March 31, 1987

822K87100

STYRENE

Health Advisory
Office of Drinking Water
U.S. Environmental Protection Agency

I. INTRODUCTION

The Health Advisory (HA) Program, sponsored by the Office of Drinking Water (ODW), provides information on the health effects, analytical methodology and treatment technology that would be useful in dealing with the contamination of drinking water. Health Advisories describe nonregulatory concentrations of drinking water contaminants at which adverse health effects would *not* be anticipated to occur over specific exposure durations. Health Advisories contain a margin of safety to protect sensitive members of the population.

Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as new information becomes available.

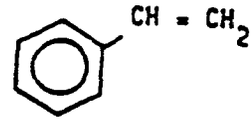
Health Advisories are developed for One-day, Ten-day, Longer-term (approximately 7 years, or 10% of an individual's lifetime) and Lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from such exposure. For those substances that are known or probable human carcinogens, according to the Agency classification scheme (Group A or B), Lifetime HAs are not recommended. The chemical concentration values for Group A or B carcinogens are correlated with carcinogenic risk estimates by employing a cancer potency (unit risk) value together with assumptions for lifetime exposure and the consumption of drinking water. The cancer unit risk is usually derived from the linear multistage model with 95% upper confidence limits. This provides a low-dose estimate of cancer risk to humans that is considered unlikely to pose a carcinogenic risk in excess of the stated values. Excess cancer risk estimates may also be calculated using the One-hit, Weibull, Logit or Probit models. There is no current understanding of the biological mechanisms involved in cancer to suggest that any one of these models is able to predict risk more accurately than another. Because each model is based on differing assumptions, the estimates that are derived can differ by several orders of magnitude.

This Health Advisory (HA) is based on information presented in the Office of Drinking Water's Health Effects Criteria Document (CD) for Styrene (U.S. EPA, 1985a). The HA and CD formats are similar for easy reference. Individuals desiring further information on the toxicological data base or rationale for risk characterization should consult the CD. The CD is available for review at each EPA Regional Office of Drinking Water counterpart (e.g., Water Supply Branch or Drinking Water Branch), or for a fee from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Rd., Springfield, VA 22161, PB # 86-118056/AS. The toll-free number is (800) 336-4700; in the Washington, D.C. area: (703) 487-4650.

II. GENERAL INFORMATION AND PROPERTIES

CAS No. 100-42-5

Structural Formula



Synonyms

Vinyl benzene, cinnamene, phenylethylene, ethenylbenzene

Use

Styrene plastics .

Properties (Hansch and Leo, 1979; Lewis et al., 1983)

Chemical Formula	C_8H_8
Molecular Weight	104.16
Physical State	Clear, colorless liquid with a characteristically sweet and pleasant odor
Melting Point	145°C
Density (20°C)	30.86 g/cm^3
Vapor Pressure (20°C)	4.53 torr
(25°C)	6.18 torr
Water Solubility	320 mg/L
Log Octanol/Water Partition Coefficient	2.95
Conversion Factors	1 mg/m^3 = 0.235 ppm 1 ppm = 4.26 mg/m^3

Occurrence

- Styrene is produced primarily from the dehydrogenation of ethylbenzene. In 1982, the U.S production of styrene totaled 5.9 billion pounds.

- National drinking water surveys indicate that styrene is an infrequent contaminant. To date, the testing of 941 ground water supplies and 102 surface water supplies has failed to result in the detection of a single positive occurrence (Boland, 1981).

- Contamination of drinking water by styrene, however, has been reported occasionally by State programs.

III. PHARMACOKINETICS

Absorption

- Available data indicate that the absorption of styrene from the gastrointestinal tract of rats is rapid and virtually complete (Plotnick and Weigel, 1979).

- Styrene uptake and absorption has been the subject of a number of human inhalation studies (Fiserova-Bergerova and Teisinger, 1965; Teramoto and Horiguchi, 1979). The findings of these studies indicate that pulmonary retention of styrene is approximately 2/3 of the administered concentration with considerable variation in measured uptake between individuals and studies (mean uptakes ranged from 59 to 89%).

Distribution

- The distribution of styrene following oral administration was studied in rats given single doses of 20 mg/kg ^{14}C-styrene in corn oil by gavage (Plotnick and Weigel, 1979). Peak tissue levels were reached within 2 to 4 hours. The organs with the highest concentrations were kidney (46 ug/g in males; 25 ug/g in females), liver (13 ug/g in males; 7 ug/g in females) and pancreas (10 ug/g in males; 6 ug/g in females) with lower concentration levels in lungs, heart, spleen, adrenals, brain, testes and ovaries.

- Results from inhalation studies in rats indicate that distribution of styrene is widespread with relatively high concentrations in adipose tissue (Withey and Collins, 1979).

- In humans, Dowty et al. (1976) found concentrations of transplacentally transferred styrene to be somewhat higher than those of maternal blood, which suggests a selective one-way transplacental transfer.

