for 127 days, no blood changes were observed in rats, guinea pigs and dogs. Slight leukopenia has been reported in rats exposed to 44 ppm, 5 hours per day, 4 days weekly for 5 to 7 weeks (202).

18.3.2 Human and Epidemiologic Studies

18.3.2.1 Short-term Toxicologic Effects

Benzene is a central nervous system depressant at high concentrations and may cause acute narcotic reactions. Depending upon the concentration and duration of exposure, these effects may range from mild manifestations such as headache and lightheadedness to more severe effects such as convulsions, respiratory paralysis and death (200). Death has resulted from single 5 to 10 minute exposures of benzene in air at concentrations of 20,000 ppm. Concentrations of 3000 to 7500 ppm may result in toxic signs within 1 hour. Exposures of 50 to 250 ppm may produce headache, lassitude and dizziness which may become more exaggerated at higher levels. No effects are reported after acute exposure to 25 ppm (12).

Ingestion of 2 mL may produce symptoms while 10 mL may be fatal (56). Ingestion of 9 to 12 g (~ 10-14 mL) has been noted to cause staggering gait, vomiting, loss of consciousness, delirium and death (12). In acute poisoning, death may be due to respiratory arrest or cardiac failure. Excessive physical activity at the time of acute exposure predisposes individuals to cardiac failure (56).

Direct contact with the liquid may cause redness and dermatitis. Absorption through human skin has been reported to be 0.004 to 0.052%, the highest absorptions occurring through the palm (194). Therefore, skin absorption is not considered to be an important route of entry in occupational situations (633).

The local effects of benzene vapor on the human eye are slight. Occasionally, hemorrhages in the retina and conjunctiva are found after systemic benzene poisoning. In rare instances these may be accompanied by edema of the retina and optic nerve. It has been suggested but not firmly established that benzene may induce inflammation of the optic nerve (19).

18.3.2.2 Chronic Toxicologic Effects

The most important effect resulting from chronic benzene exposure is its hematotoxicity, the targets being the cells of the bone marrow. At the early stages, leukopenia, anemia or thrombocytopenia (i.e. a decrease in platelet count) may be seen as well as any combination of these (195). The effects appear to be reversible at this stage (202).

Many observers agree that the lowest air levels of benzene demonstrated to produce a decrease in human circulating blood cells are in the range of 40 to 50 ppm (195). The initial symptoms tend to be non-specific and include fatigue, headache, nausea and loss of appetite (46). With continued exposure there is severe bone marrow damage which results in pancytopenia, a deficiency of all cellular elements of the blood. Human benzene toxicity is often described as aplastic or hypoplastic anemia. Pancytopenia is the more correct term since some cases of benzene-induced hematotoxicity have been reported to have hyperplastic bone marrows. It has been suggested that hyperplasia is an early bone marrow response to benzene and that hypoplasia follows after continued exposure (196). The direct, life-threatening consequences of pancytopenia result from leukopenia and thrombocytopenia which will cause an increased suseptibility to infection or hemorrhagic conditions, respectively. There is also evidence that the circulating cells contain morphological or functional abnormalities which may contribute to these effects (203).

The mechanism of benzene toxicity is thought to be due to its phenolic metabolites although this has not been proven conclusively (195). Benzene depresses incorporation of iron into circulating red blood cells and DNA synthesis in bone marrow (518). These may also play a role in its toxicity.

There is a correlation between benzene exposure and chromosomal aberrations in the bone marrow and peripheral lymphocytes of exposed individuals. Although aberrations have been reported following chronic, low-level exposures (<10 ppm), it has not been a consistent finding. Aberrations due to high exposure levels (>100 ppm) may persist for many years after exposure has been discontinued (202). Some investigators have associated irreversible chromosome damage with the eventual development of leukemia (195).

Leukemia is defined as a neoplastic condition in which there are increased numbers of white blood cells or their precursors in the blood or bone marrow. Acute myelogenous leukemia is the form most frequently related to benzene exposure although other types have also been observed. The relationship between benzene exposure and the development of leukemia has been established in numerous epidemiological studies. The International Agency for Research on Cancer believes there is sufficient evidence that benzene is carcinogenic to man (202). Studies by Aksoy and coworkers in Turkey support the causal relationship between benzene exposure and leukemia. These investigators found 26 cases of leukemia or pre-leukemia in a group of 28,500 shoe-manufacturing workers observed over an 80-month period from 1966 to 1973. The exposures were in the range of 210 to 650 ppm with durations ranging from 1 to 15 years. These cases were calculated to give an annual

incidence rate of 13 per 100,000 as opposed to a rate of 6 per 100,000 for the general population (629). The latter rate was derived from countries more developed than Turkey and is believed to be high. The investigators recently estimated the incidence of leukemia in the general population in Turkey to be 2.5 to 3 per 100,000 (630) making the increased incidence of leukemia in exposed workers more significant.

Infante and associates (631) conducted a controversial study in 2 populations of workers engaged in the production of rubber products from 1940 through 1949. Benzene was the only material in their work environment known to be associated with blood disorders (43). This group of 748 white males was followed for vital status from 1950 through 1975. A statistically significant excess of leukemia was found in comparison to 2 control groups, the white male American population and the workers in another industry not using benzene. Nine deaths resulted from all forms of leukemia in the 2 exposed groups where the expected incidence was 1.25 (518). The critical issue in this study was the estimation of the air levels of benzene in the work environments. The investigators suggested that the plants functioned within the recommended standards of 100 ppm in 1941, 50 ppm in 1947 and 35 ppm in 1948, and that the actual air concentrations were in the range of 10 - 15 ppm. These exposure levels have been refuted by other investigators who have suggested that the levels were probably greater than the prevailing standards and more likely were in the range of 95 to 950 ppm. It was also argued that environmental exposures at the plants could not have been the same since different rubber products were being manufactured at each location (631). It is also probable that there is a wide variation in absorbed doses due to variations in work habits and also due to the fact that benzene, being volatile, could drift to various locations causing actual exposures to workers thought to be unexposed. These factors make a dose-response relationship difficult to establish (518).

