabolites and if they can be used for assessing risks of occupational exposure to styrene. A population of 49 male workers exposed to styrene (average level 362.7mg/cu m) and a control group were selected. Samples of urine, blood and buccal swab were taken to determine the urinary biological indicators (phenylglyoxylic acid and mandelic acid), to quantify mRNA of CYP2E1 in blood using RT-PCR and to analyze different polymorphisms of enzyme CYP2E1 from buccal swab. /Investigators/ found decreased expression of mRNA of the enzyme, as well as decreased excretion of the styrene metabolites in individuals carrying the CYP2E1*5B heterozygote allele (c1/c2) with respect to the wild-type homozygote (c1/c1), which indicates a reduction in the inducibility of the enzyme in the presence of this polymorphism. The results show that the combined effect of both the CYP2E1 phenotype, measured by the expression of the specific mRNA in blood samples, and the CYP2E1*5B allele genotype, may explain the variability of urinary excretion of the styrene metabolites.
[Prieto-Castello MJ et al; Toxicol Lett. 192(1):34-9 (2010).] **PEER REVIEWED** PubMed Abstract

Metabolic activation is considered to be a critical step for styrene-induced pulmonary toxicity. Styrene-7,8-oxide is a primary oxidative metabolite generated by vinyl epoxidation of styrene. In addition, urinary 4-vinylphenol (4-VP), a phenolic metabolite formed by aromatic hydroxylation, has been detected in workers and experimental animals after exposure to styrene. In the present study, new oxidative metabolites of styrene, including 2-vinylphenol (2-VP), 3-vinylphenol (3-VP), vinyl-1,4-hydroquinone, and 2-hydroxystyrene glycol were detected in mouse liver microsomal incubations. The production rates of 2-VP, 3-VP, 4-VP, and styrene glycol were 0.0527 +/- 0.0045, 0.0019 +/- 0.0006, 0.0053 +/- 0.0002, and 4.42 +/- 0.33 nmol/(min x mg protein) in mouse liver microsomes, respectively. Both disulfiram (100 uM) and 5-phenyl-1-pentyne (5 ? M) significantly inhibited the formation of the VPs and styrene glycol. 2-VP, 3-VP, and 4-VP were metabolized in mouse liver microsomes at rates of 2.50 +/- 0.30, 2.63 +/- 0.13, and 3.45 +/- 0.11 nmol/(minx mg protein), respectively. The three VPs were further metabolized to vinylcatechols and/or vinyl-1,4-hydroquinone and the corresponding glycols. Pulmonary toxicity of 2-VP, 3-VP, and 4-VP was evaluated in CD-1 mice, and 4-VP was found to be more toxic than 2-VP and 3-VP.
[Shen S et al; Drug Metab Dispos. 38(11):1934-43 (2010).] **PEER REVIEWED** PubMed Abstract Full text: PMC2967389

The urine from mice exposed to styrene vapors (600 and 1200 mg/cu m, 6 hr) was analyzed for ring-oxidized metabolites of styrene. To facilitate the identification of metabolites in urine, the following potential metabolites were prepared: 2-, 3-, and 4-vinylphenol (2-, 3-, and 4-VP), 4-vinylpyrocatechol, and 2-, 3-, and 4-vinylphenylmercapturic acid (2-, 3-, and 4-VPMA). For the analysis of vinylphenols beta-glucuronidase-treated urine was extracted and derivatized with acetanhydride/triethylamine before injection into GC/MS. Three isomers, 2-, 3-, and 4-VP, were found in the exposed urine using authentic standards. Additionally, three novel minor urinary metabolites, arylmercapturic acids 2-, 3-, and 4-VPMA, were identified by LC-ESI-MS(2) by comparison with authentic standards. Excretion of the most abundant isomer, 4-VPMA, amounted to 535 +/- 47 nmol/kg and 984 +/- 78 nmol/kg, representing approximately 0.047 and 0.043% of the absorbed dose for the exposure levels of 600 and 1200 mg/cu m, respectively. The ratio of 2-VPMA, 3-VPMA, and 4-VPMA was approximately 2:1:6. In model reactions of styrene 3,4-oxide (3,4-STO) with N-acetylcysteine in aqueous solutions and of its methyl ester in methanol, 4-

vinylphenol was always the main product, while 3-vinylphenol has never been detected. No mercapturic acid was found in the reaction of 3,4-STO with N-acetylcysteine in aqueous solution at pH 7.4 or 9.7, but a small amount of 4-VPMA methyl ester was detected by LC-ESI-MS after the reaction of 3,4-STO with N-acetylcysteine methyl ester. In contrast, no mercapturic acid was found in the reaction of 3,4-STO with N-acetylcysteine in aqueous solution at pH 7.4 or 9.7. These findings indicate a capability of 3,4-STO to react with cellular thiol groups despite its rapid isomerization to vinylphenol in an aqueous environment. Moreover, the in vivo formation of 2- and 3-isomers of both VP and VPMA, neither of which was formed from 3,4-STO in vitro, strongly suggests that another arene oxide, styrene 2,3-oxide, might be a minor metabolic intermediate of styrene.
[Linhart I et al; Chem Res Toxicol. 2010 Jan;23(1):251-7 (2010).] **PEER REVIEWED** PubMed Abstract

Styrene induces lung tumors in mice but not in rats. Although metabolism of styrene to 7,8-styrene oxide (SO) by CYP2E1 has been suggested as a mediator of styrene toxicity, lung toxicity is not attenuated in CYP2E1 knockout mice. However, styrene and/or SO metabolism by mouse lung Clara cell-localized CYP2F2 to ring-oxidized cytotoxic metabolite(s) has been postulated as a key metabolic gateway responsible for both lung toxicity and possible tumorigenicity. To test this hypothesis, the lung toxicity of styrene and SO was evaluated in C57BL/6 (WT) and CYP2F2-/- knockout mice treated with styrene (400 mg/kg/day, gavage, or 200 or 400 mg/kg/day, ip) or S- or R-SO (200 mg/kg/day, ip) for 5 days. Styrene treated WT mice displayed significant necrosis and exfoliation of Clara cells, and cumulative BrdU-labeling index of S-phase cells was markedly increased in terminal bronchioles of WT mice exposed to styrene or S- or RSO. In contrast, Clara and terminal bronchiole cell toxicity was not observed in CYP2F2-/- mice exposed to either styrene or SO. This study... demonstrates that the mouse lung toxicity of both styrene and SO is critically dependent on metabolism by CYP2F2. Importantly, the human isoform of CYP2F, CYP2F1, is expressed at much lower levels and likely does not catalyze significant styrene metabolism, supporting the hypothesis that styrene-induced mouse lung tumors may not quantitatively, or possibly qualitatively, predict lung tumor potential in humans.
[Cruzan G et al; Regul Toxicol Pharmacol. 62(1):214-20 (2012).] **PEER REVIEWED** PubMed Abstract

Styrene, which is widely used in manufacturing, is both acutely and chronically toxic to mice. Styrene is metabolized by cytochromes P-450 to the toxic metabolite styrene oxide, which is detoxified via hydrolysis with microsomal epoxide hydrolase (mEH) playing a major role. The purpose of these studies was to characterize the importance of this pathway by determining the hepatotoxicity and pneumotoxicity of styrene in wild-type and mEH-deficient (mEH(-/-)) mice. While the mEH(-/-) mice metabolized styrene to styrene oxide at the same rate as the wild-type mice, as expected there was minimal metabolism of styrene oxide to glycol. mEH(-/-) mice were more susceptible to the lethal effects of styrene. Twenty-four hours following the administration of 200 mg/kg ip styrene, mice demonstrated a greater hepatotoxic response due to styrene, as measured by increased serum sorbitol dehydrogenase activity and greater pneumotoxicity as shown by increased protein levels, cell numbers, and lactate dehydrogenase activity in bronchioalveolar lavage fluid. mEH(-/-) mice were also more susceptible to styrene-induced oxidative stress, as indicated by greater decreases in hepatic glutathione levels 3 hr after styrene. Styrene oxide at a dose of 150 mg/kg did not produce hepatotoxicity in either wild-type or mEH(-/-) mice. However, styrene oxide produced pneumotoxicity that was similar in the two strains. Thus, mEH plays an important role in the detoxification of styrene but not for exogenously administered styrene oxide.
[Carlson GP; J Toxicol Environ Health A. 73(24):1689-99 (2010).] **PEER REVIEWED** PubMed Abstract

...Albumin and hemoglobin adduction derived from styrene oxide, a major reactive metabolite of styrene, has been reported in blood samples obtained from styrene-exposed workers...
[Yuan W et al; Chem Biol Interact. 186(3):323-30 (2010).] **PEER REVIEWED** PubMed Abstract Full text: PMC3463232

Cytochrome P450 2E1 (CYP2E1) is a cytochrome P450 enzyme involved in styrene metabolism. This study compared the binding affinities between styrene and 11 mammalian CYP2E1 systems using bioinformatics methods. Firstly, amino acid sequences of CYP2E1s were obtained from the Swiss-Prot database. Then, taking the crystal structure of human CYP2E1 as a template, 3D models of the CYP2E1s of other mammals were constructed using the SWISS-MODEL program. Finally, the generated homology models were applied to calculate their docking capacities against styrene and polystyrene using the Surflex-Dock program, which could automatically dock ligands into a receptor's ligand binding site using a protomol based approach and assess the affinity by an empirically derived scoring function. Docking experiments showed that the studied mammalian CYP2E1s had high binding affinities with styrene. For polystyrene, the dimer of styrene has high binding affinities with CYP2E1s, however, trimer and other high polymers were found hard to be docked into the CYP2E1s. The results of this study indicated that bioinformatics approaches might be useful tools to predict styrene and polystyrene affinities with mammalian CYP2E1s.
[Wu B et al; Ecotoxicology. 20(5):1041-6 (2011).] **PEER REVIEWED** PubMed Abstract

Styrene causes toxicity in both the lung and the liver. The study of the relationship of this toxicity to the metabolism of styrene has been aided by the use of knockout mice for both bioactivation and detoxification pathways. It has been hypothesized that CYP2E1 is primarily responsible for styrene bioactivation in mouse liver and CYP2F2 in mouse lung. Two knockout strains were used in the current studies. Mice deficient in hepatic cytochrome P450 reductase had much less hepatic metabolism of styrene to styrene oxide. Styrene (600 mg/kg, i.p.) caused significant hepatotoxicity, as determined by serum sorbitol dehydrogenase and glutathione levels, in the wild-type but not in the knockout mice. It caused lung toxicity, as determined by protein levels, cell number, and lactate dehydrogenase activity in the bronchioalveolar lavage fluid of wild-type mice, but this effect was less in the knockout mice. In CYP2F2 knockout mice there was only a small decrease in the hepatic metabolism of styrene but a very large decrease in pulmonary metabolism. As expected the CYP2F2 knockout and wild-type mice were equally susceptible to styrene-induced hepatotoxicity, but the knockout mice were less susceptible to styrene-induced pneumotoxicity. Although the results are inconsistent with the simple hypothesis that styrene pneumotoxicity is due to the bioactivation of styrene to styrene oxide by CYYP2F2, they demonstrate the importance of both liver and lung in the metabolism of styrene...
[Carlson GP; Toxicology. 294(2-3):104-8 (2012).] **PEER REVIEWED** PubMed Abstract

After a single ip dose of (14)C-styrene, rats excreted into the urine 4 known metabolites (phenylethylene glycol, mandelic acid, benzoic acid, and hippuric acid) and 4 new minor phenolic metabolites: 4-vinylphenol, p-hydroxymandelic acid, p-hydroxybenzoic acid, and p-hydroxyhippuric acid. These ring-hydroxylated metabolites are probably formed by rearrangement of unstable arene oxides. The reactive arene oxides may, therefore, be implicated in styrene toxicity.
[The Royal Society of Chemistry. Foreign Compound Metabolism in Mammals. Volume 6: A Review of the Literature Published during 1978 and 1979. London: The Royal Society of Chemistry, 1981., p. 343] **PEER REVIEWED**

Admin of styrene to rats resulted in the excretion of n-acetyl-s-(1-phenyl-2-hydroxyethyl)cysteine and n-acetyl-s-(2-phenyl-2-hydroxyethyl)cysteine. After admin of styrene the observed ratio of the diastereoisomers for both hydroxymercapturic acids was approximately 1:4. Thus, there is a stereoselective oxidation of styrene to styrene oxide, with a preference for the R-isomer.
[DELBRESSINE LP C; XENOBIOTICA 11 (9): 589-94 (1981)] **PEER REVIEWED** PubMed Abstract

Both 4-vinylphenol and mandelic acid were detected in urine samples of workers occupationally exposed to styrene. The presence of 4-vinylphenol in urine of workers exposed to styrene suggests that, in man, styrene is also metabolized via arene oxidation. However, when arene oxidation of styrene is compared to vinyl group oxidation the latter appears to be at least quantitatively by far the most important metabolic pathway.
[PFAFFLI P ET AL; TOXICOL APPL PHARMACOL 60 (1): 85-90 (1981)] **PEER REVIEWED** PubMed Abstract

In mammals, styrene is metabolized primarily in the liver and to a lesser extent in extrahepatic tissues, including kidney, intestine, and lung. The main metabolic pathway for styrene is oxidation by the microsomal monooxygenase to styrene-7,8-oxide, followed by rapid enzymatic hydration to styrene glycol or conjugation with glutathione. The styrene glycol is oxidized to mandelic acid, which is excreted in the urine. Further oxidation of mandelic acid also occurs, resulting in phenylglyoxylic acid, which is also excreted in the urine. The metabolic intermediate styrene-7,8-oxide, is biologically reactive and can bind to cellular macromolecules.
[Harkonen H; Scand J Work Environ Health 4 (Suppl 2): 104-13 (1978)] **PEER REVIEWED** PubMed Abstract

The main metabolic end products of styrene in humans are mandelic & phenylglyoxylic acid.
[NTP; Executive Summary: Styrene (Draft) p.25 (1985)] **PEER REVIEWED**

Pretreatment of /rats/ ... with phenobarbitone incr selectively biotransformation of styrene into styrene oxide, whereas admin of 2-diethylaminoethyl-2,2-diphenylvalerate hydrochloride (SKF 525-A) inhibited styrene metabolism.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 2: A Review of the Literature Published Between 1970 and 1971. London: The Chemical Society, 1972., p. 318] **PEER REVIEWED**

Oxygenated human erythrocytes catalyzed the oxidation of styrene to styrene oxide. This reaction was inhibited by carbon monoxide, but not by superoxide dismutase, catalase, & scavengers of hydroxyl radicals. In partially deoxygenated erythrocytes, styrene oxidation showed a linear relation with the molar fraction of oxyhemoglobulin. Thus, oxyhemoglobulin & not free oxygen radicals are involved in styrene metabolism.
[Tursi F et al; Experientia 39 (6): 593-94 (1983)] **PEER REVIEWED** PubMed Abstract

In rodents, styrene is metabolized to styrene glycol, hippuric acid, mandelic acid, 1-phenylethanol, 2-phenylethanol, phenylglyoxylic acid, and 4-vinylphenol along with glutathione and glucuronide conjugates. The 1- and 2-phenylethanols appear in rat urine with the glycine conjugate of phenylaceturic acid.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 5] **PEER REVIEWED**

In an experimental human study, the kinetics of styrene metabolism in 8 male workers from the plastics industry were compared with those of 8 subjects (reference) not previously exposed to solvents. The range of employment for study subjects was 7-12 yr and the mean styrene level in the factory was 44.4 mg/cu m. Both groups were experimentally exposed for 2 hr to 296 mg styrene/cu m (68.5 ppm) during light physical exercise. Approximately 63% of the styrene was absorbed. After 75 min exposure, the concentration of styrene in the blood reached steady state. At 2 hr, the mean blood concentration of styrene was significantly lower ($p< 0.05$) in pre-exposed subjects (14.07 umol/L) compared with reference subjects (21.2 umol/L). The apparent blood clearance of styrene was significantly higher ($p< 0.05$) in the pre-exposed group (2.0 L/hr kg) compared with the reference group (1.5 L/hr kg). In contrast to styrene, the blood concentration of non-conjugated styrene glycol rose continuously during exposure and reached about 3 umol/L in both groups. The mean half-life for styrene glycol was significantly lower ($p< 0.05$) in those occupationally exposed (47.0 min) compared with reference subjects (72.1 min). Significantly higher ($p< 0.05$) percentages of beta-glucuronic acid-conjugated styrene glycol were found in workers.
[Lof A et al; Br J Ind Med 43: 537-43 (1986)] **PEER REVIEWED** PubMed Abstract Full text: PMC1007702

In volunteers exposed for 2 hr to about 300 mg/cu m (70 ppm) styrene, styrene-7,8-oxide was found in venous blood at a mean concn of 0.05 umol/L (6 ug/L). Similar styrene-7,8-oxide concns, up to 0.04 umol/L (4.8 ug/L) and 4.1 ug/L, were present in venous blood of workers exposed to styrene at concns up to 371 mg/cu m (86 ppm) (mean, 99 mg/cu mg (23 ppm)) and up to 73 ppm (311 mg/cu m). Exposure to 20 ppm (87 mg/cu m) styrene gave rise to a mean styrene-7,8-oxide concn of 1 ug/L. These concns are 5-20 times lower than the corresponding concns in the blood of styrene exposed rodents. Enzymatic hydrolysis of styrene-7,8-oxide yields phenylethylene glycol, which reached a blood concn of 15-20% of the styrene concn in blood of workers exposed for 2 hr to 300 mg/ cu m (69 ppm) styrene. Phenylethylene glycol (S enantiomer:R enantiomer, about 3) and 2-phenylethanol have been found in urine of styrene-exposed workers. Phenylethylene glycol is further oxidized to mandelic and phenylglyoxylic acids, which are the main metabolites found in urine of people exposed to styrene, with 57-85% and 10-33% of an absorbed dose of styrene excreted as mandelic and phenylglyoxylic acids. Mandelic acid was excreted in styrene-exposed workers as a racemic mixture with a 1.2-fold excess of the R enantiomer. In other

studies, a 1.5-fold excess of the S enantiomer was found.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 268 (1994)] **PEER REVIEWED**

The excretion of mandelic acid in the urine appears to have a linear relationship between the exposure to styrene up to 150 ppm. Investigations have shown that the summation of mandelic acid and phenyl glyoxylic acid in the urine correlates with total exposure to styrene. Other minor metabolites of styrene metab are 4-vinyl phenol, phenylethylene glycol, phenylethanol, and hippuric acid.
[Sullivan, J.B., Krieger G.R. (eds). Clinical Environmental Health and Toxic Exposures. Second edition. Lippincott Williams and Wilkins, Philadelphia, Pennsylvania 1999., p. 1156] **PEER REVIEWED**

1-Vinylbenzene 3,4-oxide, /is/ a putative intermediate in the metabolism of styrene to 4-vinylphenol ... . /1-Vinylbenzene 3,4-oxide/
[WATABE T ET AL; MUTAT RES 93 (1): 45-56 (1982)] **PEER REVIEWED** PubMed Abstract

Styrene is metabolized in humans to styrene oxide.
[National Research Council; Prudent Practices in the Laboratory. Handling and Management of Chemical Hazards. the National Academies Press, Washington, D.C. 2011, p. 313 vol 4] **PEER REVIEWED**

Absorption, Distribution & Excretion:
The absorption of styrene in humanss proceeds by all routes, but mainly through the respiratory tract.
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 313] **PEER REVIEWED**

... Subcutaneous injections /concn not specified/ of radioactive styrene /into rats/ showed that it was rapidly metabolized, 85% of radioactivity being excreted during first 24 hr ... greatest part (about 71%) in urine, 3% in feces, 12% as respiratory co2, and 3% unchanged by lung. ... Retention after 1 hr is highest in liver (4.62%) falling to 0.11% in 24 hr, next highest in kidneys (1.82% falling to 0.01% in 24 hr). In all other organs retention at 24 hr is less than 0.02%, except for adrenals (0.03%) and small intestine (0.06%). Blood retained only 0.02% after 24 hr.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965., p. 100] **PEER REVIEWED**

Styrene vapors are absorbed through lung; percutaneous absorption of styrene during exposure to concn up to 2.5 g/cu M (600 ppm) in air is insignificant (about 2%) as compared with the respective pulmonary absorption. The percutaneous absorption of liquid styrene through skin of hand is 9-15 mg/sq cm/hr and that of aqueous soln (66-269 mg/L) is 40-180 ug/sq cm/hr. Styrene is sol in blood and has been found in fat tissue. It was found in SC fat samples froM 13/17 workers for as long as 3 days after most recent occupational exposure to more than 4.2 mg/cu M (1 ppm) styrene in air. It is rapidly depleted in breath following exposure to 420 mg/cu M (100 ppm) in air.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 244 (1979)] **PEER REVIEWED**

The tissue distribution and excretion of an oral dose of 20 mg/kg of (14)c-labeled styrene was studied in both male and female rats at various time intervals after admin. Organ with highest concn was kidney, followed by liver and pancreas. Principal route of excretion was by way of the kidneys, with 90% of dose appearing in urine within 24 hr. Less than 2% of the dose was recovered from the feces.
[PLOTNICK HB, WEIGEL WW; RES COMMUN CHEM PATHOL PHARMACOL 24 (3): 515-24 (1979)] **PEER REVIEWED** PubMed Abstract

Styrene, it has been observed, crosses the placenta.
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 313 vol 4] **PEER REVIEWED**

Exposure of rats to atmospheres containing styrene concn of between 50 and 2000 ppm showed that the concn of styrene in the perirenal fat was 10 times that in any other organ. Excluding fat, at the lowest exposure the kidney contained the highest concn of styrene. As the degree of exposure incr, greater concn were found in the liver, brain, and kidney. ... On repeated exposure (700 ppm 4 hr/day/5 days) styrene gradually accumulated in rat adipose tissue but not in other tissue.
[The Royal Society of Chemistry. Foreign Compound Metabolism in Mammals. Volume 6: A Review of the Literature Published during 1978 and 1979. London: The Royal Society of Chemistry, 1981., p. 342] **PEER REVIEWED**

Blood levels of styrene and the styrene metabolites styrene-7,8-oxide and styrene glycol were monitored in 10 men occupationally exposed to styrene in two glass-fiber reinforced plastics factories. The styrene concn in the breathing zone ranged from 5-371 mg styrene/cu m with an avg of 99 mg/cu m. Total pulmonary intake of styrene was calculated as the product of styrene concn in inspired air, pulmonary ventilation, and relative uptake (63%). The concn of styrene glycol in the blood was linearly related to styrene uptake during the preceeding 5 hr (r=0.90). The concn of styrene-7,8-oxide was at the detection limit of 0.02 umol/L in most samples.
[Lof A et al; Scand J Work Environ Health 12: 70-4 (1986)] **PEER REVIEWED** PubMed Abstract

Exposure of rats by inhalation to 1.3 mg/L styrene (300 ppm) for 2-11 wk for 6 hr daily on 6 days/wk caused a marked accum of styrene in brain and perinephric fat.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 239 (1979)] **PEER REVIEWED**

Pulmonary retention by humans ranges from 69.5% to 72.1% at 4.6 to 46 ppm; total absorbed dose can be increased sixfold with the increased respiratory rate of physical exertion.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 5] **PEER REVIEWED**

Some 90% to 97% of the styrene absorbed by humans is eliminated as urinary metabolites, with only a small fraction accounted for as parent compound in expired air or urine.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 5] **PEER REVIEWED**

Styrene partitions to human fat and concentrations therein account for approximately 8% of the inhaled compound. The human elimination halftime for styrene from adipose tissue is 2 to 4 days.
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-1634 2005., p. 5] **PEER REVIEWED**

... In an analysis of the pharmacokinetic fate of styrene in rats following a 6 hr inhalation exposure to 80, 200, 600, or 1200 ppm, there was a marked dose dependency in the elimination of styrene from the blood. ... At an exposure level of 80 ppm, the maximum styrene concn was 0.8 ug/mL, while at 1200 ppm the maximum blood concn reached a value of 64 ug/mL. Thus, as exposure concn increased by 15 fold, the maximum blood concn increased over 80 fold, indicating a dose dependency in the pharmacokinetic profile of styrene.
[Dietz FK et al; Environmental Health Perspectives 54: 9-14 (1983)] **PEER REVIEWED**

Styrene in ambient air is absorbed through the skin at 2-5% of the dose absorbed in the respiratory tract. Liquid styrene was found to penetrate the skin at a rate of 1 ug/(cm sq x min). Contact of one hand (500 sq cm) for 30 min with liquid styrene was estimated to be equivalent, in terms of absorption, to 4% of the dose retained in the body during exposure to 50 ppm (213 mg/cu m) for 8 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 265 (1994)] **PEER REVIEWED**

The absorption & distribution of styrene /was investigated/ in rats (strain unspecified) after a 4 hr exposure to styrene vapors at 500 & 1000 ppm (21 & 4333 mg/cu m). A significant enrichment of styrene in adipose tissues was reported. In another experiment, no accumulation of styrene /was found/ in the body after exposure at about 700 ppm (3033 m/cu m) for 4 hr a day for five days.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 270 (1994)] **PEER REVIEWED**

The pharmacokinetics and distribution of styrene were investigated in male Sprague Dawley rats after a 6 hr exposure to styrene at concentrations of 80, 200, 600 and l,200 ppm (347, 867, 2,600 and 5,200 mg/cu m). At each exposure level, the styrene concentration in blood increased rapidly during exposure and approached a maximum value at the end of exposure. The relationship between exposure concentration and blood concentration measured at the end of exposure was nonlinear, since a 15-fold increase in the exposure concentration resulted in a 63-fold increase in blood levels, indicating that the metabolism of styrene became saturated. The measured styrene concentrations in blood and adipose tissue were used to develop a physiologically based pharmacokinetic model.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60 270 (1994)] **PEER REVIEWED**