- Pellizzari et al. (1982) detected styrene in each of 8 milk samples collected from lactating women residing in various cities.

Metabolism

- The metabolic fate of styrene in mammals has been studied extensively. There is limited information from human studies, but similarities to the process in other mammals have been identified.

- Based on studies in rats administered styrene-7,8-oxide or styrene glycol by intraperitoneal injection, Ohtsuji and Ikeda (1971) have proposed that the metabolism of styrene proceeds via P-450 microsomal oxidations to styrene oxide, styrene glycol, and then to mandelic acid which is metabolized to either phenylglyoxylic acid or to benzoic the hippuric acid.

Excretion

- Results from a number of studies in rats (Withey and Collins, 1977, 1979; Ramsey and Young, 1978, 1980; Teramoto and Horiguchi, 1979) indicate that styrene is eliminated relatively rapidly from all tissues in test animals.

- Twenty-four hours following oral administration of 20 mg/kg ^{14}C-styrene to rats, concentrations in all tissues and organs examined were less than 1 ug/g (Plotnick and Weigel, 1979).

- The elimination of styrene from the heart, brain, liver, spleen and kidney of rats was described by biphasic log-linear kinetics after intravenous injection of 4.0 mg/kg (Withey and Collins, 1977). Half-lives ranged from 3.8 to 7.1 minutes for the alpha (fast) phase and from 20 to 37 minutes for the beta (slow) phase.

- Predictions based on a toxicokinetic model (parameters estimated from a human inhalation study) indicated that maximum concentrations of styrene in both blood and fat of humans were reached after a few repeated 8-hour daily exposures to 80 ppm styrene, suggesting no tendency for long-term accumulation (Ramsey et al., 1980; Ramsey and Young, 1978, 1980).

IV. HEALTH EFFECTS

Humans

- Results of controlled experiments using human volunteers indicate that styrene administered by inhalation at relatively high doses results in central nervous system (CNS) effects.

- Drowsiness, listlessness and an altered sense of balance were reported during a 4-hour exposure of two male subjects to styrene at 3,407 mg/m^3 (800 ppm) (Carpenter et al., 1944).

- Stewart et al. (1968) reported that volunteers exposed to styrene by inhalation at 217 mg/m^3 (50 ppm) and 499 mg/m^3 (117 ppm) for 1 and 2 hours, respectively, showed no signs of toxicity. The moderately strong initial styrene odor diminished after 5 minutes. At 921 mg/m^3 (216 ppm) nasal irritation resulted after 20 minutes. Eye and nose irritation, strong odor and altered neurological function were reported for volunteers exposed to styrene at 1,600 mg/m^3 (376 ppm) for 1 hour. Most volunteers exposed to this level exhibited reduced performance in the Crawford Manual Dexterity Collar and Pin Test, the modified Romberg Test and the Flannagan Coordination Test. Six subjects were exposed to 422 mg/m^3 (99 ppm) styrene vapor for seven hours. No serious untowed effects were noted.

° Gamberale and Hultengren (1974) exposed 12 subjects to styrene by inhalation at concentrations of 213, 639, 1,065 and 1,491 mg/m^3 (50, 150, 250 and 350 ppm) during four consecutive 30-minute intervals. A dose-related increase in single reaction time was evident. Reaction time recorded during the final 30-minute exposure was significantly increased ($p < 0.05$).

° Odkvist et al. (1982) studied the effects of styrene on the vestibulo-oculomotor functions in 10 subjects exposed to styrene by inhalation at 370 to 591 mg/m^3 (88-140 ppm) for approximately 80 minutes. The rate of movement of the eyes between two alternating light sources (saccade) increased significantly ($p < 0.05$) after exposure. Suppression of the vestibulo-oculomotor reflex was also affected.

° There is suggestive evidence that the human fetus is more sensitive than the adult to the toxic effects of styrene (Holmberg, 1977; Hemminki et al., 1980).

° The frequency of spontaneous abortions among Finnish chemical workers was analyzed by Hemminki et al. (1980). Information on spontaneous abortions (15,482 cases), induced abortions (71,235 cases) and births (193,897 cases) for 1973-1976 was obtained from the Hospital Discharge Registry of the Finnish National Board of Health and linked by social security number to the membership of the Finnish Union of Chemical Workers (approximately 900 female members). About 85% of the total number of spontaneous abortions in Finland were reportedly listed in the registry. The rate of spontaneous abortion was defined as the number of spontaneous abortions x 100/number of births. The rates of spontaneous abortion were 8.54% (N = 52) and 15.0% (N = 6) among the female union members and a subgroup in the styrene industry, respectively. These rates were significantly higher ($p<0.01$) than the rate among all Finnish women (5.52%, 15,482 spontaneous abortions). The ratios of spontaneous abortion were 16 and 32 in the female union workers and female styrene industry workers, respectively, which were significantly higher ($p<0.001$) than the rate among all Finnish women (8%).