In addition, controversy has arisen over whether it is necessary for some degree of bone marrow damage to occur before leukemia develops. Many observers believe that this is indeed the case. This suggests a yet to be proven assumption that there is a threshold for benzene-induced leukemia (195). Others argue that exposure to a carcinogen at any level carries the threat of cancer and in the case of benzene, exposures as low as 10 ppm pose a significant probability of leukemia developing (195). It is interesting to note that leukemia is observed in those industries where benzene has been used as a solvent. Industries in which benzene is either produced or used as a chemical reactant, such as the petroleum industry, do not exhibit an increased incidence of leukemia (518). This has been attributed to the fact that solvent exposure occurs indoors, in unventilated areas, whereas workers

in the petrochemical industries are in largely outdoor situations where the probability of benzene levels exceeding 1 ppm TWA is less than 5% (198).

18.3.3 Levels of Concern

The USEPA (355), based on human epidemiological data (202,630,631) and supported by experimental data in rats (201), has established an ambient water quality criterion of zero for benzene. In that attainment of a zero concentration level may be infeasible in some cases, the concentrations of benzene in water calculated to result in incremental lifetime cancer risks of 10^{-5}, 10^{-6} and 10^{-7} from ingestion of both water and contaminated aquatic organisms were estimated to be 6.6, 0.66 and 0.066 µg/L, respectively. Risk estimates are expressed as a probability of cancer after a lifetime daily consumption of two liters of water and 6.5 g of fish that have bioaccumulated benzene. Thus, a risk of 10^{-5} implies that a lifetime daily consumption of two liters of drinking water and 6.5 g of contaminated fish at the criterion level of 6.6 µg/L of benzene would be expected to produce one excess case of cancer above the normal background incidence for every 100,000 people exposed. It should be emphasized that these extrapolations are based on a number of assumptions and should be taken as crude estimates of human risk at best.

IARC (518) lists benzene in category 1 (sufficient evidence of human carcinogenicity) in its weight-of-evidence ranking for potential carcinogens. The NTP (801) has categorized benzene as providing clear evidence of carcinogenic activity (multiple sex/species/tumor sites).

For noncarcinogenic risks, the USEPA (383) has issued a Health Advisory of 0.23 mg/L for short-term (10-day) exposure to benzene in drinking water. The WHO (666) recommends a level of 10 µg/L for benzene in drinking water.

OSHA (298) currently permits exposure to 10 ppm as an 8-hour TWA with an acceptable ceiling of 25 ppm and a maximum allowable peak of 50 ppm for 10 minutes.

On the basis of reports that benzene caused both chromosomal aberrations and leukemia at levels estimated to be below 10 ppm, the U.S. Occupational Safety and Health Administration (OSHA), in 1978, issued a standard of 1 ppm (3.2 mg/m^3) TWA with a ceiling limit of 5 ppm (16 mg/m^3). An injunction against OSHA was obtained by various industrial groups which prevented the 1 ppm standard from being enforced. The case eventually reached the Supreme Court which voted to invalidate it on the basis that OSHA had neither established that there was a significant risk at 10 ppm nor that the reduction to 1 ppm would

appreciably reduce the risk of leukemia in benzene-exposed workers. Dissenting opinions suggested that OSHA was not required to find a significant risk and should be allowed the discretion to set a standard which would ensure that workers do not suffer due to medical uncertainty (195).

Recently, 2 major chemical industry groups recommended that OSHA publish a flexible proposed standard, setting a range of exposure limits from 1 ppm (3.2 mg/m^3) to 5 ppm (16 mg/m^3) (199).

OSHA, however, has issued a draft proposal to reduce the current exposure limit from 10 ppm to 1 ppm (3.2 mg/m^3) as an 8-hour time-weighted-average. In addition, it has proposed to set a 0.5 ppm (1.6 mg/m^3) ceiling limit averaged over a 15 minute period (632). At present, the 10 ppm standard remains in effect.

The ACGIH (3) has set a TLV® of 10 ppm, with the notation that benzene is a suspected human carcinogen. This value was selected not on the basis of a no-effect-level, but rather on the basis that this is the lowest level that generally can be achieved at this time.

18.3.4 Hazard Assessment

There is sufficient evidence that benzene is carcinogenic in animals and that benzene is carcinogenic for man. Several case reports (202) as well as two cohort studies (630, 631) have established a relationship between benzene exposure and leukemia. Based on these findings, the USEPA (667) calculated an upper-limit incremental unit cancer risk of 2.9×10^{-2} $(mg/kg/day)^{-1}$ for benzene.

A correlation between benzene exposure and chromosomal aberrations in bone marrow and lymphocytes of exposed individuals has also been observed at levels above 100 ppm; results are inconsistent at lower levels (202). A recent report (710) noted chromosome damage in animals at levels as low as 1 ppm. Additional studies regarding the mutagenic capability of benzene are needed to clarify the lowest effective dose.

Retardation of fetal development accompanied by a decrease in maternal weight gain have been seen in reproductive toxicity studies but there is no pattern suggestive of teratogenic activity for benzene.

Aside from the reported hematological effects of long-term benzene exposure (e.g., leucopenia, thrombocytopenia, pancytopenia), most adverse effects associated with benzene exposure are of an acute nature and occur at considerably higher concentrations (e.g., 3000-7500 ppm for one hour). Ingestion of about 10 mL is fatal (56,12) and symptoms of CNS depression have been noted following ingestion of 2 mL (56).

18.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of benzene concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of benzene, care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of benzene, one of the EPA priority pollutants, in aqueous samples include EPA Methods 602, 624, and 1624 (65). An inert gas is bubbled through the aqueous sample in a purging chamber at ambient temperature, transferring the benzene from the aqueous phase to the vapor phase and onto a sorbent trap. The trap is then heated and backflushed to desorb the benzene and transfer it onto a gas chromatographic (GC) column. The GC column is programmed to separate the volatile organics; benzene is then detected with a photo-ionization detector (Method 602) or a mass spectrometer (Methods 624 and 1624).