The pharmacokinetic behavior of styrene & styrene oxide in B6C3F1 mice & Sprague-Dawley rats was investigated. The uptake, distribution, metab, & exhalation of styrene were studied by the closed chamber technique after inhalation, ip, & oral admin to male rats & mice. In both species the rate of metab of inhaled styrene was concn dependent. Pharmacokinetic behavior of styrene was strongly influenced by physiological parameters such as blood flow & particularly the alveolar ventilation rate. Ip admin resulted in concn time courses in the atmosphere of the closed chamber. Following oral admin, concn time courses showed considerable interanimal variability. The results were used to calculate the body burden of styrene in rat, mouse & man. The pharmacokinetic parameters obtained were an essential prerequisite for computing the burden of the reactive metabolite styrene oxide resulting from styrene exposure.
[Filser JG et al; Arch Toxicol 67 (8): 517-30 (1993)] **PEER REVIEWED** PubMed Abstract

A physiologically based pharmacokinetic (PBPK) model describing the distribution and metabolism of styrene and its metabolite styrene-7,8-oxide in rats, mice, and humans was developed. The model was based on a PBPK model used previously to describe the pharmacokinetics of butadiene and butadiene-monoxide. The model represented the tissues of the body by four compartments. It assumed that styrene was metabolized by oxidation to styrene-7,8-oxide and that /this metabolite/ underwent intrahepatic first pass hydrolysis catalyzed by epoxide-hydrolase and conjugation with glutathione. Conjugation with glutathione was postulated to occur by an ordered ping pong mechanism involving glutathione, styrene-7,8-oxide, and glutathione-S-transferase. The equations in the original model were revised to reflect actual tissue styrene or styrene-7,8-oxide concentrations instead of their air equivalents. The model was tested by comparing simulated blood concentration versus time curves in rats, mice, and humans following inhalation, intravenous, oral, and ip admin of styrene or iv, oral, and ip admin of styrene-7,8-oxide with experimental data. Representative results indicated that for rat exposures, the model predictions generally agreed well with the experimental data. At low exposure concentrations, styrene was rapidly removed from the blood and the rate of metabolism was limited by the rate of blood flow through the liver. At high concentrations, the metabolism became saturated. In mice, the fraction of cardiac output perfusing the fat had to be decreased to obtain reasonable fits with experimental data. In humans at rest or performing light exercise, styrene was

predicted to be rapidly cleared from the blood immediately after the end of exposure. Pulmonary styrene clearance was biphasic: a rapid initial phase followed by a slow exhalation phase. The model predicted that only a portion of the administered styrene-7,8-oxide reached the systemic circulation because of fast acid hydrolysis occurring in the stomach. Measured blood styrene-7,8-oxide concentrations following ip admin of styrene-7,8-oxide to rodents correlated well with model predictions only when the bioavailability of styrene-7,8-oxide was decreased by 50%. Predicted blood styrene-7,8-oxide concentrations in humans agreed well with concentrations measured in male workers exposed to 11 to 72 ppm styrene for 4 hr.
[Csanady GYA et al; Arch Toxicol 68 (3): 143-57 (1994)] **PEER REVIEWED** PubMed Abstract

In man the uptake of styrene by the lungs is highly enhanced by physical activity.
[Snyder, R. (ed.) Ethel Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume 1: Hydrocarbons. Amsterdam - New York - Oxford: Elsevier, 1987., p. 201] **PEER REVIEWED**

In both animals and humans, styrene (mainly as its metabolites) is excreted >90% in urine regardless of the dose or route of exposure. A small fraction is exhaled & some is excreted in feces.
[Snyder, R. (ed.) Ethel Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume 1: Hydrocarbons. Amsterdam - New York - Oxford: Elsevier, 1987., p. 203] **PEER REVIEWED**

Dermal absorption of styrene is considered to be minimal. However, skin absorption does occur /at a rate of 0.06 mg/sq cm/hr/. Percutaneous absorption of styrene is incr if skin is injured.
[Sullivan, J.B., Krieger G.R. (eds). Clinical Environmental Health and Toxic Exposures. Second edition. Lippincott Williams and Wilkins, Philadelphia, Pennsylvania 1999., p. 1155] **PEER REVIEWED**

... An 8 hr exposure to 100 ppm styrene vapor is associated with exhalation of 2.6% of absorbed styrene, excretion of 56.9% as mandelic acid in the urine, excretion of 33.0% as phenylglyoxylic acid in urine, & a max of 7.5% excreted as hippuric acid in the urine.
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992., p. 1001] **PEER REVIEWED**

In an experimental human study, the kinetics of styrene metabolism in 8 male workers from the plastics industry were compared with those of 8 subjects (reference) not previously exposed to solvents. The range of employment for study subjects was 7-12 yr and the mean styrene level in the factory was 44.4 mg/cu m. Both groups were experimentally exposed for 2 hr to 296 mg styrene/cu m (68.5 ppm) during light physical exercise. Approximately 63% of the styrene was absorbed. After 75 min exposure, the concentration of styrene in the blood reached steady state. At 2 hr, the mean blood concentration of styrene was significantly lower ($p< 0.05$) in pre-exposed subjects (14.07 umol/L) compared with reference subjects (21.2 umol/L). The apparent blood clearance of styrene was significantly higher ($p< 0.05$) in the pre-exposed group (2.0 L/hr kg) compared with the reference group (1.5 L/hr kg). In contrast to styrene, the blood concentration of non-conjugated styrene glycol rose continuously during exposure and reached about 3 umol/L in both groups. The mean half-life for styrene glycol was significantly lower ($p< 0.05$) in those occupationally exposed (47.0 min) compared with reference subjects (72.1 min). Significantly higher ($p< 0.05$) percentages of beta-glucuronic acid-conjugated styrene glycol were found in workers.
[Lof A et al; Br J Ind Med 43: 537-43 (1986)] **PEER REVIEWED** PubMed Abstract Full text: PMC1007702

Biological Half-Life:
Seven male subjects were exposed to 210 mg/cu M of styrene in inspired air during 30 min at rest and three 30 min periods of work on a bicycle. About 24 hr after the exposure the mean concn of styrene in adipose tissue was about the same level as 2-4 hr after exposure, about 3.5 mg/kg. The est half-life of the concn of styrene in adipose tissue was 2-4 days.
[ENGSTROM J ET AL; SCAND J WORK ENVIRON HEALTH 4 (4): 315-23 (1978)] **PEER REVIEWED** PubMed Abstract

Three male employees exposed to styrene in the processing of polyester tanks were studied during a work wk. The time-weighted avg of styrene in air during the work wk was 32-85 mg/cu M. The calculated half-life in adipose tissue after exposure was 5.2 and 2.8 days. An elimination time of about 5 wk is needed before the limit of detection (0.1 mg/kg) is reached.
[ENGSTROM J ET AL; SCAND J WORK ENVIRON HEALTH 4 (4): 324-9 (1978)] **PEER REVIEWED** PubMed Abstract

The half-life for styrene in rat tissues, excluding adipose tissue, is about 2 hr.
[The Royal Society of Chemistry. Foreign Compound Metabolism in Mammals. Volume 6: A Review of the Literature Published during 1978 and 1979. London: The Royal Society of Chemistry, 1981., p. 342] **PEER REVIEWED**

Mechanism of Action:
Styrene is a volatile organic compound (VOC) that is widely used as a solvent in many industrial settings. Chronic exposure to styrene can result in irritation of the mucosa of the upper respiratory tract. Contact of styrene with epithelial cells stimulates the expression of a variety of inflammatory mediators, including the chemotactic cytokine monocyte chemoattractant protein-1 (MCP-1). To characterize the underlying mechanisms of the induction of inflammatory signals by styrene, /researchers/ investigated the influence of this compound on the induction of oxidative stress and the activation of the nuclear factor-kappa B (NF-kappaB) signaling pathway in human lung epithelial cells (A549). The results demonstrate that styrene-induced MCP-1 expression, as well as the expression of the oxidative stress marker glutathione S-transferase (GST), is associated with a concentration dependent pattern of NF-kappaB activity. An inhibitor of NF-kappaB, IKK-NBD, and the anti-inflammatory antioxidant N-acetylcysteine (NAC) were both effective in suppressing styrene-induced MCP-1 secretion. In addition, NAC was capable of inhibiting the upregulation of GST expression. /These/ findings suggest that the activation of the NF-kappaB signaling pathway by styrene is mediated via a redox-sensitive mechanism.
[Roder-Stolinski C et al; Toxicol Appl Pharmacol. 231(2):241-7 (2008).] **PEER REVIEWED** PubMed Abstract

Styrene is a widely used chemical, but it is known to produce lung and liver damage in mice. This may be related to oxidative stress associated with the decrease in the levels of reduced glutathione (GSH) in the target tissues. The purpose of this study

was to investigate the effect of styrene and its primary metabolites R-styrene oxide (R-SO) and S-styrene oxide (S-SO) on GSH levels in the lung lumen, as determined by amounts of GSH in bronchioalveolar lavage fluid (BALF) and in plasma. When non-Swiss albino (NSA) mice were administered styrene (600 mg/kg, ip), there was a significant fall in GSH levels in both BALF and plasma within 3 hr. These returned to control levels by 12 hr. The active metabolite R-SO (300 mg/kg, ip) also produced significant decreases in GSH in both BALF and plasma, but S-SO was without marked effect. Since GSH is a principal antioxidant in the lung epithelial lining fluid, this fall due to styrene may exert a significant influence on the ability of the lung to buffer oxidative damage.
[Carlson GP. J Toxicol Environ Health A. 73(11):766-72 (2010).] **PEER REVIEWED** PubMed Abstract

/Investigators/ demonstrate that intermolecular interactions, controlled by both oxygen and styrene coverage, alter reaction selectivity for styrene oxidation on oxygen-covered Au(111). Several partial oxidation products are formed--styrene oxide, acetophenone, benzoic acid, benzeneacetic acid, and phenylketene--in competition with combustion. The maximum ratio of the yields of styrene oxide to the total CO(2) produced is obtained for the maximum styrene coverage for the first two layers (0.28 ML) adsorbed on Au(111) precovered with 0.2 mL of O. Furthermore, our reactivity and infrared studies support a mechanism whereby styrene oxidation proceeds via two oxametallacycle intermediates which, under oxygen-lean conditions, lead to the formation of styrene oxide, acetophenone, and phenylketene. Benzoate, identified on the basis of infrared reflection absorption spectroscopy, is converted into benzoic acid during temperature-programmed reaction. These results demonstrate the ability to tune the epoxidation selectivity using reactant coverages and provide important mechanistic insight into styrene oxidation reactions.
[Quiller RG et al; Chem Asian J. 5(1):78-86 (2010).] **PEER REVIEWED** PubMed Abstract

Styrene is known to be hepatotoxic and pneumotoxic in rodents, and these adverse effects are related to its metabolism. Mice deficient in the enzymes responsible for both the activation and detoxification of styrene are useful in examining this relationship more closely. In the current study, mice deficient in glutathione S-transferase P1P2(-/-) (GST(-/-)) were compared with wild-type mice. Similar changes in serum sorbitol dehydrogenase, as an indicator of hepatotoxicity, and bronchioalveolar levels of protein, cells, and lactate dehydrogenase, as indicators of pneumotoxicity, were observed after styrene administration. Glutathione depletion followed a similar pattern. The administration of the toxic metabolite, styrene oxide, which is a direct substrate for glutathione metabolism, and 4-vinylphenol, which is a minor metabolite but is more potent than either styrene oxide, yielded results similar to those of styrene. The results indicate that either other isoforms of glutathione S-transferase are more important than the P1P2 form in styrene detoxification or that this pathway contributes in only a minor way to styrene detoxification, compared to other pathways.
[Carlson GP. Drug Chem Toxicol. 34(4):440-4 (2011).] **PEER REVIEWED** PubMed Abstract

Styrene is one of the most important industrial intermediates consumed in the world and is mainly used as a monomer for reinforced plastics and rubber. Styrene has been found to be hepatotoxic and pneumotoxic in humans and experimental animals. The toxicity of styrene is suggested to be metabolism-dependent. Styrene-7,8-oxide has been considered as the major metabolite responsible for styrene-induced cytotoxicity. The objective of the study was to investigate the correlation between cytotoxicity of styrene and chemical and biochemical properties of the vinyl group of styrene by development of structure activity relationships (SAR). 4-Fluorostyrene, 4-chlorostyrene and 4-bromostyrene were selected for the SAR study. Cytotoxicity of styrene and the halogenated styrene derivatives with an order of 4-bromostyrene>4-chlorostyrene>4-fluorostyrene?styrene was observed in CYP2E1 transgenic cells. Similar orders in the efficiency of the metabolism of styrene and the halogenated styrene analogues to their oxides and in the electrophilicity of the corresponding oxides were observed. Additionally, the order of the potency of cellular glutathione depletion and the degree of protein adduction induced by styrene and the halogenated styrenes were consistent with that of their cytotoxicities. The wild-type cells were less susceptible to the toxicity of the corresponding model compounds than CYP2E1 cells. The present study provided insight into the roles of the biochemical and chemical properties of styrene in its cytotoxicity.
[Chung JK et al; Toxicol Lett. 210(3):353-9 (2012).] **PEER REVIEWED** PubMed Abstract Full text: PMC3463238

In mice, styrene is hepatotoxic, pneumotoxic, and causes lung tumors. One explanation for the mechanism of toxicity is oxidative stress/damage. Previous studies have shown decreased glutathione levels, linked to increased apoptosis, in lung homogenates and isolated Clara cells 3 hr following styrene or styrene oxide (SO) administration or in vitro exposure. The objective of the current studies was to determine what effects styrene and its active metabolites, primarily styrene oxide, had on indicators of oxidative stress and attendant apoptosis in order to understand better the mechanism of styrene-induced toxicity. Three hours following in vitro exposure of Clara cells to styrene or SO there were increases in reactive oxygen species (ROS). Following administration of styrene or styrene oxide ip, increases in ROS, superoxide dismutase (SOD), and 8-hydroxydeoxyguanosine (8-OHdG) formation were observed. Since increases in ROS have been linked to increases in apoptosis ratios of bax/bcl-2, mRNA and protein expression were determined 3-240 hr following the administration of styrene and R-styrene oxide (RSO). The bax/bcl-2 mRNA ratio increased 12 and 24 hr following R-SO and 120 hr following styrene administration. However, the bax/bcl-2 protein ratio was not increased until 240 hr following R-SO, and 24 and 240 hr following styrene administration. However, only a slight increase in caspase 3 was observed. These results indicated that oxidative stress occurred 3hr following styrene or styrene oxide as evidenced by increased ROS and SOD. This increased ROS may be responsible for the increased 8-OHdG formation. Our findings of limited apoptosis in Clara cells following acute exposure to styrene or SO are in agreement with others and may reflect the minimal extent to which apoptosis plays a role in acute styrene toxicity. It is clear, however, that oxidative stress and oxidative effects on DNA are increased following exposure to styrene or styrene oxide, and these may play a role in the lung tumorigenesis in mice.
[Harvilchuck JA et al; Toxicology. 264(3):171-8 (2009).] **PEER REVIEWED** PubMed Abstract

Interactions:
The toxicity of butadiene and styrene is exerted by their metabolites. Such metabolites have been extensively scrutinized at the in vitro level demonstrating evident genotoxic properties. In monitoring, a diverse range of outcomes has been produced.

Additionally, epidemiological studies in rubber workers face difficulties of data interpretation due to the changeability and multiple exposures of the workers as well as to confounding factors inherent to the cohorts. Nevertheless, toxicity has been associated with a significant trend of increasing the risk of leukemia in employees at the styrene-butadiene rubber industry. Thus, further effort must be made to distinguish the exposures to each chemical over time and to characterize their interrelationships. The present investigation focuses on the effects and mechanisms of damage of the mixture styrene-butadiene by examining its metabolites: styrene oxide (SO), butadiene monoepoxide (BME) and butadiene diepoxide (BDE) respectively. The in vitro Comet assay on frozen lymphocytes has been employed to ascertain the DNA damage patterns for the styrene-butadiene metabolites combined and on their own. Different patterns were observed for the mixture and each of its components. This study has also led to determining the mechanism of damage of the mixture and the compounds. With regard to the presence of reactive oxygen species (ROS), co-treatment with catalase does not modulate the genotoxicity of the mixture but it does modulate its components. The outcomes also indicate that the mixture induces cross-links and this is due to the influence of BDE in the mixture, being more evident as the concentration of BDE increases. An investigation on the sensitivity of lymphocytes from occupationally un/exposed subjects to in vitro exposure of the mixture and its components revealed that occupationally exposed subjects had a substantially higher background of DNA damage and a lower sensitivity to the metabolites of styrene, 1,3-butadiene and its mixture.
[Cemeli E et al; Mutat Res. 664(1-2):69-76 (2009).] **PEER REVIEWED** PubMed Abstract

Co-admin of styrene (6 g/kg) and diethyl maleate (a depletor of reduced glutathione) to hamsters caused an incr in the hepatotoxic effect of styrene as measured by serum aminotransferase activity. Co-admin of styrene with methionine protected the liver from cell damage. ... Excretion of styrene metabolites (2.2 mmol/kg) in urine was suppressed when rats were co-injected with toluene or trichloroethylene (2-11 mmol/kg).
[The Royal Society of Chemistry. Foreign Compound Metabolism in Mammals. Volume 6: A Review of the Literature Published during 1978 and 1979. London: The Royal Society of Chemistry, 1981., p. 343] **PEER REVIEWED**

Male Sprague-Dawley rats were used to study the renal toxicity potential of subchronic exposure to non-toxic doses of a combination of styrene & toluene. Four groups (n=6) of rats were injected ip with: (1) 4 mmol styrene 2 times/day at 4 hr intervals; (2) 10 mmol toluene/kg once/day; (3) 4 mmol styrene/kg 2 times/day plus 10 mmol toluene/kg once/day; (4) Corn oil (control vehicle) once/day. All treatments were given 5 days/wk for 4 consecutive wk. The rats were placed in metab cages for 24 hr at the end of each 5 day treatment, & blood & urine were collected. At the end of 4 wk, the rats were sacrificed for removal of the kidneys. By the fourth wk, there was a significant incr ($p<0.05$) in urinary excretion of gamma-glutamyl transpeptidase, protein & glucose by the group receiving combined treatment versus those receiving treatment with either chemical alone. There was an incr in excretion of hippuric acid in the mixture treatment group, but no incr in mandelic & phenylglyoxylic acids & thioethers. Blood urinary nitrogen was not modified by the individual chemicals or the mixture. Electron microscopic exam of the kidney showed an incr of single membrane vacuoles in the proximal convoluted tubules of rats treated with a mixture of chemicals, but not with toluene or styrene alone. /Results/ indicate that subchronic exposure to a mixture of toluene & styrene may incr renal toxicity compared to either individual chemical.
[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)] **PEER REVIEWED** PubMed Abstract

Somatosensory evoked potentials (SEPs) were used to evaluate possible subclinical impairment of the nervous system. In 36 rotogravure printers with severe exposure to toluene 20 workers with severe exposure to styrene in a glass laminate manufacturing plant & a comparison group of healthy subjects. Exposure was estimated by measurements of toluene & styrene in breathing zone air hippuric acid in urine in the group exposed to toluene & urinary mandelic acid in the group exposed to styrene. Peripheral conduction velocities in the arm & leg & central conduction time after tibial nerve stimulation were decreased in both exposed groups. Prolonged latencies of peripheral & cortical SEPs were found in workers exposed to styrene. Some abnormalities in SEPs at peripheral or spinal & cortical levels were found in both groups. A trend toward increased frequency of abnormal SEPs with duration of exposure of toluene & styrene & alcohol abuse was found. Abnormalities in Saps in the exposed groups are most probably of multifactorial origin. Central SEPs abnormalities in both exposed groups could indicate early signs of subclinical dysfunction at spinal & cortical levels & could be due to toluene or styrene exposure probably potentiated by alcohol consumption in the group exposed to toluene.
[Stetkarova I et al; Br J Indust Med 50 (6): 520-7 (1993)] **PEER REVIEWED**

The metab of styrene is inhibited by ethanol as well as other solvents.
[Sullivan, J.B., Krieger G.R. (eds). Clinical Environmental Health and Toxic Exposures. Second edition. Lippincott Williams and Wilkins, Philadelphia, Pennsylvania 1999., p. 1156] **PEER REVIEWED**

Workers exposed to industrial solvents are also frequently exposed to mechanical noise. In this study, a combination of a continuous noise (100 dB SPL) and an impact noise (110 dB SPL) was used to mimic the noise exposure in the workplace. A noise band of 10-20 kHz was used to induce a cochlear injury in the same cochlear region in the rat as styrene exposure. Styrene levels of 300 and 400mg/kg were applied to induce outer hair cell (OHC) loss limited to the third row of the middle turn, but without significant cochlear functional loss. The combined exposures of the noise and styrene for 3 weeks caused greater threshold shifts than the noise alone, although the styrene alone did not induce significant threshold shift. Correspondingly, the combined exposures induced OHC losses that were greater than the summated OHC losses induced by the noise and styrene exposure alone. Apoptosis in Deiters cells was also examined after a short-term exposure (7 days) to a combined exposure of a high-level styrene (800 mg/kg) and the noise. The styrene-noise synergistic interaction was also observed in the Deiters cells. The synergistic interaction between the noise and styrene suggests that each of the exposures alone (noise or styrene) may cause stress, temporary alteration, or nonlethal injury in cochlear cells and the combined exposure strengthens the stress leading to cell death.
[Chen GD et al; Hear Res. 254(1-2):25-33 (2009).] **PEER REVIEWED** PubMed Abstract

Products having high irritancy to the human eye are formed when styrene is photo-oxidized with ozone & nitrogen dioxide as in formation of smog. Also, a potent lacrimator has been formed when styrene wastes became mixed with bromine or chlorine

wastes & reacted under the influence of sunlight.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 854] **PEER REVIEWED**

Combined occupational exposure to styrene & acetone caused monooxygenase induction in chemical workers.
[DOLARA P ET AL; ANN OCCUP HYG 27 (2): 183-88 (1983)] **PEER REVIEWED** PubMed Abstract

The objective of this study was to evaluate hearing loss among workers exposed to styrene, alone or with noise. This cross-sectional study was conducted as part of NoiseChem, a European Commission 5th Framework Programme research project, by occupational health institutes in Finland, Sweden, and Poland. Participants' ages ranged from 18-72 years (n = 1620 workers). Participants exposed to styrene, alone or with noise, were from reinforced fiberglass products manufacturing plants (n = 862). Comparison groups were comprised of workers noise-exposed (n = 400) or controls (n = 358). Current styrene exposures ranged from 0 to 309 mg/cu m, while mean current noise levels ranged from 70-84 dB(A). Hearing thresholds of styrene-exposed participants were compared with Annexes A and B from ANSI S3.44, 1996. The audiometric thresholds of styrene exposed workers were significantly poorer than those in published standards. Age, gender, and styrene exposure met the significance level criterion in the multiple logistic regression for the binary outcome 'hearing loss' (P = 0.0000). Exposure to noise (<85 dBA p = 0.0001; ?85 dB(A) p = 0.0192) interacted significantly with styrene exposure. /It was concluded that/ occupational exposure to styrene is a risk factor for hearing loss, and styrene-exposed workers should be included in hearing loss prevention programs.
[Morata TC et al; Int J Audiol. 50(10):652-60 (2011).] **PEER REVIEWED** PubMed Abstract

A copolymer of styrene and alpha-methylstyrene, was found to exhibit estrogenic action in immature intact rats and dogs when fed continuously in the diets of both species for a period of 90 days. /SRP: These effects are not described and may be due to impurities/
[USEPA; Subst Risk Notice, 8(e) p.497 (1980) EPA-560/11-80-008] **PEER REVIEWED**

The effects of pretreatment with sodium phenobarbital on styrene-induced acute nephrotoxicity were studied in male Fischer 344 rats. Sodium phenobarbital, (80 mg/kg in saline) was injected ip in rats (6/group) for 3 days. Three days after the last dose, styrene, mixed with corn oil, was injected ip at doses of 0, 0.6, or 0.9 g/kg. Control animals were injected with corn oil. Uptake of p-aminohippurate by renal cortical slices was used to assess the nephrotoxicity of styrene. The capacity of renal cortical slices from the 0.9 g/kg styrene-treated rats to accumulate p-aminohippurate was reduced 24 hr after styrene treatment, compared to the controls, but there was no difference at the 0.6 g/kg dose. Pretreatment with sodium phenobarbital followed by 0.6 or 0.9 g/kg styrene had no effect on the renal uptake of p-aminohippurate . The urinary excretion of 2 enzymes, N-acetyl-beta-D-glucosaminidase and gamma-glutamyl transpeptidase, was significantly increased (p<0.05) in the urine of rats treated with 0.9 g/kg styrene (compared with controls). Pretreatment with sodium phenobarbital followed by 0.6 or 0.9 g/kg styrene did not incr the urinary concns of the above-mentioned enzymes. Electron microscopic exam of renal cortex 24 hr after 0.9 g/kg styrene treatment showed lipid droplets and accumulations of lysosome-like bodies in proximal tubular cells, while the ultrastructure of these cells appeared normal in rats treated with 0.6 g/kg styrene or pre-treated with sodium phenobarbital followed by styrene.
[Chakrabarti SK, Tuchweber B; Toxicology 46: 343-56 (1987)] **PEER REVIEWED** PubMed Abstract

Many solvents have been implicated in central nervous disorders and some of them are known to produce hearing loss, probably mediated by damage to cochlear hair cells. Hearing loss was studied by recording the brainstem auditory evoked response (BAER) in male Long Evans rats exposed 8 hr/day for 5 days to mixtures of styrene, and trichloroethylene. Dose groups included air or solvent pairs (styrene, trichloroethylene) following concns (ppm): (0:3000, (250:2250), (500:1500), (750:750) and (1000:0). Decreased BAER amplitude, indicative of hearing loss, was correlated with blood levels of total solvent. The effects were as predicted by a linear dose-addition model, indicating neither synergistic nor antagonistic interactions at the concns studied.
[Rebert CS et al; Govt Reports Announcements & Index (GRA&I), Issue 22: (1993) NTIS/PB93-229573] **PEER REVIEWED**