° The information on the work histories of 43 Finnish mothers of children born with central nervous system (CNS) defects from June 1, 1976 to March 1, 1977 were obtained through personal interviews (Holmberg, 1977). Two of these mothers had been employed in the reinforced plastics industry with regular exposure to styrene, polyester resin, organic peroxides and acetone during pregnancy. The defects in their two children were anencephaly and congenital hydrocephaly. The overall rates of anencephaly and congenital hydrocephaly were reported to be 0.2 and 0.3, respectively, per 1000 live births in Finland. Based on these estimates, there appeared to be more than a 300 fold ~~increased rate of these malformations in~~ the reinforced plastics industry during the 9-month study period compared with the general population (2/12 vs 0.5/1000).

Animals

Short-term Exposure

- Wolf et al. (1956) reported an acute oral LD_{50} of greater than 5,000 mg/kg for rats treated with styrene by gavage. This indicates that the acute toxicity of styrene is relatively low.

- The lowest single oral dose of styrene (administered by oral intubation) causing 100% mortality in rats within two weeks of treatment was 8,000 mg/kg, while 1,600 mg/kg was the maximum dose resulting in no deaths (Spencer et al., 1942).

- The effects of styrene administration at 250, 450 or 900 mg/kg orally (method not stated) for 7 consecutive days on hepatic mixed function oxidase (MFO) enzyme activities, glutathione content and glutathione-S-transferase activity were reported by Das et al. (1981). Activities of aryl hydrocarbon hydroxylase and aniline hydroxylase were significantly enhanced at higher doses of styrene (450 and 900 mg/kg). A significant lowering of glutathione content accompanied with the inhibition of glutathione-S-transferase activity was also noted at the highest dose of styrene (900 mg/kg). Therefore, the NOAEL for effects on hepatic enzymes in this study was 250 mg/kg/day.

- Agrawal et al. (1982) studied the effects of styrene on dopamine receptor binding in rats. Styrene was administered at 200 or 400 mg/kg/day by gavage to groups of 6 eight-week old ITRC male albino rats. Styrene was administered in a single dose or in up to 90 daily doses over 90 days. Significant increases in the specific binding of ^{3}H-spiroperidol to dopamine receptors in the corpus stratum were noted at both levels after single or repeated exposure to styrene. The LOAEL for this study was identified as 200 mg/kg/day.

Long-term Exposure

- Changes in hepatic enzyme activity following oral exposure to styrene have been demonstrated by a number of investigators.

- Srivastava et al. (1982) administered styrene by gavage (at 200 or 400 mg/kg/day) to groups of 5 adult male albino ITRC rats, 6 days per week for 100 days. These animals did not exhibit any changes in weight gain or other overt signs of toxicity. There were significant dose-dependent increases in hepatic enzymes (benzo[a]pyrene hydroxylase and aminopyrine-N-demethylase) as well as decreases (glutathione-S-transferase). There were significant decreases in some mitochondrial enzymes as well. Histopathological changes were seen only at the high dose and these consisted of tiny areas of focal liver necrosis, consisting of a few degenerated hepatocytes and inflammatory cells. Therefore, the LOAEL for hepatic effects was 200 mg/kg/day.

- Groups of ten female rats were administered styrene at 66.7, 133, 400 or 667 mg/kg/day by intubation, five days a week for six months (Wolf

et al., 1956). At the two higher dose levels, decreased growth weights and increased liver and kidney weights were observed without hematologic or histopathologic effects. At the two lower dose levels, no effects were noted on body weight, organ weight or pathology. Therefore, the NOAEL for this study was 133 mg/kg/day and the LOAEL was 400 mg/kg/day.

° Beagle dogs were given styrene in a peanut oil suspension by gavage 7 days per week for 560 days (Quast et al., 1978). Dose levels were 200, 400 or 600 mg/kg bw/day. The controls received peanut oil only. At the two higher dose levels, minimal histopathologic effects were noted in the liver (increased iron deposits within the reticulo-endothelial cells) as well as hematologic effects that included increased Heinz bodies in erythrocytes and a decreased packed cell volume. At the lowest dose level, these effects were not noted. Therefore, 200 mg/kg/day was identified as the NOAEL for this study and 400 mg/kg/day can be designated as the LOAEL.

Reproductive Effects

° The reproductive/teratogenic effects of styrene oxide were assessed in Wistar rats (Sikov et al. 1981). The percentage of pregnant rats was reduced significantly.

Developmental Effects

° Investigators at the Dow Chemical Company administered styrene in peanut oil to pregnant Sprague-Dawley rats (29 to 39 dams per group) by gavage at dose levels of 0, 180 or 300 mg/kg/day (0, 90, 150 mg/kg twice daily) on days 6 through 15 of gestation (Murray et al., 1976; 1978). Maternal toxicity was indicated by significantly reduced ($p < 0.05$) body weight gain and food consumption at the higher dose level. There were no significant effects observed on maternal mortality or percent pregnancy. No teratogenic or fetotoxic effects were observed. Therefore, the NOAEL for maternal toxicity was 180 mg/kg/day.