The EPA procedures recommended for benzene analysis in soil and waste samples, Methods 8020 and 8240 (63), differ from the aqueous procedures primarily in the method by which the analyte is introduced into the GC. The recommended method involves dispersing the soil or waste sample in methanol or polyethylene glycol to dissolve the benzene. A portion of the solution is then combined with water and purged as described above. Other sample introduction techniques include direct injection and a headspace method.

Typical benzene detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.2 µg/L (Method 602)	1 µg/g (Method 8020)
4.4 µg/L (Method 624)	1 µg/g (Method 8240)
10 µg/L (Method 1624)	

ETHYLBENZENE (EB)
PHENYLETHANE, ETHYLBENZOL

Introduction:

Ethylbenzene is a colorless, flammable liquid with an aromatic odor, found in gasoline. It evaporates about 94 times more slowly than ether; and it is heavier than air, its vapors may travel a considerable distance and ignite. For all practical purposes, EB is insoluble in water but it is freely soluble in organic solvents. The properties are as follows:

Molecular formula: $C_6H_5C_2H_5$
Molecular weight: 106.16
Water solubility: 152 mg/l (at 20° C)
Specific gravity: 0.867 at 20° C
Boiling point: 136.2° C
Vapor pressure: 7 mm at 20° C
Odor threshold: 0.2 mg/l (water) and 0.62 mg/l (air)

EB is a petrochemical, largely used in the production of styrene and synthetic polymers; also as a solvent and component for automotive and aviation fuels. Ethylbenzene is produced by the alkylation of benzene with ethylene and majority of the commercial sites of production are found in Texas and Louisiana. Significant quantities of EB are present in mixed xylenes. These are used as diluents in the paint industry, in agricultural sprays for insecticides, and in gasoline blends. The U.S. production of EB in 1982 was 3.3 million tons (EPA, 1985).[1]

EB probably represents about 10 percent of the total aromatic compounds detected in air. Altschuller and Bellar (1963)[27] detected 0.01 ppm EB in the air around Los Angeles, California. Neligan et al. (1965)[28] surveyed five different sites in California, EB levels averaged 0.01 ppm. These authors have suggested that commercial sources and motor vehicles are the major contributors to EB in the atmosphere.

According to Shackelford and Keith (1976),[2] EB was present in finished drinking water in the United States, the United Kingdom, and Switzerland.

EB was also found in river water, chemical plant effluents, raw water, textile plant effluents, and well water at 15 ppb (Burnham, et al., 1972).[3] In a survey of water contaminants in the drinking water of ten cities in the U.S., EB was detected in six of ten samples. Several investigators have reported that EB is present in the ambient atmosphere at a level of approximately 0.01 ppm. EB is considered by EPA as hazardous substance and a priority toxic pollutant (EPA, 1975)[4].

The testing of 945 groundwater supplies has revealed that approximately 0.6% contain ethylbenzene and the median concentration detected was 0.87 µg/l (EPA, 1985).[1]

In a recent summary of groundwater VOC monitoring data from July 1, 1983 to April 30, 1986, the Wisconsin Department of Natural Resources reported the occurrence of ethylbenzene in public and private drinking water supplies as well as solid waste and wastewater sites as shown in Table 1.[5]

TABLE 1 (B)
GROUNDWATER MONITORING DATA FOR ETHYLBENBZENE

	Number of Wells Sampled	Wells With Detects	Highest Detected Level
Drinking Water Private Supply	1,731	56	1,400
Drinking Water Public Supply	2,371	24	1,000
Solid Waste Sites	51	5	74
Wastewater Sites	5	3	3,000

Human Exposure Routes:

Although exposure to EB comes primarily from occupational exposure, it has been found to be present in drinking water and in tne atmosphere.[11] Tne sources of atmospheric EB include (1) commercial, e.g., petroleum and petroleum by-products, (2) motor vehicle exhaust, and (3) cigarette smoke. Tne potential routes of entry for EB are inhalation, ingestion, eye and skin contact.

The NIOSH report also indicated that the population at risk for those who are residing in areas with high atmospheric smog generated by motor vehicle emissions and individuals in commercial situations where petroleum products or by-products are manufactured (e.g., rubber or plastic industry).

EB has not been reported to be present in food with an exception of the report by Kinlan et al. (1972).[31]

The absorption of ethylbenzene through the skin of the hand and the forearm in men was reported by Dutkiewicz and Tyras (1967).[6] They found that the rate of absorption of liquid ethylbenzene was 22 to 23 $mg/cm^2/hr.$, and the rates from aqueous solutions were 188 and 215 $\mu g/cm^2/hr.$; and they also concluded that the absorption of EB through the skin in men is very rapid for both the liquid ethylbenzene and its aqueous solutions.

Acute Toxicity:

The acute toxicity data on EB in both rat and rabbit via the oral, inhalation, or dermal routes indicate the low toxicity of this compound shown in Table 2.

TABLE 2 (C)
ACUTE TOXICITY OF ETHYLBENZENE*

Route of Administration	Species	Sex	No. of Animals	LD_{50}
oral	rat	both	57	3.5 gm/kg[a]
oral	rat	male	5	5.46 ml/kg[b]
skin	rabbit	male	4	1.78 ml kg[b]
inhalation	rat	female	6	4000 ppm x 4 hrs.[b]

*Sources:
[a]Wolf et al., 1956[14]
[b]Smyth et al., 1962[15]

Estimated acute LD_{50} values of 3.5 g/kg to 5.46 g/kg were reported in rats (Wolf et al., 1956).[14] An acute dermal LD_{50} value of 1.78 ml/kg (approximately 15,400 mg/kg) was reported in rabbits (Smyth et al., 1962).[15] An inhalation exposure of 4,000 ppm (approximately 17,400 mg/m^3) was lethal to 3 of 6 rats (Smyth et al., 1962).[15]

Systemic toxic effects in animals that were observed in the LD_{50} studies occurred predominantly in the liver and kidney (Wolf et al., 1956)[14] and in the central nervous system (Faustov, 1958).[16] Other acute effects include irritation of the conjunctiva (Wolf et al., 1956)[14] and slight necrosis of the cornea (Smyth et al., 1962).[15]

Based on the data available for ethylbenzene, the acute toxicity to fresh water aquatic life occurs at concentrations as low as 32,000 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of EB to sensitive fresh water aquatic life (EPA, 1980).[17]

The available data for EB indicate that acute toxicity to salt water aquatic life occurs at concentrations as low as 430 µg/l. Data on chronic toxicity of EB to sensitive salt water aquatic life were not identified in this literature review.