Exposure to styrene causes hearing loss and hair cell death in the middle frequency region in the cochlea. The current study was designed to examine the cell death pathways and the protective effect of L-NAC against styrene-induced cochlear injuries. Seventeen rats were exposed to styrene by gavage at 400 mg/kg 5 days per week for 3 weeks. Nine of the styrene-treated rats received L-NAC by intraperitoneal injection (325 mg/kg), and the remaining eight rats received saline injections as controls. The styrene-induced hearing loss was assessed by auditory brainstem responses (ABRs). Apoptotic, necrotic, and missing hair cells were quantified using combined methods, including nuclear staining with propidium iodide, F-actin staining with FITC-phalloidin, and the TUNEL assay. The styrene exposure caused a threshold shift of 15+/-4.3 dB. Both apoptosis and necrosis were involved in the pathogenesis of the cochlear lesion, but apoptosis appeared to be the major cell death pathway leading to the styrene ototoxicity. Treatment with L-NAC reduced the number of missing and dying outer hair cells (OHCs) and reduced the styrene-induced hearing loss. /The authors concluded that/ styrene exposure causes hair cell death through both apoptotic and necrotic pathways and treatment with N-acetyl-L-cysteine (L-NAC) reduces styrene ototoxicity.
[Yang WP et al; Acta Otolaryngol 129 (10): 1036-43 (2009)] **PEER REVIEWED** PubMed Abstract Full text: PMC4517195

Pharmacology:

Interactions:
The toxicity of butadiene and styrene is exerted by their metabolites. Such metabolites have been extensively scrutinized at the in vitro level demonstrating evident genotoxic properties. In monitoring, a diverse range of outcomes has been produced. Additionally, epidemiological studies in rubber workers face difficulties of data interpretation due to the changeability and

multiple exposures of the workers as well as to confounding factors inherent to the cohorts. Nevertheless, toxicity has been associated with a significant trend of increasing the risk of leukemia in employees at the styrene-butadiene rubber industry. Thus, further effort must be made to distinguish the exposures to each chemical over time and to characterize their interrelationships. The present investigation focuses on the effects and mechanisms of damage of the mixture styrene-butadiene by examining its metabolites: styrene oxide (SO), butadiene monoepoxide (BME) and butadiene diepoxide (BDE) respectively. The in vitro Comet assay on frozen lymphocytes has been employed to ascertain the DNA damage patterns for the styrene-butadiene metabolites combined and on their own. Different patterns were observed for the mixture and each of its components. This study has also led to determining the mechanism of damage of the mixture and the compounds. With regard to the presence of reactive oxygen species (ROS), co-treatment with catalase does not modulate the genotoxicity of the mixture but it does modulate its components. The outcomes also indicate that the mixture induces cross-links and this is due to the influence of BDE in the mixture, being more evident as the concentration of BDE increases. An investigation on the sensitivity of lymphocytes from occupationally un/exposed subjects to in vitro exposure of the mixture and its components revealed that occupationally exposed subjects had a substantially higher background of DNA damage and a lower sensitivity to the metabolites of styrene, 1,3-butadiene and its mixture.
[Cemeli E et al; Mutat Res. 664(1-2):69-76 (2009).] **PEER REVIEWED** PubMed Abstract

Co-admin of styrene (6 g/kg) and diethyl maleate (a depletor of reduced glutathione) to hamsters caused an incr in the hepatotoxic effect of styrene as measured by serum aminotransferase activity. Co-admin of styrene with methionine protected the liver from cell damage. ... Excretion of styrene metabolites (2.2 mmol/kg) in urine was suppressed when rats were co-injected with toluene or trichloroethylene (2-11 mmol/kg).
[The Royal Society of Chemistry. Foreign Compound Metabolism in Mammals. Volume 6: A Review of the Literature Published during 1978 and 1979. London: The Royal Society of Chemistry, 1981., p. 343] **PEER REVIEWED**

Male Sprague-Dawley rats were used to study the renal toxicity potential of subchronic exposure to non-toxic doses of a combination of styrene & toluene. Four groups (n=6) of rats were injected ip with: (1) 4 mmol styrene 2 times/day at 4 hr intervals; (2) 10 mmol toluene/kg once/day; (3) 4 mmol styrene/kg 2 times/day plus 10 mmol toluene/kg once/day; (4) Corn oil (control vehicle) once/day. All treatments were given 5 days/wk for 4 consecutive wk. The rats were placed in metab cages for 24 hr at the end of each 5 day treatment, & blood & urine were collected. At the end of 4 wk, the rats were sacrificed for removal of the kidneys. By the fourth wk, there was a significant incr ($p<0.05$) in urinary excretion of gamma-glutamyl transpeptidase, protein & glucose by the group receiving combined treatment versus those receiving treatment with either chemical alone. There was an incr in excretion of hippuric acid in the mixture treatment group, but no incr in mandelic & phenylglyoxylic acids & thioethers. Blood urinary nitrogen was not modified by the individual chemicals or the mixture. Electron microscopic exam of the kidney showed an incr of single membrane vacuoles in the proximal convoluted tubules of rats treated with a mixture of chemicals, but not with toluene or styrene alone. /Results/ indicate that subchronic exposure to a mixture of toluene & styrene may incr renal toxicity compared to either individual chemical.
[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)] **PEER REVIEWED** PubMed Abstract

Somatosensory evoked potentials (SEPs) were used to evaluate possible subclinical impairment of the nervous system. In 36 rotogravure printers with severe exposure to toluene 20 workers with severe exposure to styrene in a glass laminate manufacturing plant & a comparison group of healthy subjects. Exposure was estimated by measurements of toluene & styrene in breathing zone air hippuric acid in urine in the group exposed to toluene & urinary mandelic acid in the group exposed to styrene. Peripheral conduction velocities in the arm & leg & central conduction time after tibial nerve stimulation were decreased in both exposed groups. Prolonged latencies of peripheral & cortical SEPs were found in workers exposed to styrene. Some abnormalities in SEPs at peripheral or spinal & cortical levels were found in both groups. A trend toward increased frequency of abnormal SEPs with duration of exposure of toluene & styrene & alcohol abuse was found. Abnormalities in Saps in the exposed groups are most probably of multifactorial origin. Central SEPs abnormalities in both exposed groups could indicate early signs of subclinical dysfunction at spinal & cortical levels & could be due to toluene or styrene exposure probably potentiated by alcohol consumption in the group exposed to toluene.
[Stetkarova I et al; Br J Indust Med 50 (6): 520-7 (1993)] **PEER REVIEWED**

The metab of styrene is inhibited by ethanol as well as other solvents.
[Sullivan, J.B., Krieger G.R. (eds). Clinical Environmental Health and Toxic Exposures. Second edition. Lippincott Williams and Wilkins, Philadelphia, Pennsylvania 1999., p. 1156] **PEER REVIEWED**

Workers exposed to industrial solvents are also frequently exposed to mechanical noise. In this study, a combination of a continuous noise (100 dB SPL) and an impact noise (110 dB SPL) was used to mimic the noise exposure in the workplace. A noise band of 10-20 kHz was used to induce a cochlear injury in the same cochlear region in the rat as styrene exposure. Styrene levels of 300 and 400mg/kg were applied to induce outer hair cell (OHC) loss limited to the third row of the middle turn, but without significant cochlear functional loss. The combined exposures of the noise and styrene for 3 weeks caused greater threshold shifts than the noise alone, although the styrene alone did not induce significant threshold shift. Correspondingly, the combined exposures induced OHC losses that were greater than the summated OHC losses induced by the noise and styrene exposure alone. Apoptosis in Deiters cells was also examined after a short-term exposure (7 days) to a combined exposure of a high-level styrene (800 mg/kg) and the noise. The styrene-noise synergistic interaction was also observed in the Deiters cells. The synergistic interaction between the noise and styrene suggests that each of the exposures alone (noise or styrene) may cause stress, temporary alteration, or nonlethal injury in cochlear cells and the combined exposure strengthens the stress leading to cell death.
[Chen GD et al; Hear Res. 254(1-2):25-33 (2009).] **PEER REVIEWED** PubMed Abstract

Products having high irritancy to the human eye are formed when styrene is photo-oxidized with ozone & nitrogen dioxide as in formation of smog. Also, a potent lacrimator has been formed when styrene wastes became mixed with bromine or chlorine wastes & reacted under the influence of sunlight.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 854] **PEER REVIEWED**

Combined occupational exposure to styrene & acetone caused monooxygenase induction in chemical workers.
[DOLARA P ET AL; ANN OCCUP HYG 27 (2): 183-88 (1983)] **PEER REVIEWED** PubMed Abstract

The objective of this study was to evaluate hearing loss among workers exposed to styrene, alone or with noise. This cross-sectional study was conducted as part of NoiseChem, a European Commission 5th Framework Programme research project, by occupational health institutes in Finland, Sweden, and Poland. Participants' ages ranged from 18-72 years (n = 1620 workers). Participants exposed to styrene, alone or with noise, were from reinforced fiberglass products manufacturing plants (n = 862). Comparison groups were comprised of workers noise-exposed (n = 400) or controls (n = 358). Current styrene exposures ranged from 0 to 309 mg/cu m, while mean current noise levels ranged from 70-84 dB(A). Hearing thresholds of styrene-exposed participants were compared with Annexes A and B from ANSI S3.44, 1996. The audiometric thresholds of styrene exposed workers were significantly poorer than those in published standards. Age, gender, and styrene exposure met the significance level criterion in the multiple logistic regression for the binary outcome 'hearing loss' (P = 0.0000). Exposure to noise (<85 dBA p = 0.0001; ?85 dB(A) p = 0.0192) interacted significantly with styrene exposure. /It was concluded that/ occupational exposure to styrene is a risk factor for hearing loss, and styrene-exposed workers should be included in hearing loss prevention programs.
[Morata TC et al; Int J Audiol. 50(10):652-60 (2011).] **PEER REVIEWED** PubMed Abstract

A copolymer of styrene and alpha-methylstyrene, was found to exhibit estrogenic action in immature intact rats and dogs when fed continuously in the diets of both species for a period of 90 days. /SRP: These effects are not described and may be due to impurities/
[USEPA; Subst Risk Notice, 8(e) p.497 (1980) EPA-560/11-80-008] **PEER REVIEWED**

The effects of pretreatment with sodium phenobarbital on styrene-induced acute nephrotoxicity were studied in male Fischer 344 rats. Sodium phenobarbital, (80 mg/kg in saline) was injected ip in rats (6/group) for 3 days. Three days after the last dose, styrene, mixed with corn oil, was injected ip at doses of 0, 0.6, or 0.9 g/kg. Control animals were injected with corn oil. Uptake of p-aminohippurate by renal cortical slices was used to assess the nephrotoxicity of styrene. The capacity of renal cortical slices from the 0.9 g/kg styrene-treated rats to accumulate p-aminohippurate was reduced 24 hr after styrene treatment, compared to the controls, but there was no difference at the 0.6 g/kg dose. Pretreatment with sodium phenobarbital followed by 0.6 or 0.9 g/kg styrene had no effect on the renal uptake of p-aminohippurate . The urinary excretion of 2 enzymes, N-acetyl-beta-D-glucosaminidase and gamma-glutamyl transpeptidase, was significantly increased (p<0.05) in the urine of rats treated with 0.9 g/kg styrene (compared with controls). Pretreatment with sodium phenobarbital followed by 0.6 or 0.9 g/kg styrene did not incr the urinary concns of the above-mentioned enzymes. Electron microscopic exam of renal cortex 24 hr after 0.9 g/kg styrene treatment showed lipid droplets and accumulations of lysosome-like bodies in proximal tubular cells, while the ultrastructure of these cells appeared normal in rats treated with 0.6 g/kg styrene or pre-treated with sodium phenobarbital followed by styrene.
[Chakrabarti SK, Tuchweber B; Toxicology 46: 343-56 (1987)] **PEER REVIEWED** PubMed Abstract

Many solvents have been implicated in central nervous disorders and some of them are known to produce hearing loss, probably mediated by damage to cochlear hair cells. Hearing loss was studied by recording the brainstem auditory evoked response (BAER) in male Long Evans rats exposed 8 hr/day for 5 days to mixtures of styrene, and trichloroethylene. Dose groups included air or solvent pairs (styrene, trichloroethylene) following concns (ppm): (0:3000, (250:2250), (500:1500), (750:750) and (1000:0). Decreased BAER amplitude, indicative of hearing loss, was correlated with blood levels of total solvent. The effects were as predicted by a linear dose-addition model, indicating neither synergistic nor antagonistic interactions at the concns studied.
[Rebert CS et al; Govt Reports Announcements & Index (GRA&I), Issue 22: (1993) NTIS/PB93-229573] **PEER REVIEWED**

Exposure to styrene causes hearing loss and hair cell death in the middle frequency region in the cochlea. The current study was designed to examine the cell death pathways and the protective effect of L-NAC against styrene-induced cochlear injuries. Seventeen rats were exposed to styrene by gavage at 400 mg/kg 5 days per week for 3 weeks. Nine of the styrene-treated rats received L-NAC by intraperitoneal injection (325 mg/kg), and the remaining eight rats received saline injections as controls. The styrene-induced hearing loss was assessed by auditory brainstem responses (ABRs). Apoptotic, necrotic, and missing hair cells were quantified using combined methods, including nuclear staining with propidium iodide, F-actin staining with FITC-phalloidin, and the TUNEL assay. The styrene exposure caused a threshold shift of 15+/-4.3 dB. Both apoptosis and necrosis were involved in the pathogenesis of the cochlear lesion, but apoptosis appeared to be the major cell death pathway leading to the styrene ototoxicity. Treatment with L-NAC reduced the number of missing and dying outer hair cells (OHCs) and reduced the styrene-induced hearing loss. /The authors concluded that/ styrene exposure causes hair cell death through both apoptotic and necrotic pathways and treatment with N-acetyl-L-cysteine (L-NAC) reduces styrene ototoxicity.
[Yang WP et al; Acta Otolaryngol 129 (10): 1036-43 (2009)] **PEER REVIEWED** PubMed Abstract Full text: PMC4517195

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:
Styrene is one of the world's major organic chemicals. Styrene's production and use in plastic and resin manufacture may result in its release to the environment through various waste streams. It has been found in exhausts from combustion engines, waste incineration, and cigarette smoke. Styrene also occurs naturally in sap of some trees. If released to air, a vapor pressure of 6.40 mm Hg at 25 deg C indicates styrene will exist solely as a vapor in the ambient atmosphere. Vapor-

phase styrene will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals and ozone; the half-life for these reactions in air are estimated to be 7 and 16 hrs, respectively. Direct photochemical or photolytic reactions for styrene are slow. If released to soil, styrene is expected to have low mobility based upon an estimated Koc of 960. Volatilization from moist soil surfaces is expected to be an important fate process. For example, in 1.5 cm deep samples of a loamy soil, 26% of 2 mg/kg styrene that was added volatilized in 31 days. Styrene may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation by aerobic microorganisms may lead to extensive or complete destruction of styrene in soil. It was found that 97 and 87% of 8-14C-styrene added to soil at levels of 2.0 g/kg was converted to 14C-CO2 in 16 weeks in a landfill soil and sandy loam soil, respectively. If released into water, styrene is expected to adsorb to suspended solids and sediment based upon the estimated Koc. In lake water, 10 to 20% mineralization was observed in 3 weeks with samples containing 2.5 ug to 1.0 mg/L styrene. Degradation of styrene is rapid in sewage under aerobic conditions. Volatilization from water surfaces is expected to be rapid. Under laboratory conditions, 50% of 2 to 10 mg styrene per liter (depth not specified) was lost by volatilization in 1 to 3 hrs in lakewater samples and in 6 to 7 hrs in distilled water. A BCF of 13.5 for goldfish suggests bioconcentration in aquatic organisms is low. Styrene is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups. Occupational exposure to styrene may occur through inhalation and dermal contact with this compound at workplaces where styrene is produced or used. Monitoring data indicate that the general population may be exposed to styrene via ingestion of drinking water and by inhalation of air contaminated by industrial sources, auto exhaust, or incineration emission, and by inhalation of smoke from cigarettes. Typical concns of styrene in air and drinking water in US are 0.6 ug/cu m and 0 to 18.4 ug/L, respectively. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:
NIOSH (NOES Survey 1981-1983) has statistically estimated that 333,212 workers (86,902 of these are female) are potentially exposed to styrene in the US(1). Occupational exposure to styrene may occur through inhalation and dermal contact with this compound at workplaces where styrene is produced or used(SRC). Occupational exposure to styrene can be classified according to the types of operations in which it is present(2). In polystyrene manufacture, occupational chemical exposure is mainly styrene(2). The styrene concns found in polystyrene production are generally <21 mg/cu m (5 ppm); through occasional value of 210 mg/cu m (50 ppm) or more have been reported(2). In reinforced plastics applications, where styrene is a solvent-reactant for copolymerization, styrene is also the major air contaminant(2). Concentrations of styrene found during the production of reinforced plastics were generally much higher than those found in the polystyrene production plants, with peak concns as high as 6,300 mg/cu m (1,500 ppm)(2). The full-shift time-weighted avg (TWA) styrene exposures associated with styrene monomer and copolymer production are generally less than 10 ppm(3). Avg styrene exposures in reinforced plastics/composites plants can range from 40-100 ppm, with individual TWA and short-term exposures as high as 150-300 ppm and 1000-1500 ppm, respectively(3). Workers manufacturing boats and yachts, truck parts, tubs and showers and tanks and pipes that use reinforced plastics may be substantially exposed to styrene(4,5). Workers using certain polyester resins may be exposed to styrene(6,7), and the measured TWA ranged from 3.93-45.96 ppb(7). In the Finnish reinforced plastic industry, workers might be exposed to up to 3 g styrene per day(8). In non-production departments of pulp, paper, and paper product mills, the occupational exposure to styrene was 9.9 ppm for maintenance, construction and cleaning workers(9).
[(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available from, as of Mar 12, 2014: http://www.cdc.gov/noes/ (2) WHO; Environ Health Criteria 26 (Styrene). Geneva, Switzerland: WHO (1983) (3) Santodonato J et al; Monograph on Human Exposure to Chemicals in the Workplace: Styrene p 3-1 to 3-12 Bethesda, MD: National Cancer Institute NO1-CP-26002-03 (1985) (4) LeMasters GE et al; Am Ind Hyg Assoc J 46: 434-41 (1985) (5) Anderson KE; Diss Abstr Int B 47: 979 (1986) (6) Malek RF et al; Am Ind Hyg Asoc J 47: 524-29 (1986) (7) Bartolucci GB et al; Appl Ind Hyg 1: 125-31 (1986) (8) Hemminki K, Vianio H; Human exposure to potentially carcinogenic compounds. IARC Sci Pub1 59: 37-45 (1984) (9) Teschke K et al; Am Ind Hyg Assoc J 60: 73-83 (1999)] **PEER REVIEWED**

In Norway between 1972-1996, the average concentration of styrene in air during boat production, small items production, car body production, and other occupational environments were about 60, 40, 50 and 15 ppm, respectively(1)
[(1) Lenvik K et al; Appl Occup Environ Hygiene 14: 165-70 (1999)] **PEER REVIEWED**

Monitoring data indicate that the general population may be exposed to styrene via ingestion of food which has been packaged in polystyrene, by ingestion of contaminated finished drinking water, by inhalation of air contaminated by industrial sources, auto exhaust, or incineration emission, and by inhalation of smoke from cigarettes(1). Exposure to styrene may occur during the use of miscellaneous products containing styrene such as floor waxes and polishes, paints, adhesives, putty, metal cleaners, autobody fillers, and varnishes(2). Concn of styrene was 26-71 ppb in the indoor air of high-rise apartments(3).
[(1) IARC; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 60: 248-9 (1994) (2) NIOSH; Criteria Document: Styrene. DHEW Pub. NIOSH 83-119 p.18 (1983) (3) Tanaka T, Kogai 19: 121-28 (1984)] **PEER REVIEWED**

... Exposure to styrene may occur during the use of miscellaneous products containing styrene such as floor waxes and polishes, paints, adhesives, putty, metal cleaners, autobody fillers, and varnishes.
[NIOSH; Criteria Document: Stryene p.18 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

At fabrication facilities, workers may be exposed to unreacted monomer or monomer as a thermal degradation product.
[Hoff A et al; Scand J Work Environ Health 8 (Suppl 2): 1-60 (1982) as cited in NTP; Executive Summary: Styrene (Draft) p.6 (1985)] **PEER REVIEWED**

Body Burden:
Styrene was one of 110 chemicals monitored in blood and urine samples of 321 firefighters that responded to the Sept 11, 2001 World Trade Center collapse and 47 firefighters that were used as a control group(1). Styrene was determined to not be statistically different for these groups(1). Styrene was detected at a mean concentration of 0.06 ng/L in the blood of 43

children (3-6 year olds) living in the Phillips neighborhood of Minneapolis, MN; samples were collected Jan 2000 to Apr 2002(2). As part of the School Health Initiative: Environment, Learning, Disease study, 134 children (6-10 years old) from the Minneapolis, MN area donated blood samples for styrene analysis; 89.6% of 103 samples, 92.3% of 108 samples, 56.8% of 54 samples and 98.9% of 88 samples collected Feb 2000, May 2000, Feb 2001 and May 2001, respectively, contained measurable amounts of styrene(3).
[(1) Edelman P et al; Environ Health Perspect 111: 1906-11 (2003) (2) Sexton K et al; Environ Health Perspect 114: 453-9 (2005) (3) Sexton K et al; Environ Health Perspect 113: 342-9 (2005)] **PEER REVIEWED**

Personal air concentrations of styrene for 46 students from Philip Randolph Academy in Harlem, New York City were 1.01 and 1.68 ug/cu m in the winter and summer, respectively(1).
[(1) Kinney PL et al; Environ Health Perspect 110: 539-46 (2002)] **PEER REVIEWED**

A study done in 2000 on the exposure of school children in the inner city of Minneapolis, MN to volatile organic compounds found the following atmospheric values for styrene(1):

Sample Location/Type	% Detections winter	% Detections Summer	Median Concn (ug/cu m)
Outdoor	0	0	0.0
School	31.3	39.7	0.1
Home	91.9	91.9	0.8
Personal	93.5	85.2	0.5

[(1) Adgate JL et al; Environ Health Perspect 112: 1386-92 (2004)] **PEER REVIEWED**

Styrene was detected, but not quantified in 8 of 8 human breast milk samples from USA women in 4 cities(1). Six of 250 patients with suspected volatile organics exposure-related symptoms showed significantly elevated levels of styrene in blood(2). Concentration of styrene ranged from none detected to 1.9 ppb with a mean value of 0.6 ppb(2). A National Human Adipose Tissue Survey (NHATS) by EPA during the fiscal year 1982 detected styrene in wet adipose tissue with a frequency of 100% at a concentration range 8-350 ppb(3). Styrene, determined in the blood of 108 normal subjects from Italy was identified in 102 blood samples, with a mean concentration of 217 ng/L(4). Blood concentrations of styrene in a reference group of a nonoccupationally exposed US population averaged 0.074 ppb (number of samples = 657)(5). Urinary styrene was determined in 48 subjects, all blood donors living in urban areas, with a mean of 262 ng/L(4). Styrene has been identified in exhaled breath at mean concentrations of 0.7-1.6 ug/cu m(6).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-28 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanely JS; Broad Scan Analysis of Human Adipose Tissue Vol 1. Executive Summary. Washington, DC: USEPA-560/5-86-035 p. 22 (1986) (4) Brugnone F et al; Med Lav 85: 370-89 (1994) (5) Ashley DL et al; Clin Chem 40: 1401-4 (1994) (6) WHO; Environ Health Criteria 26 (Styrene). Geneva, Switzerland: WHO (1983)] **PEER REVIEWED**

The concentrations of styrene in the blood of service station attendants, street vendors, and office workers in Mexico City (in 1996) were 0.031 ug/L (range, 0.022-0.045 ug/L), 0.041 ug/L (range, 0.025-0.18 ug/L), and 0.025 ug/L (range, 0.022-0.049 ug/L), respectively, at the beginning of their shifts(1); post shift concentrations of styrene in blood were 0.027 ug/L (range, 0.020-0.093 ug/L), 0.031 ug/L (range, 0.022-0.073 ug/L), and 0.024 ug/L (range, 0.022-0.027 ug/L), respectively(1). The concentration of styrene in the urine and blood of reinforced plastics workers in Italy was 546.62 nmol/L (mean) and 5.65 nmol/L, respectively(2).
[(1) Romieu I et al; Environ Health Perspect 107: 511-5 (1999) (2) Gobba F et al; Scand J Work Environ Health 19: 175-82 (1993)] **PEER REVIEWED**

Blood Concentrations: Three volunteers exposed to styrene at an air concentration of approximately 50 ppm for 1 hour developed blood styrene concentrations of 0.2-0.7 mg/L; exposure to approximately 100 ppm for 8 hours produced maximal blood concentrations of 0.9-1.4 mg/L.
[Stewart RD et al; Arch Environ Health 16: 656-62 (1968) as cited in Baselt RC; Biological Monitoring Methods for Industrial Chemicals p. 238 (1980)] **PEER REVIEWED**

Blood styrene was measured by a gas chromatography-mass spectrometry method in 81 normal people and in 76 workers exposed to styrene. In the normal subjects, styrene was also tested in alveolar and environmental air. Styrene was found in nearly all (95%) blood samples. Average styrene levels in the normal subjects were 221 ng/L in blood, 3 ng/L in alveolar air, and 6 ng in environmental air. Styrene levels did not differ significantly between smokers and nonsmokers, 95% of the values being below 512 ng/L in blood, 7 ng/L in alveolar air, and 15 ng/L ln environmental air. In workers with an average exposure to styrene of 204 ug/L at the end of the workshift, mean blood styrene concentration was 1211 ug/L. In blood samples collected at the end of the Thursday shift styrene levels were significantly higher (1590 ug/L) than those found at the end of the Monday shift (1068 ug/L). A similar difference was found in samples taken the morning after exposure (60 and 119 micrograms/L respectively). Significant correlations between blood and environmental styrene were found both at the end of the shift and the morning after exposure (r = 0.61 and 0.41 respectively). In workers occupationally exposed to styrene 16 hr after the end of the workshift blood styrene (94 ug/L) was significantly higher than that found in the normal subjects (0.22 ug/L). The half life of blood styrene was 3.9 hr.
[Brugnone F et al; Int Arch Occup Environ Health 65 (2): 125-30 (1993)] **PEER REVIEWED** PubMed Abstract

A longitudinal study of 11 workers (aged 24-54 years) in the polyester resin boat industry in Germany assessed nerve

conduction velocities in 1980 and 1983. Exposure was occupational and route was by inhalation with mean air levels of 114 ppm, 97 ppm, 92 ppm over 3-7 years (mean = 4 yrs). The peripheral nervous system showed no significant difference in conduction velocities between exposed and controls for ulnar and median nerves. Mean blood levels were 0.92 mg/L in 1980 and 0.70 mg/L in 1983; mean levels of mandelic acid in urine ranged from 816 to 1660 mg/g creatinine; mean levels of phenylglyoxylic acid in urine ranged from 200-342 mg/g creatinine.
[Triebig G et al; Int Arch Occup Envir Health 5 (6): 239-47 (1985)] **PEER REVIEWED**

Average Daily Intake:
Worst-case exposure estimates for styrene of 0-0.5 ug/day from drinking water, 30 ug/day from food, and 65 mg/day from air were calculated by EPA(1); these estimates are based on the highest levels estimated or monitored and, therefore, reflect the highest potential exposure rather than typical exposure for the general population(1). The following nominal daily respiratory intakes of styrene have been estimated(1): worker in reinforced plastics industry, 2 g; worker in styrene polymerization, 100 mg; living within 1 km of a production unit, 600 ug; breathing polluted urban air, 400 ug; breathing typical urban air, 6 ug; breathing indoor air, 6-1000 ug; drinking polluted water, 2 ug; cigarette smoke (20 cigarettes per day), 400-960 ug(2). In a Boston Exposure Assessment in Microenvironments, time weighted average intake of styrene from air for 55 people living and working in the Boston area averaged 0.64 ug/cu m(3).
[(1) USEPA; Drinking water criteria document for styrene. Final draft. Cincinnati, OH: US EPA, Office of Health and Environmental Assessment. ECAO-CIN-409 (1988) (2) IARC; Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 60: 248 (1994) (3) Dodson RE et al; Environ Sci Technol 41: 8498-505 (2007)] **PEER REVIEWED**

The estimated daily intake of styrene by Canadians from various media were reported. Units for all values are ug/kg body weight/day. For the two categories 12-19 yrs and 20-70 yrs, cigarette smoking daily intakes were reported as 3.51 and 2.86 ug/kg body weight/day, respectively(1).