Mutagenicity

° Results were negative for six mutagenicity tests using Salmonella typhimurium test systems, both with and without S-9 metabolic activating system. Styrene was tested using the bacterial strains TA1535, TA1537, TA98 and TA100. De Meester et al. (1977, 1981) and Vainio et al. (1976) obtained positive results with mutant strains sensitive to base pair substitution while all tests were negative in strains sensitive to frameshift mutagens.

° Styrene oxide, a major metabolite of styrene, has been demonstrated consistently to be mutagenic in S. typhimurium TA1535 and TA100, in the presence and absence of a mammalian metabolic activating system (De Meester et al., 1977; 1981).

Carcinogenicity

- Both positive and negative results have been reported in bioassays of the potential carcinogenicity of styrene in experimental animals. Most of the long-term bioassay results, however, are characterized by inconsistent observations of elevated tumor formation and excessive mortality among treated animals (Jersey et al., 1978; Ponomarkov and Tomatis, 1978; NTP, 1979; Maltoni et al., 1982).

- Retrospective cohort mortality and case-control studies have been conducted on workers exposed to styrene in the styrene-polystyrene manufacturing industry and in the styrene-butadiene synthetic rubber industry (McMichael et al., 1976; Smith and Ellis, 1977; Meinhardt et al., 1978). There are inadequate data at present to indicate that styrene is a human carcinogen. However, an elevated incidence of tumors of the hematopoietic and lymphatic tissues have been observed. The available studies are limited because of relatively small cohort sizes or multiple chemical exposures of workers (including exposure to benzene).

V. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

Health Advisories (HAs) are generally determined for One-day, Ten-day, Longer-term (approximately 7 years) and Lifetime exposures if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. The HAs for noncarcinogenic toxicants are derived using the following formula:

$$HA = \frac{(NOAEL \text{ or } LOAEL) \times (BW)}{(UF) \times (\_\_\_ \text{ L/day})} = \_\_\_ \text{ mg/L } (\_\_\_ \text{ ug/L})$$

where:

NOAEL or LOAEL = No- or Lowest-Observed-Adverse-Effect-Level in mg/kg bw/day.

BW = assumed body weight of a child (10 kg) or an adult (70 kg).

UF = uncertainty factor (10, 100 or 1,000), in accordance with NAS/ODW guidelines.

___ L/day = assumed daily water consumption of a child (1 L/day) or an adult (2 L/day).

One-day Health Advisory

The study of Stewart et al. (1968) was seleted as the basis for calculating the One-day HA. The study invloved a controlled styrene inhalation exposure using nine healthy human male volunteers. No subjective or objective signs of toxicity were noted following one and two hour exposures to 51 ppm (217 mg/m^3) or 117 ppm (449 mg/m^3) styrene respectively. To simluate a work day, six subjects were exposed to 99 ppm (422 mg/m^3) styrene vapor for seven

hours. From a subjective standpoint, no serious untoward effects were noted except mild eye and throat irritation in three subjects. There were no objective signs of impairment of balance or coordination; however, three of the six subjects did report that they were having intermittent difficulty in performing the modified Romberg Test. In contrast, exposure to 376 ppm (1602 mg/m^3) styrene vapor for one hour resulted in abnormal neurological findings and complaints of nausea and inebriation. The result of urinalysis, hematology and blood chemistry studies were normal and unchanged from pre-exposure values.

The results of another study (Odkvist et al., 1982) using human volunteers exposed to similar styrene levels, indicate that the mean pulmonary styrene uptake was 64% of the inspired amount. Using a NOAEL of 99 ppm (422 mg/m^3) from a 7-hour exposure, the One-day Health Advisory for a 10-kg child can be derived. First the total absorbed dose (TAD) is determined.

$$TAD^* = \frac{(422\ mg/m^3)\ (20\ m^3/day)\ (7\ hours/24\ hours)\ (0.64)}{70\ kg} = 22.5\ mg/kg/day$$

where:

TAD = total absorbed dose.

442 mg/m^3 = NOAEL, based on the absence of adverse effects in humans exposed to styrene by inhalation.

7 hours/24 hours = duration of exposure.

20 m^3/day = assumed ventilation volume for 70-kg adult.

0.64 = estimated ratio of absorbed dose (Odkvist et al., 1982).

70 kg = weight of exposed individual (adult).

Therefore the One-day Health Advisory for a 10-kg child is as follows:

$$\text{One-day HA} = \frac{(22.5\ mg/kg/day)\ (10\ kg)}{(10)\ \ (1\ L/day)} = 22.5\ mg/L$$

where:

22.5 mg/kg/day = TAD.

10 kg = assumed body weight of a child.

10 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from a study in humans.