Chronic Toxicity:

The subchronic toxic effects were also observed in a gavage study in rats (Wolf et al., 1956).[14] Liver and kidney effects were observed in rats exposed orally to EB in olive oil for 182 days. Doses of 408 and 680 mg/kg caused increases in liver and kidney weights, and cloudiness and swelling of hepatocytes and renal tubular epithelium. No effects were observed in rats exposed orally to 13.6 and 136 mg/kg/day.

Human Health Effects:

Experiments with human volunteers exposured to EB via inhalation at a concentration of 100 ppm (434 mg/m^3) did not result in adverse health effects; however, exposures at higher levels resulted in sleepiness, fatigue, headache and mild eye and respiratory irritation (Bardodej and Bardodejova, 1970).[7]

Upon termination of the inhalation exposure in humans, almost all of the inhaled dose was eliminated from the system within 24 hours (Engstrom and Bjurstrom, 1978[21]; Hageman and Angerer, 1979[22]). Gerarde (1963)[23] has reviewed the acute toxicity in humans via inhalation route (Table 3).

Based on the literature review, it appears that those individuals who are involved in the use of petroleum by-products, e.g., polymerization workers involved in styrene production, may be at risk. In a study of 494 styrene workers, Lilis et al. (1978)[30] reported various neurotoxic manifestations. These included prenarcotic symptoms, incoordination, dizziness, headache and nausea involving 13 percent of the workers, 19 percent a decrease in a radial and peroneal nerve conduction velocity and 50 percent of the workers reported distal hypoasthesia involving the lower limbs. They have noted that it was difficult to assess occupational reports evaluating such a situation since these workers are exposed to a number of different precursors, by-products, and end products.

A NIOSH (1978)[18] report by Rivera and Rostand on workers exposed to various lacquer constituents (including EB in a baseball bat manufacturing facility) concluded that no health hazard existed with the exception of mucous membrane irritation and the potential for contact dermatitis under the conditions at the plant. This occupational situation illustrates the fact that (in addition to EB) these workers were exposed to more than one chemical.

It should be noted that in an industrial setting EB can be found in a number of volatile compounds with widespread industrial use including gasoline and solvents.

TABLE 3 (D)
HUMAN RESPONSE TO ETHYLBENZENE VAPORS*

Concentration mg/l	ppm	Exposure Time	Response
21.75	5000	Few seconds	Intolerable irritation of nose, eyes and throat.
8.7	2000	Few seconds	Severe eye, nose and mucous membrane irritation. Lacrimation.
8.7	2000	6 minutes	Central nervous system effects. Dizziness.
4.35	1000	Few seconds	Eye irritation.
4.35	1000	Minutes	Eye irritation diminishes.
0.87	200	Threshold limit	(a maximum concentration in which a worker is exposed to 8 hrs/day, 5 days/week over his working lifetime without hazard to health)
0.043	10	Few seconds	Odor detectable.

*Source: Gerarde, 1963 (Cited by EPA, 1980)[17]

EB is present in the respiratory tract (Conkle et al., 1975),[12] umbilical cord and maternal blood (Dowty et al., 1976),[13] and subcutaneous fat (Wolff et al., 1977)[11] of exposed humans. EB is also a defatting agent and may cause dermatitis following prolonged exposure. Individuals with pre-existing skin problems may be more sensitive to EB.

Mutagenicity:

No mutagenic activity was detected in S. typhimurium strains TA98, TA100, TA1535, TA1537 following EB exposure both with and without metabolic activation in plate assays at concentrations up to 3 mg/plate (EPA, 1985).[24] Salmona et al. (1976)[25] observed that four common metabolites of EB (d-1-mandelic, phenylglyoxylic, and hippuric acid) gave negative results in the Ames test using five tester strains. Nevertheless, they stated that, although EB metabolites do not show any mutagenic activity, styrene, an EB manufacturing product, can undergo metabolism to an epoxide intermediate, which demonstrates a positive mutagenic response in the Ames test.

Carcinogenicity:

EPA (1985)[24] has indicated that a NCI bioassay of EB has been initiated. To date, no data on the carcinogenic potential of etnylbenzene were identified in the available literature.

Teratogenicity:

In a recent study by Hardin et al. (1981),[26] ethylbenzene did not elicit maternal toxicity, embryotoxicity, fetal toxicity or teratogenicity in rats by inhalation exposures employing EB concentrations up to 1,000 ppm (4,348 mg/m^3).

Environmental Fate:

Limited information is available on the biological effects of EB in other mammalian species. Ethylbenzene possesses several sites that are potentially susceptible to oxidative microbial attack; for example, microbial oxidation with the species Pseudomonas patida (39 D strain) involves one major pathway where EB is dehydroxylated to (+)-cis-3-ethyl-3,5-cyclohexadiene-1,2-diol.[29]

Risk Assessment:

Based on the literature search, DHSS considers EB to be a non-mutagen.

IARC has not classified EB in any of its categories of carcinogenic potential. Furthermore, EPA (1985)[24] has classifed EB under Group D: Not Classified. This category is for agents with inadequate animal evidence of carcinogenicity.

The chronic exposure study by Wolf et al. (1956)[14] was selected for derivation of the Lifetime Health Advisory (EPA, 1985)[24] as well as the DHSS recommendation for groundwater standards following the procedures outlined in ss. 160.07(4) and 160.13.

In this study, rats were administered oral gavage doses of 13.6, 136, 408 or 680 mg/kg/day ethylbenzene in olive oil for 130 days of the 182-day test period.