Estimated intake (ug/kg bw per day)

Population	Ambient Air	Indoor Air	Drinking Water	Food
0-6 months	0.004-0.11	0.07	0.005-0.03	<0.58
7 months-4 yrs	0.006-0.15	0.09	0.003-0.02	<0.53
5-11 yrs	0.007-0.17	0.10	0.002-0.008	<0.30
12-19 yrs	0.006-0.14	0.09	0.001-0.006	<0.15
20-70 yrs	0.005-0.13	0.08	0.001-0.005	<0.11

[(1) Newhook R, Caldwell I; Butadiene and Styrene: Assessment of Health Hazards (Publ 127). Lyon, France: IARC, pp. 27-33 (1993)] **PEER REVIEWED**

Human exposure to styrene was calculated in the general German population based on exposure concentration in food and air(1).

Intake via:	Time frame	ug/person	ug/kg
Food	Daily	0.2-1.2	0.003-0.017
Food	Annually	80-450	1.1-6.5
Inhalation	Daily	18-54	0.3-0.8
Inhalation	Annually	6600-19,700	94.3-281

[(1) Tang W et al; Toxicology 144: 39-50 (2000)] **PEER REVIEWED**

Natural Pollution Sources:
Styrene occurs naturally in the sap of the family Styracaceae(1). Styrene has been identified in trace amounts in the gummy exudate (storax balsam) from the damaged trunks of certain trees, probably from the natural degradation of the cinnamic acid derivatives that occur in large quantities in the exudates(2). Microorganisms may also form styrene from p-hydroxycinnamic, p-coumaric, ferulic, and caffeic acids(3).
[(1) Baxter CS, Warshawsky D; Styrene, Polyphenyls, and Related Compounds. Patty's Toxicology. 6th ed. (1999-2014). New York, NY: John Wiley & Sons, Inc. On-line posting date: 17 Aug 2012 (2) IARC; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer 60: 237 (1994) (3) Verscheren K; Handbook of Environmental Data on Organic Chemicals. 4th ed. New York, NY: John Wiley & Sons Inc. 2: 1899 (2001)] **PEER REVIEWED**

Artificial Pollution Sources:
Styrene is one of the world's major organic chemicals(1). Styrene's production and use in plastic and resin manufacture, as a dental filling component, as a chemical intermediate, component in agricultural products, and as a stabilizing agent(1) may result in its release to the environment through various waste streams(SRC). It has been found in exhausts from spark-

ignition engines(2), oxyacetylene flames, cigarette smoke, and gases emitted by pyrolysis of brake linings(3). Stack emissions from waste incineration have been found to contain styrene(4).
[(1) Baxter CS, Warshawsky D; Styrene, Polyphenols, and Related Compounds. Patty's Toxicology. 6th ed. (1999-2014). New York, NY: John Wiley & Sons, Inc. On-line posting date: 17 Aug 2012 (2) Hampton CV et al; Environ Sci Technol 16: 287-98 (1982) (3) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene and Related Compounds. Washington, DC: USEPA-560/11-80-018 p. 261 (1980) (4) Junk GA, Ford CS; Chemosphere 9: 187-230 (1980)] **PEER REVIEWED**

... Styrene may be released to the environment via emissions from vents on process equipment, storage tank losses, miscellaneous leaks and spills, process wastewaters, and solid process wastes. Also, since a small percentage of styrene monomer is present in the final polymer product, the compound could diffuse out of the polymer. Another potential source of environmental entry of styrene is by the combustion of a styrene polymer product. Thermal degradation of 100 mg of polystyrene resulted in the release of 5.22 + or - 0.83 mg styrene at 350 deg C and 5.84 + or - 1.94 mg styrene at 500 deg C.
[USEPA; Health Assessment Document: Styrene (Draft) p.2-2 (1985)] **PEER REVIEWED**

Environmental Fate:
TERRESTRIAL FATE: Based on a classification scheme(1), a log Koc value of 2.96(2), indicates that styrene is expected to have low mobility in soil(SRC). Volatilization of styrene from moist soil surfaces is expected as indicated by 26% volatilization in 31 days using loamy soil and 2 mg/kg styrene(3); volatilization of styrene from moist soil surfaces would be slower than in water(4). Styrene is expected to volatilize from dry soil surfaces(SRC) based upon a vapor pressure of 6.4 mm Hg at 25 deg C(5). Styrene biodegraded 97 and 87% in 16 weeks in a landfill soil and sandy loam soil, respectively(6), and was shown to biodegrade in soil 16 to 62% at varying concentrations is other studies(3).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Schuurmann G et al; Environ Sci Technol 40: 7005-11 (2006) (3) Fu MH, Alexander M; Environ Sci Technol 26: 1540-4 (1992) (4) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (5) Chao J et al; J Phys Chem Ref Data 12: 1033-63 (1983) (6) Sielicki M et al; Appl Environ Microbiol 35: 124-28 (1978)] **PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), a log Koc value of 2.96(2), indicates that styrene is expected to adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is expected(3) based upon a Henry's Law constant of 2.75X10-3 atm-cu m/mole(4). Studies have shown that styrene will volatilize from water surfaces; 50% of 2 to 10 mg styrene per liter (depth not specified) was lost by volatilization in 1 to 3 hrs in lake water samples and in 6 to 7 hrs in distilled water, respectively(5). Styrene is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(6). According to a classification scheme(7), a BCF of 13.5 for goldfish(8), suggests bioconcentration in aquatic organisms is low(SRC). In lake water, 10 to 20% mineralization was observed in 3 weeks with samples containing 2.5 ug to 1.0 mg/L styrene, after acclimation of the indigenous microorganisms(5). A 100% of theoretical BOD using activated sludge in the Japanese MITI test(9) suggests that biodegradation is an important environmental fate process in water(SRC).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Schuurmann G et al; Environ Sci Technol 40: 7005-11 (2006) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (4) Bocek K; Experimetia, Suppl 23: 231-40 (1976) (5) Fu MH, Alexander M; Environ Sci Technol 26: 1540-4 (1992) (6) Grosjean D; Sci Total Environ 46: 41- 59 (1985) (7) Franke C et al; Chemosphere 29: 1501-14 (1994) (8) Ogata M et al; Bull Environ Contam Toxicol 33: 561-7 (1984) (9) NITE; Chemical Risk Information Platform (CHRIP). Biodegradation and Bioconcentration. Tokyo, Japan: Natl Inst Tech Eval. Available from, as of Mar 3, 2014: http://www.safe.nite.go.jp/english/db.html **PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), styrene, which has a vapor pressure of 6.4 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase styrene is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals, ozone and nitrate radical; the half-lives for these reactions in air are 2.4, 24 and 3.7 hours, respectively(3). Direct photochemical or photolytic reactions for styrene are likely to be slow(4). Styrene absorbs little light from solar radiation at wavelengths above 300 nm that reach the lower atmosphere(4). Experimental studies have shown that natural sunlight does not cause photolytic degradation in a 6 hr period of exposure(5).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Chao J et al; J Phys Chem Ref Data 12: 1033-63 (1983) (3) Atkinson R; Atmos Environ 34: 2063-101 (2000) (4) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (5) Kopczynski SL et al; Environ Sci Technol 6: 342-7 (1972)] **PEER REVIEWED**

Environmental Biodegradation:
AEROBIC: Styrene biodegraded 97 and 87% in 16 weeks in a landfill soil and sandy loam soil, respectively. Degradation was not detected in sterile soil(1). Styrene was biodegraded at all experimental concentrations in soil, but decreased with an increase in styrene concentration; 62% at 20 ug/kg to 16% at 1000 mg/kg(2). The rate of microbial transformation varied in different soils and was notably slower in an acid silt loam (pH 4.87)(2). Degradation of styrene of 2.3 to 4.3% per week and 3.8-12.0% per week in subsurface soil was shown with samples taken directly above and below aquifers from Pickett, OK and Fort Polk, LA, respectively; degradation in autoclave samples was not observed(3).
[(1) Sielicki M et al; Appl Environ Microbiol 35: 124-28 (1978) (2) Fu MH, Alexander M; Environ Sci Technol 26: 1540-4 (1992) (3) Wilson JT et al; Devel Indust Microbiol 24: 225-33 (1983)] **PEER REVIEWED**

AEROBIC: Styrene, present at 100 mg/L, reached 100% of its theoretical BOD in 2 weeks using an activated sludge inoculum at 30 mg/L in the Japanese MITI test(1). In lake water, 10 to 20% mineralization was observed in 3 weeks with samples containing 2.5 ug to 1.0 mg/L styrene(2). Transformation required several days for acclimation of the indigenous microorganisms(2). Degradation is rapid in sewage when oxygen is available(3). Styrene, incubated using a sewage seed, had CO2 production of 10-12% and 6-23% in 36 and 17 days, respectively(4). Styrene degradation of 42-80% has been reported with the Zahns-Wellen screening test(5).
[(1) NITE; Chemical Risk Information Platform (CHRIP). Biodegradation and Bioconcentration. Tokyo, Japan: Natl Inst Tech Eval. Available from, as of Mar 3, 2014: http://www.safe.nite.go.jp/english/db.html (2) Fu MH, Alexander M; Environ Sci Technol 26: 1540-4 (1992) (3) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (4) Pahren HR, Bloodgood DE; Water Pollut Contr Fed J 33: 233-38 (1961) (5) Wellens H; A Wasser

Abwasser Forsch 23: 85-98 (1990)] **PEER REVIEWED**

AEROBIC: In 11 weeks, biofilms, when provided with a mixture of organic compounds, destroyed 99% or more of the styrene in solution at initial concentrations of 81 and 280 ug/L, but the oxidation was less extensive when the water was supplemented with 8 or 21 ug/L styrene(1). Removal of >99% in an aerobic biofilm column with 20 minute detention time and 8% removal in a methanogenic biofilm column with a 2 day retention time was reported(2). Styrene was degraded in mixed propane-utilizing bacteria isolated from soil and lakes, styrene oxide was formed as a product(3).
[(1) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (2) Bouwer EJ, McCarty PL; Ground Water 22: 433-40 (1984) (3) Hou CT et al; Appl Environ Microbiol 46: 171-77 (1983)] **PEER REVIEWED**

ANAEROBIC: Methanogentic consortia derived from anaerobic sludge were shown to degrade styrene(1). The initial transformation of styrene involves the addition of water across the double bond in the unsaturated side chain, resulting in the formation of phenylethanol(1).
[(1) Grbic-Galic D; Geomicrobiology J 8: 167-200 (1990)] **PEER REVIEWED**

Environmental Abiotic Degradation:
The reaction half-live of vapor-phase styrene with photochemically-produced hydroxyl radicals, ozone and nitrate radical have been reported as 2.4, 24 and 3.7 hours, respectively(1). The atmospheric oxidation products of styrene include formaldehyde, benzaldehyde, benzoic acid, peroxybenzoyl nitrate, 2-nitrophenol, and formic acid(2-3). Styrene is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(3). Direct photochemical or photolytic reactions for styrene are likely to be slow(4). Styrene absorbs little light from solar radiation at wavelengths above 300 nm that reach the lower atmosphere(4). Experimental studies have shown that natural sunlight does not cause photolytic degradation in a 6 hr period of exposure(5).
[(1) Atkinson R; Atmos Environ 34:2063-101 (2000) (2) Kao AS; J Air Waste Manage Assoc 44: 683-96 (1994) (3) Grosjean D; Sci Total Environ 46: 41- 59 (1985) (4) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (5) Kopczynski SL et al; Environ Sci Technol 6: 342-7 (1972)] **PEER REVIEWED**

Environmental Bioconcentration:
A BCF of 13.5 for goldfish was determined for styrene(1). According to a classification scheme(2), this BCF suggests bioconcentration in aquatic organisms is low(SRC). Calculated biomagnification of styrene in water respiring organisms (zooplankton, forage and predatory fish) and air breathing organisms (reptile, amphibian, sea bird, marine mammal, terrestrial herbivore and carnivore, human) were all <1(3).
[(1) Ogata M et al; Bull Environ Contam Toxicol 33: 561-7 (1984) (2) Franke C et al; Chemosphere 29: 1501-14 (1994) (3) Kelly BC et al; Science 317: 236-9 (2007)] **PEER REVIEWED**

Soil Adsorption/Mobility:
The log Koc of styrene is reported to be 2.96(1). According to a classification scheme(2), this Koc value suggests that styrene is expected to have low mobility in soil. More than 85% of styrene is sorbed in 78 hrs on samples from a sandy aquifer(3). Styrene is retained by particulates particularly in organic matter-rich soils(3). Of styrene that had been allowed to sorb for 3 days, 61.0 and 66.7% was desorbed in 16 days from soil and aquifer soils, respectively(4).
[(1) Schuurmann G et al; Environ Sci Technol 40: 7005-11 (2006) (2) Swann RL et al; Res Rev 85: 17-28 (1983) (3) Fu MH, Alexander M; Environ Sci Technol 26: 1540-4 (1992) (4) Fu MH et al; Environ Toxicol Chem 13: 749-53 (1994)] **PEER REVIEWED**

Volatilization from Water/Soil:
The Henry's Law constant for styrene is reported as 2.75X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that styrene is expected to volatilize from water surfaces(2). Under laboratory conditions, 50% of 2 to 10 mg styrene per liter (depth not specified) was lost by volatilization in 1 to 3 hrs in lake water samples and in 6 to 7 hrs in distilled water, respectively(3). In other studies, the level of styrene in water samples fell from 23 to 3.3 and 0.4 mg/L in 2 hrs and 7 days, respectively, and from 46 to 12.5 and 1.5 mg/L in 2 hrs and 10 days, respectively(4). These findings are relevant to surface waters but not to deeper waters(4). The volatilization half-life of styrene in Rhine River water was 14 days(5). Volatilization of styrene from moist soil surfaces would be slower than in water(4). Samples at 1.5 cm deep of a loamy soil, 26% of 2 mg/kg styrene added volatilized in 31 days(3). The transfer to the air was even slower and less extensive from deep soil(4). The potential for volatilization of styrene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 6.4 mm Hg(6).
[(1) Bocek K; Experimetia, Suppl 23: 231-40 (1976) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Fu MH, Alexander M; Environ Sci Technol 26: 1540-4 (1992) (4) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (5) Zoeteman BCJ et al; Chemosphere 9: 231-49 (1980) (6) Chao J et al; J Phys Chem Ref Data 12: 1033-63 (1983)] **PEER REVIEWED**

Environmental Water Concentrations:
GROUNDWATER: In National Drinking Water Contaminant Occurrence Database (NCOD), a repository of ambient water quality data, the concentration of styrene in groundwater averaged 3.8 ug/L (range, 0.2-64 ug/L) for 21 of 4,727 stations with analyses(1). In a National water-quality assessment program run on ground water samples from across the country, styrene was detected in 2 of the 562 samples studied at 0.21 to 2.3 ug/L; samples were taken May 3, 1999 to Oct 23, 2000(2). Styrene was detected in 26 of 1202 groundwater samples collected across the US from 1985 to 2002(3). Styrene was detected in Iowa well water at 1.0 ppb(4) and detected, not quantified, in a private well in Wisconsin(5). Styrene was detected, not quantified, in ground water in England(6) and found at a maximum concentration of 10 ppb in Netherlands(7). Well water adjacent to a landfill containing buried styrene in drums at Gales Ferry, CT had styrene concentrations of 100-200 ppb in 1962(8). The maximum concentration of styrene detected in the Biscayne Aquifer near Superfund sites in Miami, FL

was 6.3 ug/L(9). Styrene was detected in 7-8% of 214 ground water samples from 30 industrial sites in samples taken in 1999 in Taiwan(10).
[(1) USEPA; National Contaminant Occurrence Database (NCOD). Styrene. Available from, as of Mar 12, 2014: http://water.epa.gov/scitech/datait/databases/drink/ncod/databases-index.cfm (2) Grady SJ; in National Water-quality Assessment Program. National Synthesis on Volatile Organic Compounds. US Geological Survey, 1-85 (2003) (3) Rowe BL et al; Environ Health Perspect 115:1539-46 (2007) (4) Kelley RD; Synthetic Organic Compounds Sampling Survey of Public Water Supplies p 38 NTIS PB 85-214427 (1985) (5) Krill RM, Sonzogni WC; J Amer Water Assoc 78: 70-75 (1986) (6) Fielding M et al; Organic Micropollutants in Drinking Water Medmenham, Eng Water Res Cent p 49 TR-159 (1981) (7) Zoetemann BCJ; Sci Total Environ 21: 187-202 (1981) (8) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene and Related Compounds p 261 USEPA-560/11-80-018 (1980) (9) Canter LW, Sabatini DA; Intern J Environmental Studies 46: 35-57 (1994) (10) Kuo MCT et al; Bull Environ Contam Toxicol 65: 654-9 (2000)] **PEER REVIEWED**

GROUNDWATER: Styrene has been found in ground water as a result of leaching from a surface impoundment in Walbro Corp, Cass City, MI. Ground water contamination with styrene has occurred at the Valley of Drums - Taylor site, Shepherdsville, KY. Leachate, leaks, and spills from discarded drums, as well as other mismanagement incidents contributed to these contaminations. Reich Farm Site is a landfill located in Dover TWP, NJ. Leaks from waste containers and "midnight dumping" contaminated the ground water in the area with styrene at a concentration of 0.012 ppm.
[SAIC/JRB; SIAC/JRB Damage Incidents Data Base (1985)] **PEER REVIEWED**

DRINKING WATER: In National Drinking Water Contaminant Occurrence Database (NCOD), a repository of drinking water quality data, the concentration of styrene in Public Water System (PWS) drinking water derived from surface water averaged 18.4 ug/L (range, 0.044-660 ug/L) for 36 of 1,490 PWS with analyses(1). The concentration of styrene in drinking water derived from ground water under the influence of surface water was 0.2 ug/L for one of 96 PWS with analyses(1). Drinking water derived from ground water averaged 1.5 ug/L (range, 0.03-10 ug/L) for 90 of 9,023 PWS with analyses(1). In a survey of Canadian drinking water supplies, the frequency of detection of styrene was low(2); when detected, it was generally at a concentration of <1 ug/L(2). Styrene was detected in the water supply of Cincinnati, OH at a concentration of 0.024 ppb(3). Styrene was detected, but not quantified, in municipal drinking water from Evansville, IN(4) and Cleveland, OH(5). Styrene was not detected in 945 finished water supplies throughout US which use ground water sources(6). Styrene was detected, not quantified, in finished drinking water in Louisiana; Cincinnati, OH; Indiana; Grand Forks, ND(7).
[(1) USEPA; National Contaminant Occurrence Database (NCOD) for Styrene. Available from, as of Mar 12, 2014: http://water.epa.gov/scitech/datait/databases/drink/ncod/databases-index.cfm (2) IARC; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer 60: 248 (1994) (3) Coleman WE et al; Arch Environ Contam Toxicol 13: 171-78 (1984) (4) Kleopfer RD, Fairless BJ; Environ Sci Technol 6: 1036-37 (1972) (5) Sanjivamurthy VA; Water Res 12: 31-33 (1978) (6) Westrick JJ et al; J Amer Water Works Assoc 76: 52-59 (1984) (7) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water. Washington, DC: USEPA-600/4-76-062 p. 213-14 (1976)] **PEER REVIEWED**

SURFACE WATER: In National Drinking Water Contaminant Occurrence Database (NCOD), a repository of ambient water quality data, the concentration of styrene in "other" surface water averaged 0.33 ug/L (range, 0.2-0.6 ug/L) for 5 of 503 stations with analyses(1). In a National water-quality assessment program run on surface water samples from across the country, styrene was detected in 1 of 169 and 2 of 202 source river and reservoir water at 2.3 and 0.41-0.97 ug/L, respectively(2). Samples were taken May 3, 1999 to Oct 23, 2000 throughout the US(2). A water sample from lower Tennesee River contained 4.2 ppb styrene(3). Styrene was detected, not quantified, in Delaware River(4) or the Great Lakes(5). Styrene was detected at 1 ppm found in Kanawha River, WV(6). No styrene was found in a 1988 survey of Canadian Rivers(7). Styrene was detected, not quantified, in samples from the Waal River, The Netherlands(8) and surface waters of England(9). A median concentration of styrene in River Elbe (Germany) in 1992 was 14 ng/L (range 6.1-46 ng/L)(10).
[(1) USEPA; National Contaminant Occurrence Database (NCOD) for Styrene. Available from, as of Mar 12, 2014: http://water.epa.gov/scitech/datait/databases/drink/ncod/databases-index.cfm (2) Grady SJ; in National Water-quality Assessment Program. National Synthesis on Volatile Organic Compounds. US Geological Survey, 1-85 (2003) (3) Goodley PC, Gordon M; Kentucky Academy of Science 37: 11-15 (1976) (4) Sheldon LS, Hites RA; Environ Sci Technol 12: 1188-94 (1978) (5) Meijers AP, Vanderlee RC; Water Res 10: 597-604 (1976) (6) National Academy of Sciences; The Alkyl Benzenes. Washington, DC National Academy Press USEPA Contract 68-01-4655 (1980) (7) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (8) Fielding M et al; Organic Micropollutants in Drinking Water Medmenham, Eng Water Res Cent p 49 TR-159 (1981) (9) Great Lakes Water Quality Board; An Inventory of Chemical Substances Identified in the Great Lakes Ecosystem Vol.1 - Summary p 195 Report to the Great Lakes Water Quality Board, Windsor, Ontario, Canada (1983) (10) Gotz R et al; Chemosphere 36: 2103-18 (1998)] **PEER REVIEWED**

SNOW: Styrene was identified in 1 of 10 early March snow samples, with a concentration of 0.08 ug/kg reported at Shosse Entuziastov, a heavy industrialized area of Moscow, Russia(1).
[(1) Poliakova OV et al; Toxicol Environ Chem 75: 181-94 (2000)] **PEER REVIEWED**

Effluent Concentrations:
Based upon gasoline vehicle emission data, the region wide emission rate (southern California, greater Los Angeles area) of styrene has been estimated to be 8500 kg/day(1); exhaust from gasoline engines was found to have the following styrene composition: catalyst equipped, 0.21 wt% of total organic gas emissions; noncatalyst equipped, 0.66 wt% of total organic gas emissions(1). Unspecified industrial wastewater in US contained styrene at a concentration <10 ppb(2). Styrene concentrations of <0.1 to 7 mg/cu m have been detected in gas emissions from solid waste landfills(3). The average concentration of styrene in emissions from Municipal landfill sanitary sites in the US was 1,517 ppbV(4).
[(1) Harley RA, Cass GR; Environ Sci Technol 28: 88-98 (1994) (2) Perry DL et al; Identification of Organic Compounds in Industrial Effluent Discharges. Washington, DC: USEPA-600/4-79-016 (1979) (3) Assmuth T, Kalevi K; Chemosphere 24: 1207-16 (1992) (4) Brosseau J, Heitz M; Atmos Environ 28: 285-93 (1994)] **PEER REVIEWED**

In a study of organic emissions from pulverized coal combustion, styrene was found to have minimum and maximum emission factors of 2.686X10-7 and 5.882X10-7 lb per 1X10+6 BTU(1). Wastewater effluent from an Louisiana oil refinery contained 31 ppb of styrene(2). Air in vicinity of oil fire contained 0.5 ppm styrene(3). The pyrolysis and combustion of scrap tires at 850 deg C with different bulk air ratios, resulted in the emission of styrene at 910 to 4700 mg/kg tires and 110 to 650 mg/kg tires, respectively(4). Pyrolysis of the scrap tires at temperatures ranging from 650 to 1050 deg C gave emission rates of 84 to 5200 mg/kg tires(4). Styrene was identified as a volatile released in car fires(5).