1 L/day = assumed daily water consumption of a child.

Ten-day Health Advisory

No information was found in the available literature that was suitable for deriving a Ten-day HA value for styrene. It is therefore recommended that the Longer-term HA for a 10-kg child (2 mg/L, calculated below) be used at this time as a conservative estimate of the Ten-day HA value.

Longer-term Health Advisory

The Quast et al. (1978) study in dogs has been chosen to serve as the basis for calculating the Longer-term HAs for styrene. In this study, beagle dogs were administered styrene by gavage at 0, 200, 400 or 600 mg/kg/day, 7 days per week, for 560 days. At the two higher doses, minimal histopathologic effects were noted in the liver (increased iron deposits within the reticulo-endothelial cells) as well as hematologic effects that included increased Heinz bodies in erythrocytes and a decreased packed cell volume. At the lowest dose level, these effects were not noted with the possible exception of the equivocal observation of low level occurrence of Heinz bodies in a single female from this group.

Based on the NOAEL of 200 mg/kg/day determined in this study, the Longer-term HAs are calculated as follows:

For a 10-kg child:

$$\text{Longer-term HA} = \frac{(200 \text{ mg/kg/day})\ (10 \text{ kg})}{(100)\ (10)\ (1 \text{ L/day})} = 2 \text{ mg/L } (2000 \text{ ug/L})$$

where:

200 mg/kg/day = NOAEL at which no decreased growth weights or increased liver and kidney weights were observed in dogs.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

10 = modifying factor for small group size (4 dogs per treatment).

1 L/day = assumed daily water consumption of a child.

For a 70-kg adult:

$$\text{Longer-term HA} = \frac{(200 \text{ mg/kg/day})\ (70 \text{ kg})}{(100)\ (10)\ (2 \text{ L/day})} = 7 \text{ mg/L } (7000 \text{ ug/L})$$

where all factors are the same except:

70 kg = assumed body weight of an adult.

2 L/day = assumed daily water consumption of an adult.

Lifetime Health Advisory

The Lifetime HA represents that portion of an individual's total exposure that is attributed to drinking water and is considered protective of noncarcinogenic adverse health effects over a lifetime exposure. The Lifetime HA is derived in a three step process. Step 1 determines the Reference Dose (RfD), formerly called the Acceptable Daily Intake (ADI). The RfD is an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, and is derived from the NOAEL (or LOAEL), identified from a chronic (or subchronic) study, divided by an uncertainty factor(s). From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined (Step 2). A DWEL is a medium-specific (i.e., drinking water) lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived from the multiplication of the RfD by the assumed body weight of an adult and divided by the assumed daily water consumption of an adult. The Lifetime HA is determined in Step 3 by factoring in other sources of exposure, the relative source contribution (RSC). The RSC from drinking water is based on actual exposure data or, if data are not available, a value of 20% is assumed for synthetic organic chemicals and a value of 10% is assumed for inorganic chemicals. If the contaminant is classified as a Group A or B carcinogen, according to the Agency's classification scheme of carcinogenic potential (U.S. EPA, 1986), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical. For Group C carcinogens, an additional safety factor of 10 is added to the DWEL.

The Lifetime HA for a 70-kg adult has been determined on the basis of the study in dogs by Quast et al. (1978) as described above.

Using the NOAEL of 200 mg/kg/day, as determined in that study, the Lifetime HA is calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(200\ mg/kg/day)}{(1,000)} = 0.2\ mg/kg/day$$

where:

200 mg/kg/day = NOAEL at which no decreased growth weights or increased liver and kidney weights were observed in dogs.

1,000 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study of less-than-lifetime duration.

Step 2: Determination of the Drinking Water Equivalent Level (DWEL)

$$DWEL = \frac{(0.2\ mg/kg/day)\ (70\ kg)}{(2\ L/day)\ (10)} = 0.7\ mg/L\ (700\ ug/L)$$

where:

0.2 mg/kg/day = RfD.

70 kg = assumed body weight of an adult.

2 L/day = assumed daily water consumption of an adult.

Step 3: Determination of the Lifetime Health Advisory

$$\text{Lifetime HA} = \frac{(7\ \text{mg/L})\ (20\%)}{(10)} = 0.14\ \text{mg/L}\ (140\ \text{ug/L})$$

where:

7 mg/L = DWEL.

20% = assumed relative source contribution from water.

10 = additional uncertainty factor per ODW policy to account for possible carcinogenicity.