A vehicle control of olive oil (2.5 ml) was run concurrently. No effects were noted in groups of rats exposed at 13.6 and 136 mg/kg/day. Increases in liver and kidney weights were reported following oral administration of 408 or 680 mg/kg/day. There were also slight histopathological changes at these dose levels. These included cloudiness and swelling of hepatocytes and renal tubular epithelium. From these results, a NOAEL of 136 mg/kg/day was established (EPA, 1985).[24]

The Uncertainty Factor of 1000 is derived as follows:

100 is appropriate for use with animal NOAEL data when comparable human data are not available.

10 is appropriate for use with data from exposure duration significantly less than lifetime.

Recommendations and Conclusions:

The Department of Health and Social Services (Division of Health) accepts EPA's NOAEL recommendation and utilized this federal number for ethylbenzene in the development of the recommended groundwater enforcement standard:

NOAEL	:	136 mg/kg/day
Uncertainty Factor	:	1000
ADI	:	0.136 mg/kg/day

Determination of Wisconsin Enforcement Standard:

$$10\text{ kg child} = \frac{(136\text{ mg/kg/day})(10\text{ kg})}{(1000)\quad(1\text{ l/day})}$$

$$= 1.36\text{ mg/l}$$
$$= 1360\ \mu\text{g/l (1360 PPB)}$$

Recommended Enforcement Standard	:	1360 µg/l (1360 PPB)
Recommended Preventive Action Limit Factor	:	20%
Recommended Prevention Action Limit	:	272 µg/l (272 PPB)

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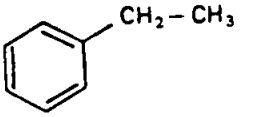
ETHYL BENZENE

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
Ethyl benzol Phenyl ethane EB	100-41-4 NIOSH NO.: DA0700000	C_8H_{10}	4.34 mg/m³ ≅ 1 ppm 0.2304 ppm ≅ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 106.16

REACTIVITY	Ethyl benzene may generate heat, react vigorously, and possibly ignite or explode in contact with oxidizing mineral acids or other strong oxidizing agents (507,51,54,511).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: colorless	(23)
	• Odor: sweet, gasoline-like	(59)
	• Odor Threshold: 2.3 ppm	(384)
	• Liquid Density (g/ml at 20°C): 0.867	(23)
	• Freezing/Melting Point (°C): -95	(23)
	• Boiling Point (°C): 136.19	(21)
	• Flash Point (°C): 15 (closed cup)	(23)
	• Flammable Limits in Air, % by Volume: 1.0-6.7	(51,506,504)
	• Autoignition Temperature (°C): 432	(510,506,504)
	• Vapor Pressure (mm Hg at 20°C): 7	(67)
	• Saturated Concentration in Air (mg/m³ at 20°C): 40,000	(67)
	• Solubility in Water (mg/L at 20°C): 152	(67)
	• Viscosity (cp at 25°C): 0.64	(599)
	• Surface Tension (dyne/cm at 20°C): 31.5	(21)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 3.15	(29)
	• Soil Adsorption Coefficient, K_{oc}: 681	(652)
	• Henry's Law Constant (atm·m³/mol at 25°C): 0.0079	(74)
	• Bioconcentration Factor: 95 (estim), 68 (estim)	(211,659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Somewhat mobile in soil-water systems, especially in aqueous phase if sufficient water is present. Volatilization losses through air-filled pores may be a minor loss pathway. Chemical is resistant to hydrolysis, but will probably biodegrade easily if microbiological populations are sufficiently numerous and active. May persist for months to years (or more) if biodegradation is not possible.
PATHWAYS OF EXPOSURE	The primary pathway of concern from a soil-water system is the migration of ethyl benzene to ground-water drinking water supplies. It is commonly found in ground water at NPL sites, illustrating the importance of this pathway. Inhalation from surface soils may also be important.
HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (38,54): Ethyl benzene primarily causes irritation of the eyes, nose, throat and skin. Irritating effects are more pronounced at higher concentrations. Narcosis can occur with very high concentrations; dizziness, drowsiness and weakness may occur. Prolonged or repeated skin contact with the liquid is defatting and may cause dermatitis.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral [rat] 3500 (47); skin [rabbit] 5000 (59); LCLo (ppm) inhalation [rat] 4000·4 hr (47)
	Long-Term Effects: Limited data suggest possible liver and kidney injury
	Pregnancy/Neonate Data: Negative
	Mutation Data: Limited evidence
	Carcinogenicity: No data
HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation • Vapor concentrations of 100-1000 ppm: chemical cartridge respirator with full facepiece and organic vapor canister • 1000-2000 ppm: any supplied-air respirator or self-contained breathing apparatus with full facepiece; gas mask with organic vapor canister • Chemical goggles if there is probability of eye contact • Impervious clothing and gloves should be used to prevent repeated or prolonged skin contact with liquid.
EMERGENCY FIRST AID TREATMENT (38,54)	Caution: Do not administer stimulants • Ingestion: Do not induce vomiting. Get medical attention immediately • Inhalation: Move victim to fresh air; give artificial respiration if necessary. Keep victim warm. Get medical attention • Skin: Remove contaminated clothing. Flush skin with water. If irritation persists after washing with soap and water, get medical attention • Eye: Irrigate immediately with large amounts of water, get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 100 ppm
- AFOSH PEL (8-hr TWA): 100 ppm; STEL (15-min): 125 ppm

Criteria
- NIOSH IDLH (30-min): 2000 ppm
- ACGIH TLV® (8-hr TWA): 100 ppm
- ACGIH STEL (15-min): 125 ppm

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories
None established

EPA Ambient Water Quality Criteria (355)
- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, 1.4 mg/L.
  - Based on ingestion of contaminated aquatic organisms only, 3.28 mg/L.
- Aquatic Life
  - Freshwater species
    acute toxicity: no criterion, but lowest effect level occurs at 32,000 µg/L.

    chronic toxicity: no criterion established due to insufficient data.
  - Saltwater species
    acute toxicity: no criterion, but lowest effect level occurs at 430 µg/L.

    chronic toxicity: no criterion established due to insufficient data.