[(1) Miller CA et al; Environ Sci Technol 28: 1150-8 (1994) (2) Keith LH; Sci Total Environ 3: 87-102 (1974) (3) Perry R; Mass Spectrometry in the Detection and Identification of Air Pollutants. Int Symp Ident Mass Environ Pollut pp. 130-37 (1971) (4) Fullana a et al; Environ Sci Technol 34: 2092-9 (2000) (5) Lonnermark A, Blomqvist P; Chemosphere 62: 1043-56 (2005)] **PEER REVIEWED**

Styrene was detected, not quantified, in various chemical, textile, and latex effluents in Louisville, KY, Calvert City, KY, Colliersville, TN, Memphis, TN and other US locations(1). In a study of volatile organic emissions from new carpets, styrene was found to have an emission rate of 16.6 mg/sq m in the first 24 hrs and 25.9 mg/sq m in the first 168 hr(2). The emission rate of styrene from dry-process photocopiers ranged from 40-220 ug/hr per copier while idle and 300-12,000 ug/hr per copier during operation(3). The emission factor of styrene from prime urethane cushions ranged from 92-94 ug/sq m hr measured for 6 hrs in a 4 L dynamic chamber, 118-192 ug/sq m hr measured for 6 hrs in a 52 L chamber, and <1-8 ug/sq m hr measured for 96 hrs in a 52 L chamber(4). The concentration of styrene released from a tufted textile floor covering with styrene-butadiene rubber (SBR) backing under equilibrium conditions ranged from 5.6 ng/L at 23 deg C to 14.9 ng/L at 71 deg C(5).
[(1) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water. Washington, DC: USEPA-600/4-76-062 pp. 213-4 (1976) (2) Hodgson AT et al; J Air Waste Manage Assoc 43: 316-24 (1993) (3) Leovic KW et al; Air Waste Manage 46: 821-9 (1996) (4) Schaeffer VH et al; J Air Waste Manage Assoc 46: 813-20 (1996) (5) Sollinger S et al; Atmos Environ 28: 2369-78 (1994)] **PEER REVIEWED**

Styrene, with o-xylene, was detected as a volatile given off of corn, alfalfa, and cereal silage, high moisture ground corn, total mixed ration, almond hulls and shells at 0.05, 0.19, 0.20, 0.17, 0.28, 0.15 and 0.12 ng/L(1). Styrene was qualitatively detected in combustion emissions in a study of simulated field burning of agricultural plastics(2).
[(1) Malkina IL et al; J Environ Qual 40:28-36 (2011) (2) Linak WP et al; JAPCA 39: 836-46 (1989)] **PEER REVIEWED**

Sediment/Soil Concentrations:
SEDIMENTS: Water/sediment sample from lower Tennessee river contained 4.2 ppb of styrene(1). Styrene was detected, not quantified, in sediments from Lake Tobin, Saskatchewan Canada(2).
[(1) Goodley PC, Gordon M; Kentucky Academy of Science 37: 11-15 (1976) (2) Samoiloff MR et al; Environ Sci Technol 17: 329-34 (1983)] **PEER REVIEWED**

SOIL: In a 1986 report of a survey of 455 hazardous waste sites, styrene was found in samples of soil from 3.5% of the sites(1); in samples in which it was present, the geometric mean was 0.53 mg/kg(2). Soil at an unspecified site in Canada contained up to 0.2 ug/kg styrene(3). Styrene was detected in 2.5% of 705 samples from 30 industrial sites in samples taken in 1999 in Taiwan(4).
[(1) Goodley PC, Gordon M; Kentucky Academy of Science 37: 11-15 (1976) (2) ATSDR; Toxicological Profile for Styrene. Sept 1992. Atlanta, GA: ATSDR p. 81-2 (1992) (3) Alexander M; Crit Rev Env Sci Technol 27: 383-410 (1997) (4) Kuo MCT et al; Bull Environ Contam Toxicol 65: 654-9 (2000)] **PEER REVIEWED**

Atmospheric Concentrations:
URBAN/SUBURBAN: In a survey of monitoring data that includes the USEPA's National Ambient Volatile Organic Compound Database, styrene was found to have been monitored at 21 different locations with 6,117 samples collected(1); the avg concentration of styrene in samples above detection limit was 0.6 ug/cu m(1). Except in highly polluted areas, styrene concentrations in outdoor air are generally < 1 ug/cu m(2). In another survey, the median concentration of styrene was 2.1 ppb from 135 samples in US(3). The mean concentration of styrene was 0.07-0.25 ppb in 3 New Jersey cities(4-6). The concentration of styrene was 0.5-3 ppb in Los Angeles, CA(6) and 0.09 ppb in Contra Costa, CA(7). The styrene concentration was 1-15 ppb in four California cities(8). The avg concentration of styrene in air from Phoenix and Tucson, AZ was 0.49-5.64 ppbv and 0.09-0.23 ppbv, respectively, during the period from 1994-1996(9). Outdoor atmospheric concentrations of styrene for 46 students from Philip Randolph Academy in Harlem, New York City were 0.43 and 0.32 ug/cu m in the winter and summer, respectively(10). Styrene was detected in 1503 of 2507 samples in urban/suburban and rural/remote locations throughout Minnesota, concentrations were 0.06-1.49 ug/cu m in positive samples(11).
[(1) Kelly TJ et al; Environ Sci Technol 28: 378A-87A (1994) (2) IARC; Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer 60: 247-8 (1994) (3) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. Menlo Park, CA: Atmospheric Science Center. SRI Intl Contract 68-02-3452 (1982) (4) Harkov R et al; J Air Pollut Control Assoc 33: 1177-83 (1983) (5) Harkov R et al; Sci Total Environ 38: 259-74 (1984) (6) Wallace LA; Toxicol Environ Chem 12: 215-36 (1986) (7) Grosjean D, Fung K; J Air Pollut Control Assoc 34: 537-43 (1984) (8) Neligan RE et al; ACS Natl Mtg pp. 118-21 (1965) (9) Zielinska B et al; J Air Waste Manage Assoc 48: 1038-50 (1998) (10) Kinney PL et al; Environ Health Perspect 110: 539-46 (2002) (11) Pratt GC et al; Environ Health Perspect 108: 815-25 (2000)] **PEER REVIEWED**

URBAN/SUBURBAN: The average concentration of styrene was less than or equal to 0.1 ppb (0.7 ppb max) in Delft, Netherlands(1). Styrene was detected, not quantified, in 6 former Soviet Union cities(2). The concentration of styrene was reported as 0.1-0.4 ppb in Dutch cities(3) and 0.2 ppb in Nagoya, Japan(4). The concentration of styrene at Porto Alegre, Brazil between March 20, 1996 and April 16, 1997 was 0.1-1.5 ppb(5). Styrene was measured at not detected to 2.0 ug/cu m in Girona, Spain; samples were collected Sep 2009 to Mar 2010(6). Styrene was detected at 0.4-12.0 ug/cu m from samples taken at 25 sites in Toronto, Canada in 1990(7). At 32 indoor and outdoor sites in Perth, Western Australia, styrene was detected at 0.0-2.4 ppb; samples were collected Aug to Dec 2000(8). Urban and suburban styrene concentrations were 0.1-61.3 and 0.1-41.7 ug/cu m, respectively; samples were collected 2005 to 2007 in London and Birmingham, England(9).
[(1) Bos R et al; Sci Total Environ 7: 69-81 (1977) (2) Ioffe BV et al; Environ Sci Technol 13: 864-68 (1979) (3) Smeyers-Verbeke NJ et al; Atmos Env 18: 2471-8 (1984) (4) IARC; Some Monomers, Plastics and Synthetic Elastomers and Acrolein 19: 231 (1979) (5) Grosjean E et al; Environ Sci Technol 33: 1970-8 (1999) (6) Alonso M et al; Environ Sci Technol 44(21): 8289-94 (2010) (7) Campbell ME et al; Can J Public Health 86: 351-7 (1995) (8) Hinwood AL et al; Chemosphere 63: 421-9 (2006) (9) Saborit JMD et al; Environ Sci Technol 43: 4582-8 (2009)] **PEER REVIEWED**

Ambient levels /of styrene/ measured worldwide are normally less than 1.0 ppb.
[NTP; Executive Summary: Styrene (Draft) p.9 (1985)] **PEER REVIEWED**

URBAN/SUBURBAN: Styrene concentrations reported in the atmosphere for newly constructed buildings in Melbourne, Australia(1).

Days After Construction	Livingroom (ug/cu m)	Bedroom (ug/cu m)	Outdoor (ug/cu m)
2	32	<30	0.4
19	27	18	0.5
72	16	2.7	
246	1.6	2.2	1.5

[(1) Brown SK; Indoor Air 12: 55-63 (2002)] **PEER REVIEWED**

RURAL/REMOTE: Styrene was detected in air of a National Forest in Alabama(1). Styrene was detected in 1503 of 2507 samples in urban/suburban and rural/remote locations throughout Minnesota, concentrations were 0.06-1.49 ug/cu m in positive samples(2). The concentration of styrene at a location 20 km from Porto Alegre, Brazil was <0.1 ppb(3). Rural styrene concentrations were 0.1-10.8 ug/cu m; samples were collected 2005 to 2007 in West Midlands and South Wales(4).
[(1) IARC; Some Monomers, Plastics and Synthetic Elastomers and Acrolein. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer 19: 231 (1979) (2) Pratt GC et al; Environ Health Perspect 108: 815-25 (2000) (3) Grosjean E et al; Environ Sci Technol 33: 1970-8 (1999) (4) Saborit JMD et al; Environ Sci Technol 43: 4582-8 (2009)] **PEER REVIEWED**

INDOOR AIR: Slightly higher styrene levels were observed (1.85 ppb before occupancy and 2.08 ppb after occupancy) in rooms in an office building after occupancy probably because of emissions from glued carpet(1). Certain solvent-based adhesives used to finish interior of office buildings emit styrene(2). In indoor air, the mean concentrations are frequently higher (< 1-6 ug/cu m), smoking making a large contribution(3); off-gassing of styrene from some styrene containing household products may also contribute to indoor air levels(3). The median concentration of styrene was 0.4 ppb in indoor air of a New Jersey city(4). The mean concentration of styrene in the indoor air of homes with smokers and nonsmokers was 2.11 ug/cu m (range, 0.49-7.02 ug/cu m) and 1.47 ug/cu m (range, 0.43-4.96 ug/cu m), respectively(5). Indoor atmospheric concentrations of styrene for 46 students from Philip Randolph Academy in Harlem, New York City were 1.25 and 0.80 ug/cu m in the winter and summer respectively(6). Air samples taken in the Boston Exposure Assessment Microenvironments study had geometric means of 3.04 and 1.19 ug/cu m in retail stores and dining areas for samples taken the summer of 2003 and winter of 2004 and 2005(7). The concentration of styrene in a parked, sun exposed new vehicle was 79.7 to 83.4 ug/cu m in a similar three year old vehicle the concentration was 10.2 to 24.9 ug/cu m(8).
[(1) Wallace LA et al; Atmos Environ 21: 385-93 (1987) (2) Girman JR et al; Environ International 12: 317-321 (1986) (3) IARC; Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer 60: 247-8 (1994) (4) Wallace L et al; J Occup Med 28: 603-7 (1986) (5) Heavner DL et al; Environ Int 21: 3-21 (1995) (6) Kinney PL et al; Environ Health Perspect 110: 539-46 (2002) (7) Loh MM et al; Environ Sci Technol 40: 6903-11 (2006) (8) Buters JTM et al; Environ Sci Technol 41(7): 2622-9 (2007)] **PEER REVIEWED**

INDOOR AIR: Styrene was detected in 33 cafes and 8 restaurants that allow smoking at 0.8-12.3 ug/cu m and at 0.5-1.2 ug/cu m in 4 non-smoking cafes and 11 non-smoking restaurants; samples were collected from Sep 2009 to Mar 2010 in Girona, Spain(1). In one case, from a survey of the indoor air in 178 buildings located in the United Kingdom, carpet was determined to be the source of styrene at 0.9 ppm(2). In a country wide study of 10 Provinces in 4 regions of Canada, 754 residential indoor air samples had a mean styrene concentration of 0.07, 0.77, 0.21 and 0.09 ug/cu m, sampled in the winter, spring, summer and fall, respectively(3). London, England office air concentrations of styrene were 0.7-5.5 and 0.3-10.4 ug/cu m in samples collected Dec 9-11 and 11-15, 1991, respectively(4). The geometric mean concentration of styrene was 0.5-<1.5 ppb in 11 homes (4 manufactured, 7 site built), that were constructed 1997 to 1998(5). Styrene was reported at 0-4 ug/cu m in 5 homes in Niigata Prefecture, Japan(6).
[(1) Alonso M et al; Environ Sci Technol 44(21): 8289-94 (2010) (2) Crump DR; Issues Environ Sci Technol 4: 109-24 (1995) (3) Fellin P, Otson R; Atmos Environ 28:3581-6 (1994) (4) Field RA et al; Environ Technol 13: 391-408 (1992) (5) Hodgson AT et al; Indoor Air 10: 178-92 (2000) (6) Sakaguchi J, Akabayashi S; Indoor Air 13: 42-9 (2003)] **PEER REVIEWED**

SOURCE DOMINATED: Ambient atmospheric styrene levels from the vicinity of six reinforced plastic processors located in Florida, Michigan, and Ohio have ranged from 0.07 to 690 ppb(1). In communities farther away from these processors, styrene was detected at a concentration range of 0.4-5.6 ppb(1). The maximum concentration of styrene in 7 sanitary and hazardous landfills in New Jersey was 15.5 ppb with a mean range of 0.12-1.53 ppb(2). As part of a 1990 Atlanta Ozone Precursor Monitoring Study, the concentration of styrene in air near roadways was 0.437 ppbC, measured in a tunnel-like underpass during periods of heavy traffic(3). A calculated styrene release rate measured from 23 locations in Minneapolis/St Paul, MN was 12 metric tons/year from publicly owned water treatment works(4). Styrene was detected inside and outside the Baltimore Harbor Tunnel tollbooths in the summer of 2001 at 0.05-1.19 and 0.05-1.68 ug/cu m(5). In the Allegheny mountain tunnel in Pennsylvania, the concentration of styrene due to vehicular traffic varied from 0.3-1.6 ppb(6). The concentration of styrene in the Caldecott Tunnel, San Francisco, CA ranged from 9.83-36.73 ppb carbon(7). Styrene was detected at all 18 sampling sites outside a tire recapping unit in Itatiaia, Brazil; concentrations were 8-96 mg/cu m, samples were collected July 6, 2001(8). Styrene was also reported at 1185 and 468 mg/cu m at the exhauster and chimney sites, respectively(8).
[(1) McKay RT et al; Environ Pollut Ser B. 4: 135-41 (1982) (2) Harkov R et al; J Environ Sci Health A20: 491-501 (1985) (3) Conner TL et al; J Air Waste Manage Assoc 45: 383-94 (1995) (4) Pratt Gc et al; Environ Sci Technol 38: 1949-59 (2004) (5) Sapkota A et al; Environ Sci Technol 39: 2936-43 (2005) (6) Hampton CV et al; Environ Sci Tech 17: 699-708 (1983) (7) Zielinska B, Fung KK; Sci Tot Environ 146/147: 281-8 (1994) (8) Correa SM et al; Bull Environ Contam Toxicol 72: 255-60 (2004)] **PEER REVIEWED**

SOURCE DOMINATED: Occupation exposure to styrene in the US trucking industry (local drivers including smoking (S) and

non-smoking (NS), loading dock and machine shop workers) from 15 cities sampled Jan 2004 to Aug 2006 gave the following results(1):

Sample Type	No. Samples	Mean (ug/cu m)	Median (ug/cu m)
Background	432	0.26	0.15
NS Driver	235	8.63	0.55
S Driver	62	1.46	0.66
Loading Dock	64	0.74	0.51
Machine Shop	19	0.60	0.49

[(1) Davis ME et al; Environ Sci Technol 41: 7152-8 (2007)] **PEER REVIEWED**

Food Survey Values:

Styrene was detected, not quantified, in roasted filbert nuts and in 4 of 7 whiskey samples(1). Styrene was tentatively identified in a commercial hickory-wood smoke flavor and in food and water stored in a refrigerator with a plastic interior(2). Styrene was also found in yogurt packaged in polystyrene containers at concentration of 2.5-34.6 ug/kg with styrene content in yogurt increasing with time(2). The concentration of 59.2 ug/kg found in butter-fat cream after 24 days, 9.3 ug/kg in cottage cheese after 27 days and 22.7 ug/kg in honey after 120 days(2). Analytical surveys of food and food packaging have shown that styrene migrates into food from both rigid and expanded polystyrene foam containers(3). The highest migration figure (235.5 ppb) was found in samples of sour cream contained in rigid polystyrene containers(4).

[(1) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene, and Related Compounds p 261 USEPA-560/11-80-018 (1980) (2) IARC; Some Monomers, Plastics and Synthetic Elastomers and Acrolein. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer 19: 231 (1979) (3) WHO; Environ Health Criteria 26 (Styrene). Geneva, Switzerland: WHO (1983) (4) Withey, JR, Collins PG; Bull Environ Contam Toxicol 19: 86-94 (1978)] **PEER REVIEWED**

Styrene has been detected as a natural constituent of a wide range of foods and beverages, the highest measured levels occurring in cinnamon(1); enzymatic degradation of cinnamic acid derivatives was proposed as the possible source of styrene(1). Styrene has been detected in plums (2 ug/kg)(2), nectarines(3), grapes(4), and scrambled eggs (103 ng/g)(5). Styrene levels of 3.9-240 ppb (avg, 20.6 ppb) were reported in a survey of 234 table-ready food items from the FDA's Total Diet Study with the highest concentration in fruit yogurt(6). The concentration of styrene in sandwich cookies, margarine, butter, and cake doughnuts was 216, 9.28, 22.4, and 23.0 ppb, respectively(6). The concentration of styrene in commercial fermented soybean curds was 34 ug/kg(7).

[(1) IARC; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 60: 247-8 (1994) (2) Gomez E et al; J Agric Food Chem 41: 1669-76 (1993) (3) Takeoka GR et al; J Agric Food Chem 36: 553-60 (1988) (4) Stevens KL et al; J Food Sci 30: 1006-7 (1965) (5) Matiella JE, Hsieh TCY; J Food Sci 56: 387-90 (1991) (6) Heikes DL et al; J Agric Food Chem 43: 2869-75 (1995) (7) Chung HY; J Agric Food Chem 47: 2690-96 (1999)] **PEER REVIEWED**

Styrene was detected in the following foods during the US FDA total diet program that was run 1996 to 2000 with samplings done four times a year. Styrene was not detected in banana, fruit flavored sherbert and carbonated cola beverage(1).

Food	No. Positive	Concn (ppb)
canned tuna in oil	1	2
fruit flavored cereal	3	2-10
peanut butter	13	16-38
raw avocado	8	3-550
raw orange	2	2-3
raw strawberries	9	12-350
coleslaw w/dressing	1	2
sweet roll/danish	13	13-91
blueberry muffins	10	8-141
cake donuts w/icing	10	6-45
graham crackers	6	4-21
sugar cookies	14	24-142
chocolate chip cookies	12	15-111
sandwich cookies	14	15-165

chocolate cake w/frosting	12	7-55
apple pie	9	10-40
potato chips	6	2-16
popcorn popped in oil	3	2-2
butter	12	11-28
margarine	10	9-20
olive/safflower oil	11	3-54
American cheese	4	2-11
cheddar cheese	3	4-70
cream cheese	2	2-3
sour cream	3	5-30
mixed nuts	14	21-104
beef frankfurters	8	4-77
bologna	7	2-78
ground beef	6	4-13
cooked hamburger	6	4-27
cooked hamburger w/cheese	5	5-22
cheese pizza	6	3-23
cheese/pepperoni pizza	7	8-20
chicken nuggets	12	10-66
french fries	12	8-68
popsicle	3	4-11

[(1) Fleming-Jones ME, Smith RE; J Agric Food Chem 51: 8120-7 (2003)] **PEER REVIEWED**

Fish/Seafood Concentrations:
The concentration of styrene in Korean salt-fermented fish and shrimp pastes were as follows: anchovy, 69.0 ng/g; big eyed herring, 223 ng/g; shrimp, 180 ng/g(1). The concentration of styrene in crabs (Charybdis feriatus) were 4.4 ug/kg dry wt for leg meat, 7.3 ug/kg dry wt for body meat, and 27.0 ug/kg for carapace meat(2).
[(1) Cha YJ, Cadwallader KR; J Food Sci 60: 19-24 (1995) (2) Chung HY; J Agric Food Chem 47: 2280-7 (1999)] **PEER REVIEWED**

Milk Concentrations:
Styrene was detected at 17.2 ug/kg in homogenized milk after 19 days storage in polystyrene packaging(1). Thirty-five milk samples from 8 grocery stores representing 8 processing plants from Arizona, California, Nevada and Utah were collected Jan-Feb 2002; styrene was detected at 0.04-1.59, 0.04-0.79 and 0.02-0.73 ng/mL in whole, 2% and 1% milk, respectively(2). Styrene was detected, but not quantified, in 8 of 8 human breast milk samples from US women in 4 cities(3).
[(1) IARC; Some Monomers, Plastics and Synthetoc Elastomers and Acrolein. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 19: 231 (1979) (2) Hiatt MH, Pia JH; Arch Environ Contam Toxicol 46: 189-96 (2004) (3) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]] **PEER REVIEWED**

Other Environmental Concentrations:
Styrene was detected in two coal tars at 0.01-0.02%(1). Styrene was qualitatively detected in a household product of liquid wax(2). Styrene has been detected at 18.0 ug/cigarette in the smoke of American domestic, filter blend cigarettes(3). The avg concentration of styrene from tobacco smoke in an exposure chamber designed to simulate passive indoor exposure ranged from 3.2-22.1 ug/cu m(4). The avg emission factor of styrene for 6 commercial brands of cigarettes was 147 ug/cigarette (range, 340-480 ug/cigarette)(5). The delivery of styrene in mainstream cigarette smoke ranges from 0.3 to 5.4 mg/cigarette(6).
[(1) Enzminger JD, Ahlert RC; Environ Technol Letters 8: 269-78 (1987) (2) Knoppel H, Schauenburg H; Environ International 15: 413-8 (1989) (3) IARC; Some Monomers, Plastics and Synthetic Elastomers and Acrolein. Geneva, Switzerland: World Health Org, Inter Agency Res Cancer. 19: 231 (1979) (4) Rothberg M et al; Ann Occup Hyg 42: 129-34 (1998) (5) Hodgson AT et al; Environ Int 22: 295-307 (1996) (6) Polzin GM et al; Environ Sci Technol 41: 1297-1302 (2007)] **PEER REVIEWED**

Environmental Standards & Regulations:

Acceptable Daily Intakes:
An ADI of 0.133 mg/kg/day was calculated on the basis of the available chronic toxicity data /for rats/.
[National Research Council. Drinking Water & Health Volume 1. Washington, DC: National Academy Press, 1977., p. 765] **PEER REVIEWED**

CERCLA Reportable Quantities:
Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1000 lb or 454 kg. The toll free number of the NRC is (800) 424-8802. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Atmospheric Standards:
This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. Styrene is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. Styrene is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990] **PEER REVIEWED**

Clean Water Act Requirements:
Styrene is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.
[40 CFR 116.4 (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Federal Drinking Water Standards:
Maximum contaminant levels (MCL) for organic contaminants apply to community and non-transient, non-community water systems: Styrene, MCL 0.1 mg/L.
[40 CFR 141.61(a) (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

EPA 100 ug/L
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93) To Present] **PEER REVIEWED**

Federal Drinking Water Guidelines:
Maximum contaminant level goal (MCLG) for organic contaminants: Styrene, MCLG 0.1 mg/L.
[40 CFR 141.50(b) (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

EPA 100 ug/L
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93) To Present] **PEER REVIEWED**

State Drinking Water Guidelines:
(AZ) ARIZONA 140 ug/L
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93) To Present] **PEER REVIEWED**

(ME) MAINE 140 ug/L
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93) To Present] **PEER REVIEWED**

FDA Requirements:
Styrene is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Styrene is a food additive permitted for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant in accordance with the following conditions: a) they are used in the minimum quantity required to produce their intended effect, and otherwise in accordance with all the principles of good manufacturing practice, and 2) they consist of one or more of the following, used alone or in combination with flavoring substances and adjuvants generally recognized as safe in food, prior-sanctioned for such use, or regulated by an appropriate section in this part.
[21 CFR 172.515 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:
C8-H8
[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983., p. 1270] **PEER REVIEWED**

Molecular Weight:
104.150
[Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-488] **PEER REVIEWED**

Color/Form:
Colorless to yellowish, oily liquid
[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1638] **PEER REVIEWED**

VISCOUS LIQUID
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60: 233 (1994)] **PEER REVIEWED**

Solventy, rubbery
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)] **PEER REVIEWED**

Odor:
Extremely penetrating
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975., p. 519] **PEER REVIEWED**

An aromatic odor
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads, Hazardous Materials Systems (BOE), 1987., p. 653] **PEER REVIEWED**

Sweet, floral odor
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

If pure, sweet and pleasant, but usually contains aldehydes that have a typical penetrating smell, sharp, sweet, and unpleasant.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. Volumes 1-2. 4th ed. John Wiley & Sons. New York, NY. 2001, p. 1899] **PEER REVIEWED**

Boiling Point:
145.3 deg C
[Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 4-388] **PEER REVIEWED**

Melting Point:
-30.65 deg C
[Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-488] **PEER REVIEWED**

Corrosivity:

Styrene will corrode copper and copper alloys
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

Critical Temperature & Pressure:
Critical temperature: 363.7 deg C; critical pressure: 36.3 atm
[Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985., p. 187] **PEER REVIEWED**

Density/Specific Gravity:
0.9016 g/cu cm at 25 deg C
[Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-488] **PEER REVIEWED**

Heat of Combustion:
-4,395.63 kJ/mol at 25 deg C
[Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985., p. 187] **PEER REVIEWED**

Heat of Vaporization:
10.50 kcal/mol at 25 deg C
[Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985., p. 187] **PEER REVIEWED**

Octanol/Water Partition Coefficient:
log Kow = 2.95
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995., p. 40] **PEER REVIEWED**

Solubilities:
In water, 300 mg/L at 25 deg C
[Yalkowsky, S.H., He, Yan, Jain, P. Handbook of Aqueous Solubility Data Second Edition. CRC Press, Boca Raton, FL 2010, p. 468] **PEER REVIEWED**

Soluble in carbon disulfide, alcohol, ether, methanol, acetone
[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1638] **PEER REVIEWED**

Miscible with benzene
[Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-488] **PEER REVIEWED**

Soluble in ... toluene, ethanol, n-heptane, carbon tetrachloride ...
[NIOSH; Criteria Document: Stryene p.17 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