Evaluation of Carcinogenic Potential

- Data on an increased incidence of lung tumors (adenomas and carcinomas) in O_{20} strain mice (Ponomarkov and Tomatis, 1978) were used for the quantitative assessment of cancer risk due to styrene. Based on the data from this study and using the linearized multistage model, a carcinogenic potency factor (q_1^*) for humans of 1.34 $(mg/kg/day)^{-1}$ was calculated from the data for male mice and a q_1^* of 2.47 $(mg/kg/day)^{-1}$ was calculated from the data for female mice (Ponomarkov and Tomatis, 1978). Because the data cannot accommodate a tumor incidence of 100% when only a single dose is tested, the tumor response for female mice was adjusted from 32/32 and the transformed dose reduced by multiplying the calculated transformed dose, 25.7 mg/kg/day, by the ratio 31/32 to arrive at an adjusted transformed dose of 24.9 mg/kg/day. The higher of the two q_1^* values is the basis for the estimation of cancer risk levels. The doses corresponding to increased lifetime cancer risks of 10^{-4}, 10^{-5} and 10^{-6} for a 70-kg adult are 3×10^{-3}, 3×10^{-4}, 3×10^{-5} mg/kg/day, respectively. Assuming a water consumption of 2 liters/day, the corresponding concentrations of styrene in water are 1.4, 1.4×10^{-1} and 1.4×10^{-2} ug/L, respectively. These criteria, which reflect lifetime exposure, are uncertain because of short exposure duration (13% of lifetime) and the small number of animals in each dose group.

- IARC evaluated styrene in February of 1979 and found insufficient evidence to reach a conclusion as to its carcinogenicity rating (IARC, 1979).

- Applying the criteria described in EPA's guideline for assessment of carcinogenic risk (U.S. EPA, 1986), styrene may be classified in Group C: Possible human carcinogen. This category is for agents with limited evidence of carcinogenicity in animals in the absence of human data.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- The OSHA Standard for styrene is an 8-hour TWA concentration of 100 ppm, a ceiling concentration of 200 ppm and a maximum peak concentration (29 CFR 1910.1000; Table Z-2) of 600 ppm for 5 minutes or less in any 3-hour period.

- The ACGIH (1982) has established the TWA-TLV for styrene in workroom air as 50 ppm with an STEL of 100 ppm. The TLV was reduced from 100 ppm in 1981 (ACGIH, 1981).

- NIOSH (1983) recommended a styrene concentration limit in workplace air of 50 ppm TWA for up to a 10-hour day, 40 hour work-week and a ceiling concentration 100 ppm determined during any 15 minute sampling period.

VII. ANALYTICAL METHODS

- Styrene content is determined by a purge-and-trap gas chromatographic procedure used for the determination of volatile aromatic and unsaturated organic compounds in water (U.S. EPA, 1985b). This method calls for the bubbling of an inert gas through the sample and trapping styrene on an adsorbant material. The adsorbant material is heated to drive off styrene onto a gas chromatographic column which is temperature programmed to separate the method analytes which are then detected by the photoionization detector. This method is applicable to the measurement of styrene over a concentration range of 0.05 to 1,500 ug/L. Confirmatory analysis for styrene is by mass spectrometry which has a detection limit of 0.3 ug/L (U.S. EPA, 1985c).

VIII. TREATMENT TECHNOLOGIES

- Information is available on the removal of styrene from water by air stripping, adsorption and oxidation. Styrene has a Henry's Law Constant of 12 atm which makes it suitable for removal from water by air stripping (U.S. EPA, 1985d).
- Decarbonaters which have some aeration function have been evaluated for their efficacy in styrene removal. When the influent styrene concentration was 0.076 ug/L, the decarbonators tested were able to remove 51.3% (U.S. EPA, 1985d).

- Tests evaluating adsorption of styrene by granular activated carbon showed that an average of 40% was removed over a 10-month period (U.S. EPA, 1985d). The influent styrene concentration was 0.03 ug/L.

- The ethenyl double bond found in the styrene molecule makes it amendable to oxidation. It is, therefore, possible that oxidative techniques may be effective in removing styrene from potable water. Bench scale evaluations of ozone treatment of styrene-contaminated water conducted by Avigne (1983, as cited by U.S. EPA, 1985b) indicate that the reaction rate constant for a 0.007 mM styrene solution (pH 2) is 300,000 L/mole-sec. The pH was maintained at 2 to inhibit the

decomposition of ozone. Oxidation of styrene to benzaldehyde and hydrogen peroxide was reported by Legube (1983, as cited by U.S. EPA, 1985b). Using an ozone application rate of 10^7 mg/hr at 12 L/hr 0.9 moles ozone per mole of styrene was required to completely oxidize the styrene. The initial styrene concentration was 1.1×10^{-4} mole/L. It was suggested that further oxidation of benzaldehyde to benzoic acid might occur.

- It is possible that other oxidizing agents such as permanganate could be effective in oxidizing styrene. However, no studies of tests of these alternative oxidizing situations were available.

IX. REFERENCES

ACGIH. 1981. American Conference of Governmental Hygienists. TLVs. Threshold limit values for chemical substances and physical agents in the workroom environment with intended changes for 1981. Cincinnati, OH. p. 50.

ACGIH. 1982. American Conference of Governmental Hygienists. TLVs. Threshold limit values for chemical substances and physical agents in the Workroom environment with intended changes for 1982. Cincinnati, OH. p. 29.