REGULATORY STATUS (as of October 1, 1985)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)
Ethyl benzene is designated a hazardous substance under CWA. It has a reportable quantity (RQ) limit of 454 kg (347,556). It is also listed as a toxic pollutant (351). Water quality criteria have been set. No effluent limitations specific to this chemical have been set.

Toxic Substances Control Act (TSCA)
Manufacturers, processors or distributors of ethyl benzene must report production, usage and disposal information to EPA (334).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
Ethyl benzene is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing ethyl benzene but these depend upon the concentration of the chemicals present in the waste stream (556).

Occupational Safety and Health Act (OSHA)
Employee exposure to ethyl benzene in any 8-hour work-shift of a 40-hour work-week shall not exceed an 8-hour time-weighted- average (TWA) of 100 ppm (298).

Hazardous Materials Transportation Act (HMTA)
The Department of Transportation has designated ethyl benzene as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

- State Water Programs

Missouri has a maximum limit of 320 µg/L for protection of aquatic life (731).

Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs

Clean Water Act (CWA)
Effluent guidelines for ethyl benzene have been proposed in the organic chemicals, plastics and synthetic fibers category (357).

Resource Conservation and Recovery Act (RCRA)
EPA has proposed listing spent solvent mixtures containing 10% or more ethyl benzene as non-specific sources of hazardous wastes (780).

- State Water Programs
  No proposed regulations are pending.

EEC Directives

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment, and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparations (Solvents) (544)
Ethyl benzene is listed as a Class II/c harmful substance and is subject to packaging and labeling regulations.

Directive on Toxic and Dangerous Wastes (542)
Any installation, establishment, or undertaking which produces, holds and/or disposes of certain toxic and dangerous wastes including phenols and phenol compounds; organic-halogen compounds, excluding inert polymeric materials and other substances referred to in this list or covered by other Directives concerning the disposal of toxic and dangerous waste; chlorinated solvents; organic solvents; biocides and phyto-pharmaceutical substances; ethers and aromatic polycylic compounds (with carcinogenic effects) shall keep a record of the quantity, nature, physical and chemical characteristics and origin of such waste, and of the methods and sites used for disposing of such waste.

Directive on the Classification, Packaging and Labeling of Dangerous Substances (787)
Ethyl benzene is classified as a harmful substance and is subject to packaging and labeling regulations.

20.1 MAJOR USES

The major application of ethyl benzene is as an intermediate in the production of styrene. It is also used in the manufacture of cellulose acetate and synthetic rubber. Significant quantities are consumed in connection with xylene, which may contain as much as 20% ethyl benzene as a solvent or diluent. These xylene/ethyl benzene mixtures are used as diluents in the paint industry, in agricultural sprays for insecticides and in gasoline blends (54,21).

20.2 ENVIRONMENTAL FATE AND EXPOSURE PATHWAYS

20.2.1 Transport in Soil/Ground-water Systems

20.2.1.1 Overview

Ethyl benzene may move through the soil/ground-water system when present at low concentrations (dissolved in water and sorbed on soil) or as a separate organic phase (resulting from a spill of significant quantities of the chemical). In general, transport pathways for low soil concentrations can be assessed by using an equilibrium partitioning model, as shown in Table 20-1. These calculations predict the partitioning of ethyl benzene among soil particles, soil water and soil air. Ethyl benzene associated with the water and air phases of the soil is more mobile than the adsorbed portion.

The estimates for the unsaturated topsoil model indicate that nearly all of the ethyl benzene (98%) is sorbed to the soil. A much smaller amount (0.75%) is expected to be present in the soil-water phase and can thus migrate by bulk transport (e.g., the downward movement of infiltrating water), dispersion and diffusion. For the portion of ethyl benzene in the gaseous phase of the soil (0.7%), diffusion through the soil-air pores up to the ground surface, and subsequent removal by wind, will be a significant loss pathway. There is no significant difference in the partitioning calculated for 25°C and 10°C.

In saturated, deep soils (containing no soil air and negligible soil organic carbon), a much higher fraction of the ethyl benzene (26%) is likely to be present in the soil-water phase (Table 20-1) and transported with flowing ground water.

20.2.1.2 Sorption on Soils

The mobility of ethyl benzene in the soil/ground-water system (and its eventual migration into aquifers) is strongly affected by the

TABLE 20-1 (E)

EQUILIBRIUM PARTITIONING CALCULATIONS FOR ETHYL BENZENE IN MODEL ENVIRONMENTS[a]

Soil Environment	Estimated Percent of Total Mass of Chemical in Each Compartment		
	Soil	Soil-Water	Soil-Air
Unsaturated topsoil[b,c]			
at 25°C	98.5	0.75	0.74
at 10°C	98.8	0.76	0.42
Saturated deep soil[d]	74.1	25.9	-

a) Calculations based on Mackay's equilibrium partitioning model (34,35,36); see Introduction for description of model and environmental conditions chosen to represent an unsaturated topsoil and saturated deep soil. Calculated percentages should be considered as rough estimates and used only for general guidance.

b) Utilized estimated soil sorption coefficient: K_{oc} = 681 (Estimated by Arthur D. Little, Inc.)

c) Henry's law constant taken as 0.00790 atm·m^3/mol at 25°C (74), and 0.00430 atm·m^3/mol at 10°C (latter calculated using 25°C/10°C ratio of H values from Brown and Wasik (521)).

d) Used sorption coefficient (K_p) calculated as a function of K_{oc} assuming 0.1% organic carbon: $K_p = 0.001 \times K_{oc}$.

extent of its sorption on soil particles. In general, sorption on soils is expected to:

- increase with increasing soil organic matter content;
- increase slightly with decreasing temperature;
- increase moderately with increasing salinity of the soil water; and
- decrease moderately with increasing dissolved organic matter content of the soil water.

Based upon its octanol-water partition coefficient of 1410, the soil sorption coefficient (K_{oc}) is estimated to be 681. This number is indicative of a moderate soil sorption potential.