Spectral Properties:
Index of refraction: 1.5440 at 25 deg C
[Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-488] **PEER REVIEWED**

MAX ABSORPTION (ALCOHOL): 245.3 NM (LOG E= 4.18)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979., p. C-500] **PEER REVIEWED**

IR: 81 (Sadtler Research Laboratories IR Grating Collection)
[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V1: 954] **PEER REVIEWED**

UV: 94 (Sadtler Research Laboratories Spectral Collection)
[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V1: 954] **PEER REVIEWED**

NMR: 6408 (Sadtler Research Laboratories Spectral Collection)
[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V1: 954] **PEER REVIEWED**

MASS: 53473 (NIST/EPA/MSDC Mass Spec Database, 1990 version); 312 (Atlas of Mass Spectral Data, John Wiley & Sons, NY)
[Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V1: 954] **PEER REVIEWED**

Surface Tension:

32.3 dynes/cm at 20 deg C
[Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985., p. 187] **PEER REVIEWED**

Vapor Density:
3.6 (Air = 1)
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60: 234 (1994)] **PEER REVIEWED**

Vapor Pressure:
6.40 mm Hg at 25 deg C
[Chao J et al; J Phys Chem Ref Data 12: 1033-63 (1983)] **PEER REVIEWED**

Viscosity:
0.696 cP at 25 deg C
[Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985., p. 187] **PEER REVIEWED**

Other Chemical/Physical Properties:
Percent in saturated air at 760 mm Hg & 15 deg C: 0.57; density of saturated vapor-air mixture at 760 mm Hg & 15 deg C: 1.02 (Air = 1)
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963., p. 1223] **PEER REVIEWED**

Heat of polymerization: -154 cal/g (-6.35X10+5 J/kg)
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.] **PEER REVIEWED**

Styrene dissolves rubber
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

Latent heat of fusion: 10.95 kJ/mole (at melting point); Latent heat of sublimation: 43.9 kJ/mole (25 deg C); Heat of formation: 103.8 kJ/mole (25 deg C); Ionization potential: 8.42 eV
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.4 (1981)] **PEER REVIEWED**

When heated to 200 deg C it is converted into polymer, polystyrene, which is clear plastic having excellent insulating properties even at ultrahigh radio frequencies.
[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1638] **PEER REVIEWED**

Enthalpy, 24.83 kcal/mol (liquid), 35.22 kcal/mol (gas); Gibbs (free) energy of formation, 48.37 kcal/mol (liquid), 51.10 kcal/mol (gas); entropy, 56.78 cal/deg/mol (liquid), 82.48 cal/deg/mol (gas); heat capacity, 43.64 cal/deg/mol (liquid), 29.18 cal/deg/mol (gas)
[Dean, J.A. Handbook of Organic Chemistry. New York, NY: McGraw-Hill Book Co., 1987., p. 5-37] **PEER REVIEWED**

Liquid molar volume = 0.115714 cu m/kmol; Heat of formation = 1.4736E+08 J/kmol; Heat of fusion at melting pt = 1.0950E+07 J/kmol
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.] **PEER REVIEWED**

Henry's Law constant = 0.00275 atm cu m/mole at 25 deg C
[Bocek K; Experimetia, Suppl 23: 231-40 (1976)] **PEER REVIEWED**

Hydroxyl radical reaction rate constant = 5.8X10-11 cu cm/molecule-sec at 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 1, p. 231 (1989)] **PEER REVIEWED**

Chemical Safety & Handling:

Hazards Summary:
The major hazards encountered in the use and handling of styrene stem from its toxicologic properties and flammability. Toxic by all routes (ie, inhalation, ingestion, and dermal contact), exposure to this colorless-to-yellow, sweet-smelling liquid may occur from its presence in the manufacture and use of plastics, synthetic rubber, resins, coatings, paints, floor waxes, adhesives, putty, metal cleaners, autobody fillers, and varnishes. Effects from exposure may include headache, fatigue, nausea, sensation of drunkenness, central nervous system depression, and irritation of the eyes, skin, and respiratory tract (including pulmonary edema). Also, the International Agency for Research on Cancer (IARC) has classified styrene as a Group 2B carcinogen (defined as an agent that is possibly carcinogenic to humans). OSHA has established a TWA limit for styrene of

100 ppm. Mechanical ventilation should be used if necessary to maintain airborne levels of styrene at or below the permissible limit. In activities and situations where over-exposure may occur, wear protective clothing (neoprene is recommended), and a self-contained breathing apparatus. If contact should occur, irrigate exposed eyes with copious amounts of tepid water for at least 15 minutes, and wash exposed skin thoroughly with soap and water. Contaminated clothing should be removed and left at the worksite for cleaning. Styrene is easily ignited by heat, sparks (including static discharge), or flames. Its heavier-than-air vapor may travel considerable distances to a source of ignition and flash back, or form explosive concentrations in enclosed spaces such as sewers. Also, containers of styrene may explode in the heat of a fire. For fires involving styrene, extinguish with dry chemical, CO2, Halon, water spray (solid stream may spread the fire), or standard foam. Fight fire from as far a distance as possible, and consider evacuation of one half mile radius, especially if a tank car or truck is involved. Styrene (inhibited) may be shipped domestically via air, rail, road, and water, in containers bearing the label, "Flammable liquid." Styrene should be stored in air-tight containers, and away from sources of ignition or physical damage, moisture, heat, metal salts, peroxides, and strong acids. Small spills of styrene should be taken up with vermiculite, dry sand, or earth, and placed into containers for later disposal. Large spills on land should be diked using soil, sand bags, foamed polyurethane, or foamed concrete, and the bulk liquid absorbed with fly ash, cement powder, or commercial sorbents. Spills in bodies of water should be encircled by natural barriers or oil spill control booms, and a "universal" gelling agent injected to solidify the material. Apply activated carbon, and remove the trapped material with suction hoses, or mechanical lifts or dredges. Before implementing land disposal of styrene waste, consult with environmental regulatory agencies for guidance.
PEER REVIEWED

DOT Emergency Guidelines:
/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Fire or Explosion: HIGHLY FLAMMABLE: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Those substances designated with a "P" may polymerize explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water. Substances may be transported hot. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Health: Inhalation or contact with material may irritate or burn skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Public Safety: CALL Emergency Response Telephone Number ... As an immediate precautionary measure, isolate spill or leak area for at least 50 meters (150 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Protective Clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. CAUTION: For mixtures containing alcohol or polar solvent, alcohol-resistant foam may be more effective. Small fire: Dry chemical, CO2, water spray or regular foam. Large fire: Water spray, fog or regular foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from tanks engulfed in fire. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ Spill or Leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spill: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

/GUIDE 128P: FLAMMABLE LIQUIDS (NON-POLAR/WATER-IMMISCIBLE)/ First Aid: Move victim to fresh air. Call 911 or

emergency medical service. Give artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. In case of burns, immediately cool affected skin for as long as possible with cold water. Do not remove clothing if adhering to skin. Keep victim warm and quiet. Ensure that medical personnel are aware of the material(s) involved and take precautions to protect themselves. /Styrene monomer, stabilized/
[U.S. Department of Transportation. 2012 Emergency Response Guidebook. Washington, D.C. 2012] **PEER REVIEWED**

Odor Threshold:

Detection in water: 0.73 ppm; Chemically pure
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978., p. 151] **PEER REVIEWED**

Recognition in air: 0.047 ppm; Chemically pure
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978., p. 152] **PEER REVIEWED**

Odor Threshold Range: 0.15 to 25 ppm
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.1 (1981)] **PEER REVIEWED**

Odor detection in air, 0.05 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978., p. 152] **PEER REVIEWED**

Odor detection in water, 37 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978., p. 152] **PEER REVIEWED**

Odor (low) 0.4300 mg/cu m; Odor (high) 860.00 mg/cu m; Irritating concn 4300.00 mg/cu m. /Styrene, inhibited/
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)] **PEER REVIEWED**

During acute inhalation exposures to >10 ppm (0.04 mg/l), odor is not detectable; at 60 ppm (0.26 mg/l), odor is detectable, but nonirritant; at 100 ppm (0.43 mg/l), odor is strong, but without excessive discomfort; at 200-400 ppm (0.85-1.7 mg/l), odor is objectionably strong; at 376 ppm (1.6 mg/l) for 1 hr, neurological impairment is noted; at 600 ppm (2.6 mg/l), odor is very strong, producing strong eye & nasal irritation. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994., p. 1353] **PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

Acute exposure to high concn of styrene may produce irritation of the mucous membranes of the upper respiratory tract, nose and mouth.
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.71 (1981)] **PEER REVIEWED**

HAZARD WARNING: Primary irritant to mucosal surfaces at vapor concn above 200 ppm, but pungent odor usually gives adequate warning.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-152] **PEER REVIEWED**

Irritating to skin ...
[Commission of the European Communities. Legislation on Dangerous Substances - Classification and Labelling in the European Communities. Vol. II. London and Trotman Ltd., 1989., p. 224] **PEER REVIEWED**

Exposure to concn of styrene above 200 ppm causes irritation of the eyes and upper respiratory tract.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

At high concns (higher than 100 ppm), styrene is a respiratory and mucous membrane irritant. Skin contact may result in the development of primary irritant dermatitis.
[Young, L.Y., M.A. Koda-Kimble (eds.). Applied Therapeutics. The Clinical Use of Drugs. 6th ed. Vancouver, WA., Applied Therapeutics, Inc. 1995., p. 594] **PEER REVIEWED**

The principal acute hazards from worker exposure to styrene /is/ ... irritation of the skin, eyes, and upper respiratory tract.
[NIOSH; Criteria Document: Styrene p.15 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

Fire Potential:

Flammable liquid.
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 49-138] **PEER REVIEWED**

A very dangerous fire hazard when exposed to flame, heat, or oxidants. ... May ignite when heated with air + polymerizing polystyrene.
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

NFPA Hazard Classification:
Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection.
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 325-104] **PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 325-104] **PEER REVIEWED**

Instability: 2. 2= Materials that can undergo violent chemical changes at elevated temperatures and pressures. This also includes materials that may react violently with water or that may form potentially explosive mixtures with water. In advanced or massive fires involving these materials, fire fighting should be done from a safe distance or from a protected location.
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 325-104] **PEER REVIEWED**

Flammable Limits:
Lower flammable limit: 0.9% by volume; Upper flammable limit: 6.8% by volume
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 325-104] **PEER REVIEWED**

Flash Point:
34.4 deg C (Tag closed cup); 36.7 deg C (Tag open cup).
[NIOSH; Criteria Document: Stryene p.17 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

Autoignition Temperature:
914 deg F (490 deg C)
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 325-104] **PEER REVIEWED**

Fire Fighting Procedures:
Use water spray to cool unopened containers.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Wear self contained breathing apparatus for fire fighting if necessary.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Container explosion may occur under fire conditions. Vapors may form explosive mixture with air.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Use water spray, dry chemical, foam, or carbon dioxide. Fight fire from protected location or maximum possible distance. Use water spray to keep fire-exposed containers cool. /Styrene monomer, inhibited/
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 49-138] **PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, dry chemical, or carbon dioxide. /Styrene monomer, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 842] **PEER REVIEWED**

Toxic Combustion Products:
... Toxic gases and vapors (such as carbon monoxide) may be released in a fire involving styrene. Styrene fumes are very acrid.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

Firefighting Hazards:
Electrical ignition hazard: May be ignited by static discharge.
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.4 (1981)] **PEER REVIEWED**

Vapors are heavier than air and may travel to a source of ignition and flash back. Liquid floats on water and may travel to a source of ignition and spread fire. Hazardous polymerization may occur under fire conditions. Closed containers may rupture violently when heated. /Styrene monomer, inhibited/
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 49-138] **PEER REVIEWED**

Explosive Limits & Potential:
... Readily undergoes polymerization when heated or exposed to light or a peroxide catalyst. The polymerization releases heat and may become explosive.
[Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 1186] **PEER REVIEWED**

Vapors form explosive mixtures with air.
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.4 (1981)] **PEER REVIEWED**

Lower explosive limit: 1.1%, Upper explosive limit: 6.1%
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 3027] **PEER REVIEWED**

Exposure of unstabilised styrene to oxygen at 40-60 deg C generated a styrene oxygen interpolymeric peroxide which, when isolated, exploded violently on gentle heating.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990, p. 744] **PEER REVIEWED**

Explosive in the form of vapor when exposed to heat or heat or flame.
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:
Oxidizers, catalysts for vinyl polymers, peroxides, strong acids, aluminum chloride [Note: May polymerize if contaminated or subjected to heat. Usually contains an inhibitor such as tert-butylcatechol].
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

... Styrene readily reacts with low concentrations of halogens in the presence of uv light to form a potent lacrimator.
[Adams EM, Schneider EJ; Proc Air Pollut Smoke Prev Assoc 45: 61-64 (1952) as cited in NIOSH; Criteria Document: Styrene p.164 (1983) DHEW Pub. NIOSH 83-119] **PEER REVIEWED**

Mixing styrene monomer and chlorosulfonic acid in a closed container caused the temp and pressure to incr. ... Mixing styrene monomer and 96% sulfuric acid in a closed container caused the temp and pressure to incr.
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 491-187] **PEER REVIEWED**

Reacts with oxygen above 40 deg C to form a heat-sensitive explosive peroxide. Violent or explosive polymerization may be initiated by alkali-metal-graphite composites; butyllithium; dibenzoyl peroxide; other initiators (e.g., azoisobutyronitrile; di-tert-butyl peroxide). Reacts violently with chlorosulfonic acid; oleum; sulfuric acid; chlorine + iron(III)chloride (above 50 deg C). May ignite when heated with air + polymerizing polystyrene. Can react vigorously with oxidizing materials.
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Hazardous Decomposition:
When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Hazardous Polymerization:
Polymerizes slowly at room temperature and readily at temp > 65 deg C.
[Environment Canada; Tech Info for Problem Spills: Styrene (Draft) p.3 (1981)] **PEER REVIEWED**

Polymerization may occur iF heated above 150 deg f; metal salts, peroxides, & strong acids may also cause polymerization.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.] **PEER REVIEWED**

Styrene is stabilized by a polymerization inhibitor (often tertbutylcatechol). If this is not present in adequate concentrations, styrene can polymerize and explode its container. ...
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

Upon exposure to light and air, styrene undergoes self-polymerization and oxidation with formation of peroxides; therefore, inhibitors are added to stabilize pure styrene solns..
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992., p. 999] **PEER REVIEWED**

Violent or explosive polynerization may be initiated by alkali-metal graphite composites, butylithium, dibenzoyl peroxide, other initiators (e.g., azoisobutyronitrile, di-tert-butyl peroxide).
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Immediately Dangerous to Life or Health:
700 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Protective Equipment & Clothing:
Approved organic vapor cartridge respirator can be used for short periods up to 1000 ppm vapor. Use self-contained or air-supplied breathing equipment for higher or unknown concn or oxygen deficient atmospheres. A full facepiece is required above 400 ppm. ...
[General Electric Co; Material Safety Data Sheet #351 (1979)] **PEER REVIEWED**

Possible exposure to higher concn ... make it necessary for workman to wear safety goggles ... apron, and neoprene gloves. Neoprene is actually recommended because it is completely inert to styrene.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968., p. 78] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... dispensers of liq detergent /should be available./ ... Safety pipettes should be used for all pipetting. ... In animal laboratory, personnel should ... wear protective suits (preferably disposable, one-piece and close-fitting at ankles and wrists), gloves, hair covering and overshoes. ... In chemical laboratory, gloves and gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, and disposable plastic aprons might provide addnl protection. ... gowns ... /should be/ of distinctive color, this is a reminder that they are not to be worn outside the laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 8] **PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Respirator Recommendations: Up to 500 ppm:

Assigned Protection Factor (APF)	Respirator Recommendations
APF = 10	Any chemical cartridge respirator with organic vapor cartridge(s). Substance reported to cause eye irritation or damage; may require eye protection.
APF = 10	Any supplied-air respirator. Substance reported to cause eye irritation or damage; may require eye protection.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Respirator Recommendations: Up to 700 ppm:

Assigned Protection Factor (APF)	Respirator Recommendations
APF = 25	Any supplied-air respirator operated in a continuous-flow mode. Substance reported to cause eye irritation or damage; may require eye protection.

APF = 50	Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s).
APF = 50	Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister.
APF = 25	Any powered, air-purifying respirator with organic vapor cartridge(s). Substance reported to cause eye irritation or damage; may require eye protection.
APF = 50	Any self-contained breathing apparatus with a full facepiece.
APF = 50	Any supplied-air respirator with a full facepiece.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Respirator Recommendations: Escape:

Assigned Protection Factor (APF)	Respirator Recommendations
APF = 10,000	Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode.
APF = 10,000	Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained positive-pressure breathing apparatus.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Respirator Recommendations: Escape:

Assigned Protection Factor (APF)	Respirator Recommendations
APF = 50	Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Compatible protective equipment construction materials include: Polyethylene, polyvinyl alcohol, viton. /Styrene, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 843] **PEER REVIEWED**

Preventive Measures:
SRP: The scientific literature for the use of contact lenses by industrial workers is inconsistent. The benefits or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

Ventilation in workshop must allow maintenance of permitted level.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968., p. 78] **PEER REVIEWED**

Immediately remove any clothing that becomes wet /with styrene/ to avoid flammability hazard.

[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.169 (1983)] **PEER REVIEWED**

Waste-gas outlets from ovens and furnaces should carry gases to the open air; Continuous processes should be given preference over batch techniques; Manual operations should be mechanized, and wide use should be made of automation and remote control; Ducting, piping and pipe joints should be leak-tight; Glandless pumps and measuring and control instruments should be used ...
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983., p. 2115] **PEER REVIEWED**

Clothing wet with liquid styrene should be placed in closed containers for storage until it can be discarded or until provision is made for the removal of styrene from the clothing ... the person performing the operation should be informed of styrene's hazardous properties.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 3] **PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water. /Styrene monomer, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 842] **PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to knock-down vapors. /Styrene monomer, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 842] **PEER REVIEWED**

Avoid contact with skin and eyes. Avoid inhalation of vapor or mist. Keep away from sources of ignition - No smoking. Take measures to prevent the build up of electrostatic charge.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Smoking, drinking, eating, storage of food or of food and beverage containers or utensils, and the application of cosmetics should be prohibited in any laboratory. All personnel should remove gloves, if worn, after completion of procedures in which carcinogens have been used. They should ... wash ... hands, preferably using dispensers of liq detergent, and rinse ... thoroughly. Consideration should be given to appropriate methods for cleaning the skin, depending on nature of the contaminant. No standard procedure can be recommended, but the use of organic solvents should be avoided. Safety pipettes should be used for all pipetting. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 8] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": In animal laboratory, personnel should remove their outdoor clothes and wear protective suits (preferably disposable, one-piece and close-fitting at ankles and wrists), gloves, hair covering and overshoes. ... clothing should be changed daily but ... discarded immediately if obvious contamination occurs ... /also,/ workers should shower immediately. In chemical laboratory, gloves and gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, and disposable plastic aprons might provide addnl protection. If gowns are of distinctive color, this is a reminder that they should not be worn outside of lab. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 8] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... operations connected with synth and purification ... should be carried out under well-ventilated hood. Analytical procedures ... should be carried out with care and vapors evolved during ... procedures should be removed. ... Expert advice should be obtained before existing fume cupboards are used ... and when new fume cupboards are installed. It is desirable that there be means for decreasing the rate of air extraction, so that carcinogenic powders can be handled without ... powder being blown around the hood. Glove boxes should be kept under negative air pressure. Air changes should be adequate, so that concn of vapors of volatile carcinogens will not occur. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 8] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Vertical laminar-flow biological safety cabinets may be used for containment of in vitro procedures ... provided that the exhaust air flow is sufficient to provide an inward air flow at the face opening of the cabinet, and contaminated air plenums that are under positive pressure are leak-tight. Horizontal laminar-flow hoods or safety cabinets, where filtered air is blown across the working area towards the operator, should never be used ... Each cabinet or fume cupboard to be used ... should be tested before work is begun (eg, with fume bomb) and label fixed to it, giving date of test and avg air-flow measured. This test should be repeated periodically and after any structural changes. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 9] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Principles that apply to chem or biochem lab also apply to microbiological and cell-culture labs ... Special consideration should be given to route of admin. ... Safest method of administering volatile carcinogen is by injection of a soln. Admin by topical application, gavage, or intratracheal instillation should be performed under hood. If chem will be exhaled, animals should be kept under hood during this period. Inhalation exposure requires special equipment. ... unless specifically required, routes of admin other than in the diet should be used. Mixing of carcinogen in diet should be carried out in sealed mixers under fume hood, from which the exhaust is fitted with an efficient particulate filter. Techniques for cleaning mixer and hood should be devised before expt begun. When mixing diets, special protective clothing and, possibly, respirators may be required. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 9] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When ... admin in diet or applied to skin, animals should be kept in cages with solid bottoms and sides and fitted with a filter top. When volatile carcinogens are given, filter tops should not be used. Cages which have been used to house animals that received carcinogens should be decontaminated. Cage-cleaning facilities should be installed in area in which carcinogens are being used, to avoid moving of ... contaminated /cages/. It is difficult to ensure that cages are decontaminated, and monitoring methods are necessary. Situations may exist in which the use of disposable cages should be recommended, depending on type and amt of carcinogen & efficiency with which it can be removed. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 10] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": To eliminate risk that ... contamination in lab could build up during conduct of expt, periodic checks should be carried out on lab atmospheres, surfaces, such as walls, floors and benches, and ... interior of fume hoods and airducts. As well as regular monitoring, check must be carried out after cleaning-up of spillage. Sensitive methods are required when testing lab atmospheres. ... Methods ... should ... where possible, be simple and sensitive. ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 10] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Rooms in which obvious contamination has occurred, such as spillage, should be decontaminated by lab personnel engaged in expt. Design of expt should ... avoid contamination of permanent equipment. ... Procedures should ensure that maintenance workers are not exposed to carcinogens. ... Particular care should be taken to avoid contamination of drains or ventilation ducts. In cleaning labs, procedures should be used which do not produce aerosols or dispersal of dust, ie, wet mop or vacuum cleaner equipped with high-efficiency particulate filter on exhaust, which are avail commercially, should be used. Sweeping, brushing and use of dry dusters or mops should be prohibited. Grossly contaminated cleaning materials should not be re-used ... If gowns or towels are contaminated, they should not be sent to laundry, but ... decontaminated or burnt, to avoid any hazard to laundry personnel. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 10] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Doors leading into areas where carcinogens are used ... should be marked distinctively with appropriate labels. Access ... limited to persons involved in expt. ... A prominently displayed notice should give the name of the Scientific Investigator or other person who can advise in an emergency and who can inform others (such as firemen) on the handling of carcinogenic substances. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 11] **PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning. **PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard (i.e., for liquids with a flash point <100 deg F).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Handle in accordance with good industrial hygiene and safety practice. Wash hands before breaks and at the end of workday.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good

laboratory practices. Wash and dry hands.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Stability/Shelf Life:
On exposure to light and air it slowly undergoes polymerization and oxidation with formation of peroxides.
[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1638] **PEER REVIEWED**

... Styrene is stabilized by a polymerization inhibitor (often tertbutylcatechol). If this is not present in adequate concn, styrene can polymerize and explode its container. The polymerization is also speeded up by temperatures above 66 deg C (150 deg F).
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 2] **PEER REVIEWED**

Shipment Methods and Regulations:
No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (USDOT); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 25, 2014: http://www.ecfr.gov **PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[International Air Transport Association. Dangerous Goods Regulations. 47th Edition. Montreal, Quebec Canada. 2006., p. 257] **PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[International Maritime Organization. IMDG Code. International Maritime Dangerous Goods Code Volume 2 2006, p. 99] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Procurement ... of unduly large amt ... should be avoided. To avoid spilling, carcinogens should be transported in securely sealed glass bottles or ampoules, which should themselves be placed inside strong screw-cap or snap-top container that will not open when dropped and will resist attack from the carcinogen. Both bottle and the outside container should be appropriately labelled. ... National post offices, railway companies, road haulage companies and airlines have regulations governing transport of hazardous materials. These authorities should be consulted before ... material is shipped. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 13] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When no regulations exist, the following procedure must be adopted. The carcinogen should be enclosed in a securely sealed, watertight container (primary container), which should be enclosed in a second, unbreakable, leakproof container that will withstand chem attack from the carcinogen (secondary container). The space between primary and secondary container should be filled with absorbent material, which would withstand chem attack from the carcinogen and is sufficient to absorb the entire contents of the primary container in the event of breakage or leakage. Each secondary container should then be enclosed in a strong outer box. The space between the secondary container and the outer box should be filled with an appropriate quantity of shock-absorbent material. Sender should use fastest and most secure form of transport and notify recipient of its departure. If parcel is not received when expected, carrier should be informed so that immediate effort can be made to find it. Traffic schedules should be consulted to avoid ... arrival on weekend or holiday ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 13] **PEER REVIEWED**

Storage Conditions:
Must be inhibited during storage.
[Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 1186] **PEER REVIEWED**

Store in a cool, dry, well-ventilated place. Separate from oxidizing materials, peroxides, and metal salts. /Styrene monomer, inhibited/
[National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 49-138] **PEER REVIEWED**

Copper or copper containing alloys should be avoided as containers. Glass is particularly suitable for storing small quantities in refrigerators or cold boxes. Large quantities can be safely stored in vented metal storage tanks with certain safe-guards for polymerization. In hot climates, store in tank with a temp alarm system. Outdoors or detached storage is preferable. Indoor storage should be in a standard flammable liquid storage room. The monomer must be checked at least weekly to determine inhibitor and polymer content if the material is being stored for any period of time in excess of 30 days at 88 deg C. Storage vessels should be free of internal superstructure and should be suitably diked. In addn, they are electrically grounded to

prevent static electricity. An inert blanket, preferably nitrogen, can ... be used. Centrifugal pumps must not be allowed to run with a closed discharge line, because this will cause polymerization in the pump. Keep away from oxidizing agents.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988., p. 495] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Storage site should be as close as practicable to lab in which carcinogens are to be used, so that only small quantities required for ... expt need to be carried. Carcinogens should be kept in only one section of cupboard, an explosion-proof refrigerator or freezer (depending on chemicophysical properties ...) that bears appropriate label. An inventory ... should be kept, showing quantity of carcinogen and date it was acquired ... Facilities for dispensing ... should be contiguous to storage area. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 13] **PEER REVIEWED**