Agrawal, A.K., S.P. Srivastava and P.K. Seth. 1982. Effect of styrene on dopamine receptors. Bull. Environ. Contam. Toxicol. 29(4):400-403.

Boland, P.A. 1981. National screening program for organics in drinking water. EPA contract 68-01-4666. SRI International.

Carpenter, C.P., C.B. Shaffer, C.S. Weil and H.F. Smyth. 1944. Studies on the inhalation of 1:3-butadiene with a comparison to its narcotic effect with benzol, toluol and styrene, and a note on the elimination of styrene by the human. J. Ind. Hyg. Toxicol. 26(3):69-78.

Das, M., R. Dixit, M. Mushtaq, S.P. Srivastava and P.K. Seth. 1981. Effect of styrene on hepatic mixed function oxidasaes, glutathione content and glutathione-S-transferase activity in rats. Drug Chem. Toxicol. 4(3):219-227.

De Meester, C., F. Poncelet, M. Roberfroid, J. Rondelet and M. Mercier. 1977. Mutagenicity of styrene and styrene oxide. Mutat. Res. 56(2):147-152.

De Meester, C., M. Durverger-Van Bogaert, M. Lambotte-Vandepaer, M. Mercier and F. Poncelet. 1981. Mutagenicity of styrene in the Salmonella typhimurium test system. Chem. Biol. Interact. 20(2):163-170.

Dowty, B.J., J.L. Laseter and J. Storer. 1976. Transplacental migration and accumulation in blood of volatile organic constituents. Pediatr. Res. 10:696-701.

Fiserova-Bergerova, V., and Teisinger. 1965. Pulmonary styrene vapor retention. Ind. Med. Surg. 34:620-622.

Gamberale, F., and M. Hultengren. 1974. Exposure to styrene. II. Psychological functions. Work Environ. Health 11(2):86-93.

Hansch, C., and A.J. Leo. 1979. Substituent constants for correlation analysis in chemistry and biology. John Wiley and Sons, New York, NY.

Hemminki, K., E. Franssila and H. Vainio. 1980. Spontaneous abortion among female chemical workers in Finland. Int. Arch. Occup. Health 45:123-126.

Holmberg, P.C. 1977. Central nervous defects in two children of mothers exposed to chemicals in the reinforced plastics industry. Scand. J. Work Environ. Health 5:333-335.

IARC. 1979. International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Some monomers, plastics and synthetic elastomers, and acrolein. 19, 97-115.

Jersey, G., M. Balmer, J. Quast et al. 1978. Two year chronic inhalation toxicity and carcinogenicity study on monomeric styrene in rats. Dow Chemical study for Manufacturing Chemical Association. December 6.

Lewis, P.J., C. Hagopian and P. Koch. 1983. Styrene. In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. M. Grayson and D. Eckroth, eds. John Wiley and Sons, Inc. New York. Vol. 21, pp. 770-801.

Maltoni, C., A. Cilberti and D. Carrietti. 1982. Experimental contributions in identifying brain potential carcinogens in the petrochemical industry. Ann. New York Acad. Sci. 381:216-249.

McMichael, A.J., R. Spirtas, J.F. Gamble and P.M. Tousey. 1976. Mortality among rubber workers: Relationship to specific jobs. J. Occup. Med. 18:178-185.

Meinhardt, T., R. Young and R. Hartle. 1978. Epidemiologic investigations of styrene-butadiene rubber production and reinforced plastic production. Scand. J. Work Environ. Health. 8(4):250-259.

Murray, F.J., J.A. John, H.D. Haberstoh et al. 1976. Teratologic evaluation of styrene monomers administered rats by gavage. Dow Chemical Study for Manufacturing Chemical Association. August 26.

Murray, F.J., J.A. John, M.F. Balmer and B.A. Schwetz. 1978. Teratologic evaluation of styrene given to rats and rabbits by inhalation or by gavage. Toxicology 11(4):335-343.

NIOSH. 1983. National Institute for Occupational Safety and Health. Criteria for a recommended standard ... occupational exposure to styrene. DHHS (NIOSH) Publ. No. 83-119. U.S. DHHS, Cincinnati, OH.

NTP. 1979. National Toxicology Program. National Cancer Institute Carcinogenesis Technical Report Series No. 185. Bioassay of styrene for possible carcinogenicity.

Odkvist, L.M., B. Larsby, R. Tham et al. 1982. Vestibulo-oculomotor disturbances in humans exposed to styrene. Acta Oto-Laryngol. 94(5-6):487-493.

Ohtsuji, M., and M. Ikeda. 1971. Metabolism of styrene in the rat and the stimulatory effect of phenobarbital. Toxicol. Appl. Pharmacol. 18(2):321-328.