20.2.1.3 Volatilization from Soils

Transport of ethyl benzene vapors through the air-filled pores of unsaturated soils is an important transport mechanism for near-surface soils. In general, important soil and environmental properties influencing the rate of volatilization include soil porosity, temperature, convection currents and barometric pressure changes; important physicochemical properties include the Henry's law constant, the vapor-soil sorption coefficient, and, to a lesser extent, the vapor phase diffusion coefficient (31). No data are available from laboratory or field studies to indicate the actual rate of volatilization, but the rate should not be much different than for toluene (see Chapter 19).

The Henry's law constant (H), which provides an indication of a chemical's tendency to volatilize from solution, is expected to increase significantly with increasing temperature. Moderate increases in H are also expected with increasing salinity due to a decrease in ethyl benzene's solubility (517).

20.2.2 Transformation Processes in Soil/Ground-water Systems

The persistence of ethyl benzene in soil/ground-water systems has not been studied. In most cases, it should be assumed that the chemical will persist for months to years (or more). Ethyl benzene that has been released into the air will eventually undergo photochemical oxidation; an estimated tropospheric lifetime of 15 hours has been reported (10).

Ethyl benzene under normal environmental conditions is not expected to undergo hydrolysis (10,33).

The available data indicate that ethyl benzene would be biodegradable in the soil/ground-water environment (10,55). Some species of soil bacteria are capable of using ethyl benzene as the sole carbon source. The data from Tabak *et al.* (55) indicate that the chemical would be fairly easily biodegraded in a biological wastewater treatment plant. However, in most soil/ground-water systems, the concentration of microorganisms capable of biodegrading chemicals such as ethyl benzene is very low and drops off sharply with increasing depth. Thus, biodegradation in the soil/ground-water system should be assumed to be of minimal importance except, perhaps, in landfills with active microbiological populations.

20.2.3 Primary Routes of Exposure From Soil/Ground-water Systems

The properties of ethyl benzene and the above discussion of fate pathways suggest that ethyl benzene is highly volatile in aqueous solutions, may be moderately adsorbed by soil and has a moderate potential for bioaccumulation. This compound may volatilize from soil surfaces. The portion of the compound not removed by volatilization may be adsorbed, but some of the ethyl benzene may migrate to ground water. These fate characteristics suggest several potential exposure pathways.

Volatilization of ethyl benzene from a disposal site, particularly during drilling or restoration activities, could result in inhalation exposures. In addition, the potential for ground water contamination is high, particularly in sandy soils. Mitre (1983) reported that ethyl benzene has been found at 47 of 546 National Priority List (NPL) sites. It was detected at 32 sites in ground water, 13 sites in surface water and 7 sites in air.

This compound was also reported in the USEPA (531) Groundwater Supply Survey (GWSS). This survey examined 945 finished water supplies that use ground-water sources. The results for ethyl benzene are shown below:

Sample Type	Occurrences* No.	%	Median of Positives (µg/L)	Maximum (µg/L)
Random				
Supplies serving <10,000 people (280 samples)	2	0.7	0.94	1.1
Supplies serving >10,000 people (186 samples)	1	0.5	0.74	0.74
Non-Random				
Supplies serving <10,000 people (321 samples)	5	1.6	1.6	12.0
Supplies serving >10,000 people (158 samples)	0	0	-	-

*Samples having levels over quantification limit of 0.5 µg/L.

The random results are intended to statistically represent the U.S. ground-water drinking water supplies. The non-random samples were chosen by the states as being potentially contaminated. Ethyl benzene has also been detected in the National Organic Monitoring Survey (NOMS) (90).

These survey results indicate that this compound has the potential for movement in soil/ground-water systems. This compound may

eventually reach surface waters by this mechanism, suggesting several other exposure pathways:

- Surface waters may be used as drinking water supplies, resulting in direct ingestion exposure;
- Aquatic organisms residing in these waters may bioaccumulate this chemical and be consumed, also resulting in ingestion exposures;
- Recreational use of these waters may result in dermal exposures;
- Domestic animals may consume or be dermally exposed to contaminated ground or surface waters; the consumption of meats and poultry could then result in ingestion exposures.

In general, exposures associated with surface water contamination can be expected to be lower than exposure from drinking contaminated ground water. The Henry's law constant for ethyl benzene suggests that it will volatilize upon reaching surface waters. However, if ethyl benzene is available, the bioconcentration factor for this compound suggests moderate bioaccumulation in aquatic organisms or domestic animals.

20.2.4 Other Sources of Exposure

The volatility of ethyl benzene suggests that it may be found in air. Brodzinsky and Singh (84) compiled all available atmospheric monitoring data for a number of volatile organics. For ethyl benzene, they had data for 861 locations. In rural and remote areas, the median concentration was 2.0 $\mu g/m^3$. In urban and suburban areas, the median concentration was 5.2 $\mu g/m^3$ and in source-dominated locations, the median concentration was 2.7 $\mu g/m^3$. These results suggest there are inhalation exposures to individuals, even in remote areas.

20.3 HUMAN HEALTH CONSIDERATIONS

20.3.1 Animal Studies

20.3.1.1 Carcinogenicity

No carcinogenicity data are available.

20.3.1.2 Mutagenicity

In the sole study available, ethyl benzene was found to be a weak inducer of sister chromatid exchange in human lymphocytes (209).

20.3.1.3 Teratogenicity, Embryotoxicity and Reproductive Effects

Hardin et al. (208) conducted teratogenicity tests in rats and rabbits. Both species were exposed to vapor concentrations of 100 or 1000 ppm ethyl benzene for 6 to 7 hours daily. Rats were exposed for 3 weeks prior to mating as well as on days 1 through 19 of gestation. Rabbits were exposed only on days 1 through 24 of gestation. No significant maternal or fetal toxicity was seen in rabbits. In rats, a possible reduction in fertility was noted at both exposure levels, but no dose-response was evident. Maternal toxicity in the form of increased spleen, liver and kidney weights was seen in the 1000 ppm group. In the fetuses, there was a significant increase in the incidence of extra ribs at both exposure levels.