Keep container tightly closed in a dry and well-ventilated place. Containers which are opened must be carefully resealed and kept upright to prevent leakage. Recommended storage temperature: 2-8 deg C. Light sensitive
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

It is a storage hazard above 32 deg C.
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 3313] **PEER REVIEWED**

Cleanup Methods:
If styrene is spilled or leaked ... /in/ small quantities, absorb on paper towels. Evaporate in a safe place (such as a fume hood). Allow sufficient time for evaporating vapors to completely clear the hood ductwork. Burn the paper in a suitable location away from combustible materials. Large quantities can be collected and atomized in a suitable combustion chamber. Combustion may be improved by mixing with a more flammable liq.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 4] **PEER REVIEWED**

Environmental considerations- Land spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using soil, sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder, or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard. /Styrene monomer, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 842] **PEER REVIEWED**

Environmental considerations- Water spill: Use natural barriers or oil spill control booms to limit spill travel. Use surface active agent (eg detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10 ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates. /Styrene monomer, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 842] **PEER REVIEWED**

Environmental considerations: Air spill: Apply water spray or mist to knock down vapors. /Styrene monomer, stabilized/
[Association of American Railroads; Bureau of Explosives. Emergency Handling of Hazardous Materials in Surface Transportation. Association of American Railroads, Pueblo, CO. 2005, p. 842] **PEER REVIEWED**

Contain spillage, and then collect with an electrically protected vacuum cleaner or by wet-brushing and place in container for disposal according to locatl regulations ...
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Use personal protective equipment. Avoid breathing vapors, mist or gas. Ensure adequate ventilation. Remove all sources of ignition. Beware of vapors accumulating to form explosive concentrations. Vapors can accumulate in low areas.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

Environmental precautions: Prevent further leakage or spillage if safe to do so. Do not let product enter drains. Discharge into the environment must be avoided.
[Sigma-Aldrich; Material Safety Data Sheet for Styrene. Product number: S4972, Version 4.14 (Revision Date 06/12/2014). Available from, as of August 25, 2014: http://www.sigmaaldrich.com/safety-center.html **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": A high-efficiency particulate arrestor (HEPA) or charcoal filters can be used to minimize amt of carcinogen in exhausted air ventilated safety cabinets, lab hoods, glove boxes or animal rooms ... Filter housing that is designed so that used filters can be transferred into plastic bag without contaminating maintenance staff is avail commercially. Filters should be placed in plastic bags immediately after removal ... The plastic bag should be sealed immediately ... The sealed bag should be labelled properly ... Waste liquids ... should be placed or collected in proper containers for disposal. The lid should be secured and the bottles properly labelled. Once filled, bottles should be placed in plastic bag, so that outer surface ... is not contaminated ... The plastic bag should also be sealed and labelled. ... Broken glassware ... should be

decontaminated by solvent extraction, by chemical destruction, or in specially designed incinerators. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 15] **PEER REVIEWED**

Disposal Methods:
SRP: The most favorable course of action is to use an alternative chemical product with less inherent propensity for occupational harm/injury/toxicity or environmental contamination. Recycle any unused portion of the material for its approved use or return it to the manufacturer or supplier. Ultimate disposal of the chemical must consider: the material's impact on air quality; potential migration in soil or water; effects on animal and plant life; and conformance with environmental and public health regulations.
PEER REVIEWED

1. By absorbing it in vermiculite, dry sand, earth or a similar material and disposing in a secured sanitary landfill. 2. By atomizing in a suitable combustion chamber. Combustion may be improved by mixing with a more flammable liq.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981., p. 4] **PEER REVIEWED**

/Styrene is a/ waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-9 (1981) EPA 68-03-3025] **PEER REVIEWED**

Incineration. In some cases, recovery and recycle of styrene monomer is economic and technology is available.
[Pohanish, R.P. (ed). Sittig's Handbook of Toxic and Hazardous Chemical Carcinogens 5th Edition Volume 1: A-H,Volume 2: I-Z. William Andrew, Norwich, NY 2008, p. 2316] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": There is no universal method of disposal that has been proved satisfactory for all carcinogenic compounds & specific methods of chem destruction ... published have not been tested on all kinds of carcinogen-containing waste. ... summary of avail methods and recommendations ... /given/ must be treated as guide only. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 14] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Incineration may be only feasible method for disposal of contaminated laboratory waste from biological expt. However, not all incinerators are suitable for this purpose. The most efficient type ... is probably the gas-fired type, in which a first-stage combustion with a less than stoichiometric air:fuel ratio is followed by a second stage with excess air. Some ... are designed to accept ... aqueous and organic-solvent solutions, otherwise it is necessary ... to absorb soln onto suitable combustible material, such as sawdust. Alternatively, chem destruction may be used, esp when small quantities ... are to be destroyed in laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 15] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": HEPA (high-efficiency particulate arrestor) filters ... can be disposed of by incineration. For spent charcoal filters, the adsorbed material can be stripped off at high temp and carcinogenic wastes generated by this treatment conducted to and burned in an incinerator. ... LIQUID WASTE: ... Disposal should be carried out by incineration at temp that ... ensure complete combustion. SOLID WASTE: Carcasses of lab animals, cage litter and misc solid wastes ... should be disposed of by incineration at temp high enough to ensure destruction of chem carcinogens or their metabolites. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 15] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... small quantities of ... some carcinogens can be destroyed using chem reactions ... but no general rules can be given. ... As a general technique ... treatment with sodium dichromate in strong sulfuric acid can be used. The time necessary for destruction ... is seldom known ... but 1-2 days is generally considered sufficient when freshly prepd reagent is used. ... Carcinogens that are easily oxidizable can be destroyed with milder oxidative agents, such as saturated soln of potassium permanganate in acetone, which appears to be a suitable agent for destruction of hydrazines or of compounds containing isolated carbon-carbon double bonds. Concn or 50% aqueous sodium hypochlorite can also be used as an oxidizing agent. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 16] **PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Carcinogens that are alkylating, arylating or acylating agents per se can be destroyed by reaction with appropriate nucleophiles, such as water, hydroxyl ions, ammonia, thiols and thiosulfate. The reactivity of various alkylating agents varies greatly ... and is also influenced by sol of agent in the reaction medium. To facilitate the complete reaction, it is suggested that the agents be dissolved in ethanol or similar solvents. ... No method should be applied ... until it has been thoroughly tested for its effectiveness and safety on material to be inactivated. For example, in case of destruction of alkylating agents, it is possible to detect residual compounds by reaction with 4(4-nitrobenzyl)-pyridine. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979., p. 17] **PEER REVIEWED**

The following wastewater treatment technologies have been investigated for Styrene: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-47 (1982)] **PEER REVIEWED**

The following wastewater treatment technologies have been investigated for styrene: Stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-97 (1982)] **PEER REVIEWED**

The following wastewater treatment technologies have been investigated for styrene: Solvent extraction.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-112 (1982)] **PEER REVIEWED**

The following wastewater treatment technologies have been investigated for styrene: Activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-147-8 (1982)] **PEER REVIEWED**

Spray by mist into a furnace. Incineration will become easier by mixing with a more flammable solvent. Recommendable methods: Incineration and use as a boiler fuel. /Styrene polymer/
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985., p. 283] **PEER REVIEWED**

Occupational Exposure Standards:

OSHA Standards:
Permissible Exposure Limit: Table Z-2 8-hr Time Weighted Avg: 100 ppm.
[29 CFR 1910.1000 (USDOL); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Permissible Exposure Limit: Table Z-2 Acceptable Ceiling Concentration: 200 ppm.
[29 CFR 1910.1000 (USDOL); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Permissible Exposure Limit: Table Z-2 Acceptable maximum peak above the acceptable ceiling concentration for an 8-hour shift. Concentration: 600 ppm. Maximum Duration: 5 minutes in any 3 hours.
[29 CFR 1910.1000 (USDOL); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of February 21, 2014: http://www.ecfr.gov/cgi-bin/ECFR?page=browse **PEER REVIEWED**

Threshold Limit Values:
8 hr Time Weighted Avg (TWA): 20 ppm; 15 min Short Term Exposure Limit (STEL): 40 ppm.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 53] **PEER REVIEWED**

A4; Not classifiable as a human carcinogen. /Styrene, monomer/
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 53] **PEER REVIEWED**

Biological Exposure Index (BEI): Determinant: mandelic acid plus phenylglyoxylic acid in urine; Sampling Time: end of shift; BEI: 400 mg/g creatinine; Notation: The determinant is nonspecific, since it is also observed after exposure to other chemicals.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 118] **PEER REVIEWED**

Biological Exposure Index (BEI): Determinant: (styrene in venous blood); Sampling Time: (end of shift); BEI: (0.2 mg/L); Notation: (The biological determinant is an indicator of exposure to the chemical, but the quantitative interpretation of the measurement is ambiguous. These determinants should be used as a screening test if a quantitative test is not practical, or as a confirmatory test if the quantitative test is not specific and the origin of the determinant is in question.)
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 118] **PEER REVIEWED**

NIOSH Recommendations:
Recommended Exposure Limit: 15 Minute Short-Term Exposure Limit: 100 ppm (425 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Recommended Exposure Limit: 10 Hour Time-Weighted Average: 50 ppm (215 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Immediately Dangerous to Life or Health:
700 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. Department of Health & Human Services, Centers for Disease Control & Prevention. National

Institute for Occupational Safety & Health. DHHS (NIOSH) Publication No. 2010-168 (2010). Available from: http://www.cdc.gov/niosh/npg **PEER REVIEWED**

Other Standards Regulations and Guidelines:
Emergency Response Planning Guidelines (ERPG): ERPG(1) 50 ppm (no more than mild, transient effects) for up to 1 hr exposure. Odor should be detectable near ERPG-1. ; ERPG(2) 250 ppm (without serious, adverse effects) for up to 1 hr exposure; ERPG(3) 1000 ppm (not life threatening) up to 1 hr exposure.
[2013 Emergency Response Planning Guidelines (ERPG) & Workplace Exposure Level (WEEL). American Industrial Hygiene Association, Falls Church, VA 2013, p. 29] **PEER REVIEWED**

Manufacturing/Use Information:

Uses:
Manufacture of plastics; synthetic rubber; resins; insulator
[O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1638] **PEER REVIEWED**

Polystyrene; SBR /styrene-butadiene-rubber/, ABS /acrylonitrile-butadiene-styrene/ and SAN /styrene-acrylonitrile/ resins; protective coatings (styrene-butadiene latex; alkyds); styrenated polyesters; rubber-modified polystyrene; copolymer resins; intermediate.
[Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 1186] **PEER REVIEWED**

Glass fiber-reinforced, unsaturated polyester resins used in construction materials & boats; used in synthesis of styrene-divinylbenzene copolymers as matrix for ion-exchange resins; as synthetic flavoring substance & adjuvant; as cross-linking agent in polyester resins; in rubber articles (5% wt max), when intended for use in contact with food.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19: 234 (1979)] **PEER REVIEWED**

Used in plastic and resins and as a dental filling component, chemical intermediate, component in agricultural products, and stabilizing agent.
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4: 307] **PEER REVIEWED**

Monomer for straight and impact polystyrene; comonomer for styrene-butadiene elastomers and for other copolymers, eg, acrylic ester-styrene; chem intermed for styrenated phenols and styrene oxide, styrenated oils; cross-linking agent in unsaturated polyester resin manufacture.
[SRI] **PEER REVIEWED**

FDA-approved flavoring agent, eg, for ice cream & candy
[SRI] **PEER REVIEWED**

Polymerizes with many other monomers and polymers to produce wide variety of plastics /such as styrofoam/, paints and lacquers.
[Kuney, J.H., J.M. Mullican (eds.). Chemcyclopedia. Washington, DC: American Chemical Society, 1994., p. 111] **PEER REVIEWED**

Manufacturers:
Styrene - Producer and Manufacture Data (2012)

Company	Site	Address	Manufacture	Import
Shell Chemical LP	Shell Norco Chemical Plant East Site	15536 River Road, Norco LA 70079-2537	Yes	No data
Shell Chemical LP	One Shell Plaza	910 Louisiana St, Houston TX 77002	No data	Yes
Lyondell Chemical Co	Lyondell Channel View Facility, Lyondell Chemical Co	Channelview TX 77350-2681	CBI	CBI
Total Petrochemicals & Refining USA Inc	Total Petrochemicals & Refining USA Inc Styrene Joint Venture	6325 LA Highway 75 PO Box 11, Carville LA 70721-0011	Yes	No data
Solvchem Inc	Solvents & Chemicals	4704 Shank Rd, Pearland TX 77581	Yes	No data

Dow Chemical Co	The Dow Chemical Co	1790 Building Washington St, Midland MI 48667	CBI	No data
Bayer Group	Bayer Material Science	100 Bayer Rd, Pittsburgh PA 15205-0741	No data	CBI
Styrolution America LLC	INEOS Nova LLC	25846 Southwest Frontage Rd, Channahon IL 60410-5222	No data	CBI
Dow Chemical Co	The Dow Chemical Co	2020 Dow Center, Midland MI 48674	No data	CBI
Americas Styrenics LLC	Americas Styrenics - St James Plant	9901 Hwy 18, St James LA 70086	Yes	No data
Monument Chemicals	Advanced Aromatics LLC	5501 W Baker Rd, Baytown TX 77520	Yes	No data
Transammonia Inc	Trammochem, a Div of Transammonia Inc	17 Old King's Highway South Suite 100, Darien CT 06820	No data	Yes
Styrolution America LLC	Nova Chemicals Inc	950 Worcester St, Springfield (Indian Orchard) MA 01151-1043	No data	Yes
Westlake Chemical Corp	Westlake Styrene LLC - Styrene Monomer Production Facility	900 Hwy 108, Sulphur LA 70665-8527	Yes	No data
Deltech Corp	Deltech Corp	11911 Scenic Hwy, Baton Rouge LA 70807-1318	Yes	No data
Cook Composites & Polymers Co	CCP Composites US	5851 FM 1998, Marshall TX 75672	Yes	No data
Cook Composites & Polymers Co	CCP Composites US	10124 Rocket Blvd, Orlando FL 32824	Yes	No data
Cook Composites & Polymers Co	CCP Composites US	920 Tightsqueeze Industrial Rd, Chatham VA 24531-3488	Yes	No data
Cook Composites & Polymers Co	CCP Composites US	2434 Holmes Rd, Houston TX 77051-1016	Yes	No data
Styrolution America LLC	INEOS Styrenics LLC	12222Port Rd, Pasadena TX 77507	Yes	No data
BASF Corp	BASF Corp	100 Campus Rd, Florham Park NJ 07932-1089	No data	CBI
Styrolution America LLC	INEOS Styrenics LLC	Loop 197 and 6th St S, Texas City TX 77590	Yes	No data

[US EPA; Chemical Data Reporting (CDR). Non-confidential 2012 Chemical Data Reporting information on chemical production and use in the United Sates. Available from, as of Mar 11, 2014: http://java.epa.gov/oppt_chemical_search/ **PEER REVIEWED**

Methods of Manufacturing:

Direct dehydrogenation of ethylbenzene to styrene accounts for 85% of commercial production. The reaction is carried out in the vapor phase with steam over a catalyst consisting primarily of iron oxide. The reaction is endothermic, and can be accomplished either adiabatically or isothermally.
[James DH, Castor WM; Styrene. Ullmann's Encyclopedia of Industrial Chemistry 7th ed. (1999-2014). NY, NY: John Wiley & Sons. Online Posting Date: October 15, 2011] **PEER REVIEWED**

Many different techniques have been investigated for the manufacture of styrene monomer. Of these, the following methods have been used ... for commercial production: 1) dehydrogenation of ethylbenzene; 2) oxidation of ethylbenzene to ethylbenzene hydroperoxide, which reacts with propylene to give alpha-phenylethanol and propylene oxide, after which alcohol is dehydrated to styrene; 3) oxidative conversion of ethylbenzene to alpha-phenylethanol by way of acetophenone and subsequent dehydration of the alcohol; 4) side-chain chlorination of ethylbenzene followed by dehydrochlorination; 5) side-chain chlorination of ethylbenzene, hydrolysis to the corresponding alcohols, followed by dehydration; and 6) pyrolysis of petroleum and recovery from various petroleum processes. The 1st two methods are the only commercially utilized routes to styrene: dehydrogenation of ethylbenzene accounts for over 90% of the total world production. ... The two commercially important routes to styrene are based on ethylbenzene produced by alkylation of benzene with ethylene.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V22: 969 (1997)] **PEER REVIEWED**

General Manufacturing Information:

Styrene was discovered in 1827 as a result of the pyrolytic decarboxylation of organic acids of Storax balsam ... By early 1900s styrene was recognized as an impurity of industrial processes using coal tar & petroleum cracking. ... Styrene monomer production requires large amounts of raw materials produced by the coal tar & petroleum industries. In fact, styrene production consumes 50% of the world's capacity of benzene which, in the form of ethylbenzene, is the base of styrene manufacturing.
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988., p. 956] **PEER REVIEWED**

Styrene monomer is one of the world's major organic chemicals.
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4: 307] **PEER REVIEWED**

Styrene polymer is used in the manufacture of photocopier toner. /Styrene polymer/
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V20: 111 (1996)] **PEER REVIEWED**

Formulations/Preparations:

... Available in USA as polymer grade ... purity, 99.6% min; polymer, 10 mg/kg (ppm) max; sulfur, 25 mg/kg (ppm) max; chlorine, 50 mg/kg (ppm) max; hydrogen peroxide, 100 mg/kg (ppm) max; benzaldehyde, 200 mg/kg (ppm) max; and tertiary-butyl catechol (as inhibitor), 12-15 mg/kg (ppm). ... Free from suspended matter and is clear.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19: 232 (1979)] **PEER REVIEWED**

Purity, 99.6-99.9% min; ethylbenzene, 85 ppm max; polymer content, 10 ppm max; para-tert-butylcatechol (inhibitor), 10-15 ppm or 45-55 ppm; aldehydes (as benzaldehyde), 200 ppm; peroxides (as H2O2), 0.0015 wt% or 100 ppm max; benzene, 1 ppm max; sulfur, 25 ppm max; chlorides (as chlorine), 50 ppm max
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60: 234 (1994)] **PEER REVIEWED**

Clear, colorless grades
[Kuney, J.H., J.M. Mullican (eds.). Chemcyclopedia. Washington, DC: American Chemical Society, 1994., p. 111] **PEER REVIEWED**

Impurities:

Polymer, <10 ppm by wt; C8, 400-800 ppm by wt; C9, 500-1000 ppm by wt; benzaldehyde, <50 ppm by wt; peroxides, <30 ppm by wt; inhibitor (tertbutylcatechol), 10-50 ppm by wt; chlorides, <10 ppm by wt
[NCI/DCE; Monograph On Human Exposure To Chemicals In The Workplace: Styrene p.1-1, 1985] **PEER REVIEWED**

Ethylbenzene, 85 ppm max; polymer content, 10 ppm max; para-tert-butylcatechol (inhibitor), 10-15 ppm or 45-55 ppm; aldehydes (as benzaldehyde), 200 ppm; peroxides (as H2O2), 0.0015 wt% or 100 ppm max; benzene, 1 ppm max; sulfur, 25 ppm max; chlorides (as chlorine), 50 ppm max
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60: 234 (1994)] **PEER REVIEWED**

Consumption Patterns:
MONOMER OR COMONOMER FOR POLYSTYRENES, 67%; FOR ACRYLONITRILE-BUTADIENE/STYRENE RESINS, 9%; FOR STYRENE-BUTADIENE ELASTOMERS, 7%; FOR STYRENE-BUTADIENE COPOLYMER LATEXES, 6%; FOR STYRENE-ACRYLONITRILE RESINS, 1%; CROSS-LINKING AGENT IN POLYESTER MANUFACTURING, 5%; OTHER USES, 5% (1982)
[SRI] **PEER REVIEWED**

Polystyrene, 55%; acrylonitrile-butadiene-styrene (ABS), 9%; styrene-butadiene rubber, 7%; styrene-butadiene latex, 6%; unsaturated polyester resins, 6%; miscellaneous uses including other copolymers and styrene-acrylonitrile (SAN), 4%; export, 13% (1985)
[CHEMICAL PROFILE: Styrene (1986)] **PEER REVIEWED**

Polystyrene, 58%; ABS and SAN resins, 12%; SB elastomer, 8%; SB Latex, 7%; unsaturated polyester, 7%; miscellaneous, 8% (1984) /estimate/
[CHEMICAL PROFILE: Styrene (1984)] **PEER REVIEWED**

CHEMICAL PROFILE: Styrene. Polystyrene, 55%; acrylonitrile- butadiene-styrene (ABS), 9%; styrene-butadiene rubber (SBR), 7%; styrene- butadiene latex, 6%; unsaturated polyester resins, 6%; miscellaneous uses, including other copolymers and styrene-acrylonitrile (SAN), 4%; exports, 13%.
[Kavaler AR; Chemical Marketing Reporter 230 (5): 50 (1986)] **PEER REVIEWED**

CHEMICAL PROFILE: Styrene. Demand: 1985: 7.6 billion lb; 1986: 7.8 billion lb; 1990 /projected/: 8.65 billion lb. (Represents total apparent domestic consumption, including production of about 1 billion lb per year for export sales and imports of 200 million lb per year.)
[Kavaler AR; Chemical Marketing Reporter 230 (5): 50 (1986)] **PEER REVIEWED**

CHEMICAL PROFILE: Styrene. Polystyrene, 55%; acrylonitrile-butadiene-styrene (ABS), 10%; styrene-butadiene rubber (SBR), 5%; styrene-butadiene latex, 5%; unsaturated polyester resins, 5%; miscellaneous uses, including other copolymers and styrene-acrylonitrile (SAN), 7%; exports, 13%.
[Kavaler AR; Chemical Marketing Reporter 236 (7): 46 (1989)] **PEER REVIEWED**

CHEMICAL PROFILE: Styrene. Demand: 1988: 8,580 million lb; 1989: 8,700 million lb; 1993 /projected/: 9,950 million lb. (Includes exports, but not imports, which totaled 470 million lb last year.)
[Kavaler AR; Chemical Marketing Reporter 236 (7): 46 (1989)] **PEER REVIEWED**

Polystyrene, 54%; expandable polystyrene, 12%; acrylonitrile-butadiene-styrene resins, 10%; styrene-butadiene rubber, 7%; styrene-butadiene latexes, 6%; other, including unsaturated polyester resins, acrylic ester-styrene copolymers, and styrenated alkyds, 11%
[Chemical Marketing Reporter; Chemical Profile: Styrene. Sept 21 (1992)] **PEER REVIEWED**

Demand: (1999) 10.584 billion lbs; (2000) 10.796 billion lbs; (2004) 11.960 billion lbs (est)
[ChemExpo; Chemical Profile Database on Styrene (100-42-5). May 14, 2001. Available from, as of Sept 11, 2001: http://www.chemexpo.com/news/PROFILE010514.cfm **PEER REVIEWED**

Polystyrene (66%); acrylonitrile-butadiene-styrene (ABS) resins and styrene- acrylonitrile resins (SAN) (11%); styrene-butadiene rubber (SBR) (7%); styrene-butadiene latex (6%); unsaturated polyester resins (5%); misc (5%).
[ChemExpo; Chemical Profile Database on Styrene (100-42-5). May 14, 2001. Available from, as of Sept 11, 2001: http://www.chemexpo.com/news/PROFILE010514.cfm **PEER REVIEWED**

Approximately 60% of the styrene produced goes into polystyrene ... Approximately 18% goes into styrene-acrylonitrile copolymer (SAN) and terpolymers of acrylonitrile, butadiene, and styrene (ABS) ... Approximately 5% goes into styrene-butadiene rubber elastomers (SBR) ... Approximately 6% goes to styrene-butadiene latexes ... A further 5% is combined with unsaturated polyester resins ... The remainder goes into miscellaneous uses.
[James DH, Castor WM; Styrene. Ullmann's Encyclopedia of Industrial Chemistry 7th ed. (1999-2014). NY, NY: John Wiley & Sons. Online Posting Date: October 15, 2011] **PEER REVIEWED**

U. S. Production:
(1977) 3.12X10+12 G
[SRI] **PEER REVIEWED**

(1982) 2.70X10+12 G
[SRI] **PEER REVIEWED**

(1983) > 5942 million pounds.
[USEPA; Health and Environmental Effects Profile for Styrene (Final Draft) p.2 (1984) ECAO-CIN-P103] **PEER REVIEWED**

(1986) 3.56X10+12 g
[CHEM WEEK 140 (13): 30, 1987] **PEER REVIEWED**

(1986) 7.8X10+9 lb
[USITC; SYN ORG CHEM-US PROD PRELIMINARY FEBRUARY 1988 (SERIES C/P-87-5)] **PEER REVIEWED**

(1987) 8.0X10+9 lb

[USITC; SYN ORG CHEM-US PROD/SALES 1987 p.3-2] **PEER REVIEWED**

(1990) 8.02 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)] **PEER REVIEWED**

(1991) 8.12 billion lb
[Chem & Engineering News 71 (15): 11 (4/12/93)] **PEER REVIEWED**

(1992) 9.00 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)] **PEER REVIEWED**

(1993) 10.07 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)] **PEER REVIEWED**

(1999) 10.58 billion lbs; (2000) 10.79 billion lbs
[ChemExpo; Chemical Profile Database on Styrene (100-42-5). May 14, 2001. Available from, as of Sept 11, 2001: http://www.chemexpo.com/news/PROFILE010514.cfm **PEER REVIEWED**

Benzene, ethenyl- is listed as a High Production Volume (HPV) chemical (65FR81686). Chemicals listed as HPV were produced in or imported into the U.S. in >1 million pounds in 1990 and/or 1994. The HPV list is based on the 1990 Inventory Update Rule. (IUR) (40 CFR part 710 subpart B; 51FR21438).
[EPA/Office of Pollution Prevention and Toxics; High Production Volume (HPV) Challenge Program. Benzene, ethenyl- (100-42-5). Available from, as of February 21, 2014: http://www.epa.gov/hpv/pubs/general/opptsrch.htm **PEER REVIEWED**

Production volumes for non-confidential chemicals reported under the Inventory Update Rule.