Pellizzari, E.D., T.D. Hartwell, B.S.H. Harris, R.D. Waddell, D.A. Whitaker and M.D. Erickson. 1982. Purgeable organic compounds in mother's milk. Bull. Environ. Contam. Toxicol. 28(3):322-328.

Plotnick, H.B., and W.W. Weigel. 1979. Tissue distribution and excretion of ^{14}-C-styrene in male and female rats. Res. Commun. Chem. Pathol. Pharmacol. 24(3):515-524.

Ponomarkov, V.I., and L. Tomatis. 1978. Effects of long-term oral administration of styrene to mice and rats. Scand. J. Work Environ. Health. 4(Suppl.2):127-135.

Quast, J.F., R.P. Kalnins, K.J. Olson, et. al. 1978. Results of a toxicity study in dogs and teratogenicity studies in rabbits and rats administered monomeric styrene. Toxicol. Appl. Pharmacol. 45:293-294.

Ramsey, J.C., and J.D. Young. 1978. Pharmacokinetics of inhaled styrene in rats and humans. Scand. J. Work and Health 4(Suppl.2):84-91.

Ramsey, J.C., and J.D. Young. 1980. Comparative pharmacokinetics of inhaled styrene in rats and humans. In: Proc. 10th Conference on Environmental Toxicology, OH. November, 1979. AFAMRL-TR-79-121. Wright Patterson Air Force Base, OH. pp. 103-117.

Ramsey, J.C., J.D. Young, R.J. Karbowski, M.B. Chenoweth, L.P. McCarty and W.H. Braun. 1980. Pharmacokinetics of inhaled styrene in human volunteers. Toxicol. Appl. Pharmacol. 53(1):54-63.

Sikov, M.R., W.C. Cannon, D.B. Carr, R.A. Miller, L.F. Montgomery and D.W. Phelps. 1981. Teratologic Assessment of butylene oxide, styrene oxide and methyl bromide. Study performed by Battelle Pacific Northwest Laboratory, Richland, W.A. for National Institute of Occupational Safety and Health, Division of Biochemical and Behavioral Science, Experimental Toxicol. Branch, Cincinnati, OH. DHHS (NIOSH) Publ. No. 81-124.

Smith, A.H., and L. Ellis. 1977. Styrene butadiene rubber synthetic plants and leukemia (letter to the editor). J. Occup. Med. 19(7):441.

Spencer, H.C., D.D. Irish, E.M. Adams and V.K. Rowe. 1942. The response of laboratory animals to monomeric styrene. J. Ind. Toxicol. 24(10):295-301.

Srivastava, S.P., M. Das, M. Mushtaq, S.V. Chandra and P.K. Seth. 1982. Hepatic effects of orally administered styrene in rats. J. Appl. Toxicol. 2(4):219-222.

Stewart, R.D., H.C. Dodd, E.D. Baretta and A.W. Schaffer. 1968. Human exposure to styrene vapor. Arch. Environ. Health 16(5):656-662.

Teramoto, K., and S. Horiguchi. 1979. Absorption, distribution and elimination of styrene in man and experimental animals. Arch. Hig. Rada Toksikol. 30(Suppl):431-439.

U.S. EPA. 1985a. U.S. Environmental Protection Agency. Draft health effects criteria document for styrene. Office of Drinking Water.

U.S. EPA. 1985b. U.S. Environmental Protection Agency. Method 503.1. Volatile aromatic organic compounds in water by purge and trap gas chromatography. Environmental Monitoring and Support Laboratory, Cincinnati, Ohio 45268.

U.S. EPA. 1985c. U.S. Environmental Protection Agency. Method 524.1. Volatile organic compounds in water by purge and trap gas chromatography/ mass spectrometry. Environmental Monitoring and Support Laboratory, Cincinnati, Ohio 45268.

U.S. EPA. 1985d. U.S. Environmental Protection Agency. Draft technologies and costs for removal of synthetic organic chemicals from portable water supplies. Science and Technology Branch, CSD, ODW, U.S. EPA Washington, D.C.

U.S. EPA. 1986. U.S. Environmental Protection Agency. Guidelines for carcinogen risk assessment. Federal Register. 51(185):33992-34003. September 24.

Vainio, H., R. Paakonen, K. Ronnholm, V. Raunio and O Pelkonen. 1976. A study on the mutagenic activity of styrene and styrene oxide. Scand. J. Work Environ. 3:147-151.

Withey, J.R., and P.G. Collins. 1977. Pharmacokinetics and distribution of styrene monomer in rats after intravenous administration. J. Toxicol. Environ. Health 3(5-6):1011-1120.

Withey, J.R., and P.G. Collins. 1979. The distribution and pharmacokinetics of styrene monomer in rats by the pulmonary route. J. Environ. Pathol. Toxicol. 2(6):1329-1342.

Wolf, M.A., V.K. Rowe, D.D. McCollister, R.L. Hollingsworth and F. Oyen. 1956. Toxicological studies of certain alkylated benzene and benzene. Arch. Ind. Health 14:387-398.