Year	Production Range (pounds)
1986	>1 billion
1990	>1 billion
1994	>1 billion
1998	>1 billion
2002	>1 billion

[US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Benzene, ethenyl- (100-42-5). Available from, as of February 24, 2014: http://epa.gov/cdr/tools/data/2002-vol.html **PEER REVIEWED**

Production volume for non-confidential chemicals reported under the 2006 Inventory Update Rule. Chemical: Benzene, ethenyl-. Aggregated National Production Volume: 1 billion pounds and greater.
[US EPA; Non-Confidential 2006 Inventory Update Reporting. National Chemical Information. Benzene, ethenyl- (100-42-5). Available from, as of February 24, 2014: http://cfpub.epa.gov/iursearch/index.cfm **PEER REVIEWED**

Non-confidential 2012 Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. Chemical: Benzene, ethenyl-. National Production Volume: 10,245,086,182 lb/yr.
[USEPA/Pollution Prevention and Toxics; 2012 Chemical Data Reporting Database. Benzene, ethenyl- (100-42-5). Available from, as of February 24, 2014: http://java.epa.gov/oppt_chemical_search/ **PEER REVIEWED**

U. S. Imports:
(1978) 1.40X10+10 G
[SRI] **PEER REVIEWED**

(1983) 3.35X10+10 G
[SRI] **PEER REVIEWED**

(1986) 1.45X10+11 g
[CHEM WEEK 140 (13): 30, 1987] **PEER REVIEWED**

(1986) 3.18X10+8 lb
[BUREAU OF THE CENSUS. US IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1986 P.1-493] **PEER REVIEWED**

(1999) 1.038 million lbs; (2000) 1.265 million lbs
[ChemExpo; Chemical Profile Database on Styrene (100-42-5). May 14, 2001. Available from, as of Sept 11, 2001: http://www.chemexpo.com/news/PROFILE010514.cfm **PEER REVIEWED**

U. S. Exports:
(1978) 3.57X10+11 G
[SRI] **PEER REVIEWED**

(1983) 4.88X10+11 G

[SRI] **PEER REVIEWED**

(1986) 5.93X10+11 g
[CHEM WEEK 140 (13): 30, 1987] **PEER REVIEWED**

(1987) 1.13X10+9 lb (Styrene monomer)
[BUREAU OF THE CENSUS; US EXPORTS, SCHEDULE E, DECEMBER 1987, P.2-73] **PEER REVIEWED**

(1999) 2.552 billion lbs; (2000) 2.730 billion lbs
[ChemExpo; Chemical Profile Database on Styrene (100-42-5). May 14, 2001. Available from, as of Sept 11, 2001: http://www.chemexpo.com/news/PROFILE010514.cfm **PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:
Styrene is one of the most important industrial chemicals, with an enormously high production volume worldwide. The urinary mercapturic acids of its metabolite styrene-7,8-oxide, namely N-acetyl-S-(2-hydroxy-1-phenylethyl)-L-cysteine (PHEMA 1) and N-acetyl-S-(2-hydroxy-2-phenylethyl)-L-cysteine (PHEMA 2), are specific biomarkers for the determination of individual internal exposure to this highly reactive intermediate of styrene. /Investigators/ have developed and validated a fast, specific and very sensitive method for the accurate determination of the sum of phenylhydroxyethyl mercapturic acids (PHEMAs) in human urine with an automated multidimensional liquid chromatography-tandem mass spectrometry method using (13)C(6)-labelled PHEMAs as internal standards. Analytes were stripped from the urinary matrix by online extraction on a restricted access material, transferred to the analytical column and subsequently determined by tandem mass spectrometry. The limit of quantification (LOQ) for the sum of PHEMAs was 0.3 ug/L urine and allowed us to quantify the background exposure of the (smoking) general population. Precision within series and between series ranged from 1.5 to 6.8% at three concentrations ranging from 3 to 30 ug/L urine; the mean accuracy was between 104 and 110%. We applied the method to spot urine samples from 40 subjects of the general population with no known occupational exposure to styrene. The median levels (range) for the sum of PHEMAs in urine of non-smokers (n = 22) were less than 0.3 ug/L (less than 0.3 to 1.1 ug/L), whereas in urine of smokers (n = 18), the median levels were 0.46 ug/L (less than 0.3 to 2.8 ug/L). Smokers showed a significantly higher excretion of the sum of PHEMAs (p = 0.02)...
[Reska M et al; Anal Bioanal Chem. 397(8):3563-74 (2010).] **PEER REVIEWED** PubMed Abstract

Biomonitoring of chemicals in the workplace provides an integrated characterization of exposure that accounts for uptake through multiple pathways and physiological parameters influencing the toxicokinetics. /Investigators/ used the case of styrene to (i) determine the best times to sample venous blood and end-exhaled air, (ii) characterize the inter-individual variability in biological levels following occupational exposure and (iii) propose biological limit values using a population physiologically based pharmacokinetic (PBPK) model. /They/ performed Monte Carlo simulations with various physiological, exposure and workload scenarios. Optimal sampling times were identified through regression analyses between levels in biological samples and 24-hr area under the arterial blood concentration vs. time curve. /Investigators/ characterized the variability in levels of styrene in biological samples for exposures to a time weighted average (TWA) of 20 ppm. Simulations suggest that the best times to sample venous blood are at the end of shift in poorly ventilated workplaces and 15 min after the shift in highly ventilated workplaces. Exhaled air samples are most informative 15 min after the shift. For a light workload, simulated styrene levels have a median (5th-95th percentiles) of 0.4 mg/L (0.2-0.6) in venous blood at the end of shift and 0.5 ppm (0.3-0.8) in exhaled air 15 min after the end of shift. /The authors concluded that/ this study supports the current BEI(R) of the ACGIH of 0.2 mg/L of styrene in venous blood at the end of shift and indicates a biological limit value of 0.3 ppm in end-exhaled air 15 min after the end of shift.
[Verner MA et al; Toxicol Lett. 213(2):299-304 (2012).] **PEER REVIEWED** PubMed Abstract

Styrene and 1,3-butadiene are important intermediates used extensively in the plastics industry. They are metabolized mainly through cytochrome P450-mediated oxidation to the corresponding epoxides, which are subsequently converted to diols by epoxide hydrolase or through spontaneous hydration. The resulting styrene glycol and 3-butene-1,2-diol have been suggested as biomarkers of exposure to styrene and 1,3-butadiene, respectively. Unfortunately, poor ionization of the diols within electrospray mass spectrometers becomes an obstacle to the detection of the two diols by liquid chromatography/electrospray ionization-mass spectrometry (LC/ESI-MS). /The authors/ developed an LC/ESI-MS approach to analyze styrene glycol and 3-butene-1,2-diol by means of derivatization with 2-bromopyridine-5-boronic acid (BPBA), which not only dramatically increases the sensitivity of diol detection but also facilitates the identification of the diols. The analytical approach developed was simple, quick, and convincing without the need for complicated chemical derivatization. To evaluate the feasibility of BPBA as a derivatizing reagent of diols, /the authors/ investigated the impact of diol configuration on the affinity of a selection of diols to BPBA using the established LC/ESI-MS approach. /They/ found that both cis and trans diols can be derivatized by BPBA. In conclusion, BPBA may be used as a general derivatizing reagent for the detection of vicinal diols by LC/MS.
[Shen S et al; Anal Biochem. 386(2):186-93 (2009).] **PEER REVIEWED** PubMed Abstract Full text: PMC3960292

Mandelic acid and phenylglyoxylic acid were determined in urine as an index of exposure to styrene by high-performance liquid chromatography. Detection at 212 nm allows both acids to be measured at the same time with maximum sensitivity. The analysis takes approx 20 min to perform.
[GAETANI E ET AL; MED LAV 73 (4): 408-11 (1982)] **PEER REVIEWED** PubMed Abstract

Gas chromatography with flame ionization detection and mass spectrometry has been used to determine styrene and related hydrocarbons in the sc fat of workers in a styrene polymerization plant. The limit of detection was 50 ug/kg (ppb).

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V13 237 (1979)] **PEER REVIEWED**

Ultra-violet spectrophotometric methods using absorption at 247 or 245 nm have been used to determine styrene ... in biological fluids of exptl animals, with a limit of detection of 1000 ng/sample.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 237 (1979)] **PEER REVIEWED**

Analytic Laboratory Methods:
A convenient and reliable gas chromatographic method was developed for the simultaneous determination of six aromatic acid metabolites of styrene and styrene-oxide in rat urine; i.e., benzoic (BA), phenylacetic (PAA), mandelic (MA), phenylglyoxylic (PGA), hippuric (HA) and phenylaceturic (PAUA) acids. The method involves a one-pot esterification-extraction procedure, performed directly on urine without prior treatment. Analyses were performed on a RTX-1701 capillary column and the recovered isopropyl esters derivatives were detected by flame ionization detection. The analytical method was validated for selectivity, linearity, detection and quantification limits, recovery and intra-day and inter-day precisions. Calibration curves showed linearity in the range of 8-800 mg/L, except for HA and PAUA (40-800 mg/L). Limits of detection were between 0.2 (PPA) and 7.0 (PAUA) mg/L. The intra-day precisions determined at three concentrations levels were less than 5% for BA, PAA, MA and PGA and 9% for HA and PAUA, respectively. The corresponding mean inter-day precisions for these two groups were 8 and 16%, respectively. The method was successfully applied to quantitatively analyze styrene, styrene-oxide, ethylbenzene and toluene metabolites in urine samples from rats exposed by inhalation to these compounds at levels close to the occupational threshold limit values. Provided that this method can be transposed to human urine, it could have applications as part of biological monitoring for workers exposed to styrene or related compounds.
[Cosnier F et al; J Anal Toxicol. 2012 Jun;36(5):312-8 (2012).] **PEER REVIEWED** PubMed Abstract

Styrene oxide-cysteine adduction is predominantly involved in protein covalent modification after exposure in vivo to styrene or styrene oxide. In the present study, /researchers/ developed an alkaline permethylation- and GC/MS-based approach to detect styrene oxide-derived protein adduction. Permethylation of the protein adducts produced two methylthiophenylethanols, namely 2-methylthio-2-phenyl-1-ethanol and 2-methylthio-1-phenyl-1-ethanol. To improve the permethylation efficiency, reaction conditions, including temperature, time, NaOH strength, and molar ratio of CH(3)I/NaOH, were explored. Under optimized conditions, the yields of the analyte formation resulting from permethylation of authentic standard alpha- and beta-mercapturic acids, representing alpha and beta isomers of cysteine adducts, were 35% and 28%, respectively. Permethylation of styrene oxide-modified bovine serum albumin released the two methylthiophenylethanols with an alpha-/beta-adduction ratio of 1.5. A concentration-dependent increase in both alpha- and beta-adduction was observed in mouse liver microsomes incubated with styrene at various concentrations. CD-1 mice were administered intraperitoneally with styrene at doses of 0, 50, and 400mg/kg daily for 5 days. The formation of protein adducts derived from styrene oxide in whole blood in 400mg/kg group was observed with an alpha/beta ratio of 4.8, suggesting that the reaction of styrene oxide with cysteine residues took place more likely at the alpha-carbon than the beta-carbon of styrene oxide.
[Dai J, et al; Anal Biochem. 405(1):73-81 (2010).] **PEER REVIEWED** PubMed Abstract Full text: PMC3463237

Method: NIOSH 1501, Issue 3; Procedure: gas chromatography with flame ionization detection; Analyte: styrene; Matrix: air; Detection Limit: 0.4 ug/sample.
[CDC; NIOSH Manual of Analytical Methods, 4th ed. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.cdc.gov/niosh/docs/2003-154/ **PEER REVIEWED**

Method: NIOSH 3800, Issue 2; Procedure: extractive fourier transform infrared (FTIR) spectrometry; Analyte: styrene; Matrix: air; Detection Limit: 1.84 ppm for 10 meter absorption pathlength.
[CDC; NIOSH Manual of Analytical Methods, 4th ed. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.cdc.gov/niosh/docs/2003-154/ **PEER REVIEWED**

Method: OSHA 89; Procedure: gas chromatography with flame ionization detector; Analyte: styrene; Matrix: air; Detection Limit: 100 ppb (426 ug/cu m.
[U.S. Department of Labor/Occupational Safety and Health Administration's Index of Sampling and Analytical Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.osha.gov/dts/sltc/methods/toc.html **PEER REVIEWED**

Method: ASTM D5790; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: validated for treated drinking water, wastewater, and ground water; Detection Limit: 0.18 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-EAD 1625; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: water; Detection Limit: 10 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-NERL 502.2; Procedure: gas chromatography with photoionization detector; Analyte: styrene; Matrix: finished drinking water, raw source water, or drinking water in any treatment stage; Detection Limit: 0.01 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-NERL 524.2; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: surface water, ground water, and drinking water in any stage of treatment; Detection Limit: 0.06 ug/L.

[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-OGWDW/TSC 524.3; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: finished drinking waters; Detection Limit: 0.011 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-RCA 5030C; Procedure: purge and trap; Analyte: styrene; Matrix: water; Detection Limit: not provided.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-RCA 8021B; Procedure: gas chromatography with photoionization detector; Analyte: styrene; Matrix: ground water, aqueous sludges, caustic liquors, waste solvents, oily wastes, mousses, tars, fibrous wastes, polymeric emulsions, filter cakes, spent carbons, spent catalysts, soils, and sediments; Detection Limit: 0.01 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-RCA 8021B; Procedure: gas chromatography with electrolytic conductivity detection; Analyte: styrene; Matrix: ground water, aqueous sludges, caustic liquors, waste solvents, oily wastes, mousses, tars, fibrous wastes, polymeric emulsions, filter cakes, spent carbons, spent catalysts, soils, and sediments; Detection Limit: not provided.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: EPA-RCA 8260B; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: various; Detection Limit: not provided.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: Standard Methods 6200B; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: water; Detection Limit: 0.03 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: Standard Methods 6200C; Procedure: gas chromatography; Analyte: styrene; Matrix: water; Detection Limit: 0.02 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Method: USGS-NWQL O-4127-96; Procedure: gas chromatography/mass spectrometry; Analyte: styrene; Matrix: surface- or ground-water; Detection Limit: 0.039 ug/L.
[National Environmental Methods Index; Analytical, Test and Sampling Methods. Styrene (100-42-5). Available from, as of February 24, 2014: http://www.nemi.gov **PEER REVIEWED**

Gas chromatography can be used to determine styrene in waste-waters in concentrations of 4.5 to 63 ug/L (ppb): Pakhomova AD, Berendeeva VL; Khim Tekhnol (Kiev) 3: 12-3 (1974), & lower levels have been measured after extraction with freon & concentration of the sample in a Kuderna-Danish apparatus: Austern BM et al; Environ Sci Technol 9: 588-90 (1975).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 237 (1979)] **PEER REVIEWED**

Residual styrene in styrene polymers can be determined by gas chromatography: 1) by a headspace method, with a limit of detection of 1 mg/kg (ppm): Steinchen RJ; Anal Chem 48: 1398-1402 (1976); 2) with a limit of detection of 10 mg/kg (ppm) ... 3) in concentrations of 0.03 to 1.0% ... & 4) with a limit of detection of 1 mg/kg (ppm) after extraction in water vapor & concentration in a suitable solvent ...
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V13 237 (1979)] **PEER REVIEWED**

Raman spectral analysis has been used to determine residual styrene in commercial styrene-butadiene latexes at concn in range of 0.6 to 12.4 wt percent. The Raman results agree with those obtained by high performance liquid chromatography within 0.25%: Wancheck PL, Wolfram LE; Appl Spectrosc 30: 542-44 (1976).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19 237 (1979)] **PEER REVIEWED**

Biological monitoring includes quantitation of urinary styrene, creatinine, mandelic acid, and phenylglyoxylic acid. /Biomonitoring in urine/
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 308] **PEER REVIEWED**

Styrene and its metabolite styrene 7,8-oxide can be monitored in blood by a variety of analytical techniques. Biomarkers of styrene exposure measured in blood lymphocytes include 06-guanine DNA adducts, styrene oxide-DNA adducts, DNA strand breaks, mutant frequencies in the hypoxanthine guanine phosphoribosyltransferase gene, micronuclei, and sister-chromatid exchanges. /Biomonitoring in blood/
[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. V4 308] **PEER

REVIEWED**

Sampling Procedures:
NIOSH Method 1501. Substance: Styrene; Nominal volume of air, 5 L in 5 min; Maximum volume of air, 14 L; Flow rate, equal to or less than 1.0 L/min; Range at nominal volume 426 to 1710 mg/cu m; Sampler: solid sorbent tube (coconut shell charcoal, 100 mg/50 mg); Blanks: 2 to 10 field blanks per set; Bulk sample: desirable, 1 to 10 mL; ship in separate containers from samples. Overall precision: 0.058 (relative standard deviation).
[U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed. Methods A-Z & Supplements. Washington, DC: U.S. Government Printing Office, Aug 1994.]
PEER REVIEWED

Special References:

Special Reports:
VAINIO H ET AL; ADV EXP MED BIOL 136A (BIOL REACT INTERMED-2 CHEM MECH BIOL EFF PT A): 257-74 (1982). A REVIEW WITH 63 REFERENCES ON THE METABOLISM & MUTAGENICITY OF STYRENE.

USEPA; Health Assessment Document: Styrene (Draft) (1985)

Environment Canada; Tech Info for Problem Spills: Styrene (Draft) (1981)

NIOSH; Criteria Document: Styrene (1983) DHEW Pub. NIOSH 83-119

NCI/DCE; Monograph On Human Exposure To Chemicals In The Workplace: Styrene (1985)

USEPA; Health and Environmental Effects Profile for Styrene (Final Draft) (1984) ECAO-CIN-P103

DHHS/ATSDR; Toxicological Profile for Styrene TP-91/25 (1992)

DHEW/NCI; Bioassay of Styrene for Possible Carcinogenicity (1979) Technical Rpt Series No. 185 DHEW Pub No. (NIH) 79-1741

Groth-Marnat G; Precept Mot Skills 77 (3 pt 2): 1139-49 (1993). Neuropsychological effcts of styrene exposure, a review of current literature.

Pahwa R, Kalra J; Vet Human Toxicol 35 (6): 516-20 (1993). A critical review of the neurotoxicity of styrene in humans.

USEPA/ECAO; Drinking Water Criteria Document for Styrene (1991) EPA Contract No. EPA-68-03-3112 NTIS/PB91-143370

Bond JA; CRC Critical Reviews Toxicol 19 (3): 227-49 (1989). Review of the toxicology of styrene.

U.S. Department of Health & Human Services/National Toxicology Program; Twelfth Report on Carcinogens (2011). The Report on Carcinogens is an informational scientific and public health document that identifies and discusses substances (including agents, mixtures, or exposure circumstances) that may pose a carcinogenic hazard to human health. Styrene (100-42-5) is listed as reasonably anticipated to be a human carcinogen. First listed in the Twelfth Report on Carcinogens (2011).
[Available from, as of February 24, 2014: http://ntp.niehs.nih.gov/

Synonyms and Identifiers:

Related HSDB Records:
2646 [STYRENE-7,8-OXIDE] (METABOLITE)

Synonyms:
BENZENE, ETHENYL-
PEER REVIEWED

BENZENE, VINYL-
PEER REVIEWED

CINNAMENE
PEER REVIEWED

CINNAMENOL
PEER REVIEWED

CINNAMOL
PEER REVIEWED

DIAREX HF 77
PEER REVIEWED

Ethenylbenzene
PEER REVIEWED

ETHYLENE, PHENYL-
PEER REVIEWED

FEMA number 3234.
PEER REVIEWED

NCI-C02200
PEER REVIEWED

PHENETHYLENE
PEER REVIEWED

PHENYLETHENE
PEER REVIEWED

PHENYLETHYLENE
PEER REVIEWED

STIROLO (ITALIAN)
PEER REVIEWED

STYREEN (DUTCH)
PEER REVIEWED

STYREN (CZECH)
PEER REVIEWED

STYRENE MONOMER
PEER REVIEWED

STYROL
PEER REVIEWED

STYROLE
PEER REVIEWED

STYROLENE
PEER REVIEWED

STYROL (GERMAN)
PEER REVIEWED

STYRON
PEER REVIEWED

STYROPOL
PEER REVIEWED

STYROPOR
PEER REVIEWED

VINYLBENZEN (CZECH)
PEER REVIEWED

VINYLBENZEN (DUTCH)
PEER REVIEWED

VINYLBENZENE
PEER REVIEWED

VINYLBENZOL
PEER REVIEWED

Styropol SO
PEER REVIEWED

Formulations/Preparations:
... Available in USA as polymer grade ... purity, 99.6% min; polymer, 10 mg/kg (ppm) max; sulfur, 25 mg/kg (ppm) max; chlorine, 50 mg/kg (ppm) max; hydrogen peroxide, 100 mg/kg (ppm) max; benzaldehyde, 200 mg/kg (ppm) max; and tertiary-butyl catechol (as inhibitor), 12-15 mg/kg (ppm). ... Free from suspended matter and is clear.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V19: 232 (1979)] **PEER REVIEWED**

Purity, 99.6-99.9% min; ethylbenzene, 85 ppm max; polymer content, 10 ppm max; para-tert-butylcatechol (inhibitor), 10-15 ppm or 45-55 ppm; aldehydes (as benzaldehyde), 200 ppm; peroxides (as H2O2), 0.0015 wt% or 100 ppm max; benzene, 1 ppm max; sulfur, 25 ppm max; chlorides (as chlorine), 50 ppm max
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V60: 234 (1994)] **PEER REVIEWED**

Clear, colorless grades
[Kuney, J.H., J.M. Mullican (eds.). Chemcyclopedia. Washington, DC: American Chemical Society, 1994., p. 111] **PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:
UN 2055; Styrene monomer, stabilized

IMO 3; Styrene monomer, stabilized

Standard Transportation Number:
49 072 65; Styrene monomer, inhibited

Administrative Information:

Hazardous Substances Databank Number: 171

Last Revision Date: 20140904

Last Review Date: Reviewed by SRP on 5/15/2014

Update History:
Complete Update on 2014-09-04, 94 fields added/edited/deleted
Field Update on 2008-09-02, 2 fields added/edited/deleted
Field Update on 2008-08-23, 1 fields added/edited/deleted
Field Update on 2008-08-22, 1 fields added/edited/deleted
Field Update on 2008-08-21, 1 fields added/edited/deleted
Field Update on 2008-08-15, 25 fields added/edited/deleted
Field Update on 2007-06-07, 1 fields added/edited/deleted
Field Update on 2006-04-18, 2 fields added/edited/deleted
Field Update on 2006-04-17, 2 fields added/edited/deleted
Complete Update on 2005-06-24, 2 fields added/edited/deleted
Field Update on 2005-04-29, 4 fields added/edited/deleted
Field Update on 2005-01-29, 2 fields added/edited/deleted
Complete Update on 11/08/2002, 1 field added/edited/deleted.
Complete Update on 10/16/2002, 1 field added/edited/deleted.
Complete Update on 08/06/2002, 1 field added/edited/deleted.
Complete Update on 06/27/2002, 87 fields added/edited/deleted.
Field Update on 05/13/2002, 1 field added/edited/deleted.
Field Update on 01/14/2002, 1 field added/edited/deleted.
Field Update on 08/08/2001, 1 field added/edited/deleted.
Complete Update on 09/12/2000, 1 field added/edited/deleted.
Complete Update on 06/12/2000, 1 field added/edited/deleted.
Complete Update on 02/08/2000, 1 field added/edited/deleted.
Complete Update on 02/02/2000, 1 field added/edited/deleted.
Complete Update on 11/18/1999, 1 field added/edited/deleted.
Complete Update on 11/02/1999, 2 fields added/edited/deleted.
Complete Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 08/26/1999, 1 field added/edited/deleted.
Complete Update on 07/20/1999, 9 fields added/edited/deleted.
Complete Update on 05/04/1999, 1 field added/edited/deleted.

Complete Update on 03/29/1999, 1 field added/edited/deleted.
Complete Update on 02/24/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 02/25/1998, 1 field added/edited/deleted.
Complete Update on 09/25/1997, 2 fields added/edited/deleted.
Complete Update on 08/11/1997, 1 field added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 01/09/1997, 2 fields added/edited/deleted.
Complete Update on 06/27/1996, 1 field added/edited/deleted.
Complete Update on 06/11/1996, 1 field added/edited/deleted.
Complete Update on 04/16/1996, 9 fields added/edited/deleted.
Field Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 01/16/1996, 1 field added/edited/deleted.
Complete Update on 06/09/1995, 1 field added/edited/deleted.
Complete Update on 06/07/1995, 78 fields added/edited/deleted.
Field Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 10/13/1994, 2 fields added/edited/deleted.
Complete Update on 08/04/1994, 1 field added/edited/deleted.
Complete Update on 06/08/1994, 1 field added/edited/deleted.
Complete Update on 05/05/1994, 1 field added/edited/deleted.
Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 11/05/1993, 1 field added/edited/deleted.
Complete Update on 09/15/1993, 1 field added/edited/deleted.
Complete Update on 08/20/1993, 1 field added/edited/deleted.
Complete Update on 08/07/1993, 1 field added/edited/deleted.
Complete Update on 08/04/1993, 1 field added/edited/deleted.
Complete Update on 04/30/1993, 1 field added/edited/deleted.
Field update on 12/11/1992, 1 field added/edited/deleted.
Complete Update on 12/02/1992, 1 field added/edited/deleted.
Complete Update on 11/20/1992, 3 fields added/edited/deleted.
Complete Update on 11/09/1992, 1 field added/edited/deleted.
Complete Update on 09/03/1992, 2 fields added/edited/deleted.
Complete Update on 05/29/1992, 3 fields added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 04/03/1992, 1 field added/edited/deleted.
Complete Update on 01/23/1992, 1 field added/edited/deleted.
Complete Update on 09/26/1991, 2 fields added/edited/deleted.
Complete Update on 07/03/1990, 107 fields added/edited/deleted.
Field Update on 05/04/1990, 1 field added/edited/deleted.
Field Update on 01/15/1990, 1 field added/edited/deleted.
Complete Update on 05/15/1987
Created 19830401 by AR