20.3.1.4 Other Toxicologic Effects

20.3.1.4.1 Short-term Toxicity

Acute toxicity data on oral and dermal routes in both rats and rabbits indicate a low toxicity for ethyl benzene. An oral LD_{50} value in rats of 3500 mg/kg has been reported; dermal LD_{50} values in rabbits of 500 mg/kg (59) and 17,800 mg/kg (47) have been recorded.

Wolf et al. (210) evaluated the ability of ethyl benzene to produce injury to the eye and skin of rabbits. They found that two drops applied to the eye produced slight conjunctival irritation but no corneal injury. Ten to twenty applications to the ear and abdomen for 2 to 4 weeks produced moderate redness, swelling, superficial necrosis and blistering.

20.3.1.4.2 Chronic Toxicity

Chronic inhalation exposure of guinea pigs, monkeys, rabbits and rats at concentrations ranging from 400 to 2200 ppm for 7 to 8 hours per day, 5 days per week for 6 months produced no effects in guinea pigs, monkeys and rabbits; rats exhibited a slight increase in liver and kidney weights (210). The same investigators noted changes in the liver and kidney in rats administered 408 or 680 mg/kg/day ethyl benzene in olive oil, 5 days per week for 6 months. No effects on the bone marrow were observed (210).

20.3.2 Human and Epidemiologic Effects

Ethyl benzene is primarily an irritant to the skin, eyes and upper respiratory tract. Systemic absorption causes central nervous system depression (38). Inhalation of ethyl benzene might exacerbate the symptoms of obstructive airway diseases (e.g., emphysema) due to its irritant properties or reflex bronchospasm. Aspiration of small amounts causes extensive edema and hemorrhage of lung tissue (38).

No human ingestion data are available and inhalation data are limited. At 200 ppm (870 mg/m^3), the vapor has a transient irritant effect on the eyes. At 2000 ppm, eye irritation and lacrimation are immediate and severe and are accompanied by moderate nasal irritation. Tolerance to these effects develops after several minutes. Central nervous system effects begin after about 6 minutes at this level. At 5000 ppm, the irritation of the eyes, nose and throat becomes intolerable (19,2,211). Redness and inflammation may result from skin contact with the liquid (51). The rate of absorption through the skin of the hand and forearm is 22 to 33 mg/cm^2 per hour (46). Ethyl benzene is not known to be toxic to the liver or kidneys; however, concern for these organs has been expressed since they are the primary routes of metabolism and excretion, respectively (54).

20.3.3.3 Levels of Concern

The USEPA (355) has established an ambient water quality criterion for the protection of human health for ethyl benzene of 1.4 mg/L. This criterion is based on the threshold limit value (100 ppm) for occupational exposure to vapors, which was set to prevent irritation rather than chronic effects. An uncertainty factor of 1000, 50% absorption (assumed), a bioconcentration factor of 37.5 for fish and consumption of two liters of water and 6.5 g of contaminated fish per day were also utilized to calculate the criterion.

Both OSHA (298) and the ACGIH (3) have set an occupational exposure limit of 100 ppm (435 mg/m^3) for ethyl benzene, based on preventing eye irritation.

20.3.3.4 Hazard Assessment

The extent and quality of health effects data available for ethyl benzene are inadequate. Available data deal primarily with the irritant properties of ethyl benzene. The limited nature of these studies, linked with the lack of information on chronic and subchronic toxicity, carcinogenic activity and mutagenicity make estimation of the hazards of long-term low-level human exposure to this compound difficult to define.

20.4 SAMPLING AND ANALYSIS CONSIDERATIONS

Determination of ethyl benzene concentrations in soil and water requires collection of a representative field sample and laboratory analysis. Due to the volatility of ethyl benzene, care is required to prevent losses during sample collection and storage. Soil and water samples should be collected in airtight containers with no headspace; analysis should be completed within 14 days of sampling. In addition to the targeted samples, quality control samples such as field blanks, duplicates, and spiked matrices may be specified in the recommended methods.

EPA-approved procedures for the analysis of ethyl benzene, one of the EPA priority pollutants, in aqueous samples include EPA Methods 602, 624, and 1624 (65). An inert gas is bubbled through the aqueous sample in a purging chamber at ambient temperature, transferring the ethyl benzene from the aqueous phase to the vapor phase and onto a sorbent trap. The trap is then heated and backflushed to desorb the ethyl benzene and transfer it onto a gas chromatographic (GC) column. The GC column is programmed to separate the volatile organics; ethyl benzene is then detected with a photo-ionization detector (Method 602) or a mass spectrometer (Methods 624 and 1624).

The EPA procedures recommended for ethyl benzene analysis in soil and waste samples, Methods 8020 and 8240 (65), differ from the aqueous procedures primarily in the method by which the analyte is introduced into the GC. The recommended method involves dispersing the soil or waste sample in methanol or polyethylene glycol to dissolve the ethyl benzene. A portion of the solution is then combined with water and purged as described above. Other sample introduction techniques include direct injection and a headspace method.

Typical ethyl benzene detection limits that can be obtained in wastewaters and non-aqueous samples (wastes, soils, etc.) are shown below. The actual detection limit achieved in a given analysis will vary with instrument sensitivity and matrix effects.

Aqueous Detection Limit	Non-Aqueous Detection Limit
0.2 µg/L (Method 602)	1 µg/g (Method 8020)
7.2 µg/L (Method 624)	1 µg/g (Method 8240)
10 µg/L (Method 1624)	

TOLUENE

Introduction:

Toluene is produced during the petroleum refining process as a by-product of styrene production and coke-oven operation. It is used in the manufacture of benzene derivatives, dyes, solvents, TNT, saccharin, perfumes, medicines, detergent, gasoline blending, and as a raw material in the production of numerous organic chemicals. Toluene has a fresh-water solubility of 534.8 mg/l (ppm) and is highly soluble in other organic solvents. Due to its lipophilic properties, toluene possesses a significant potential for uptake by tissues with a high lipid content.

Toluene has been detected in finished and raw drinking water from several communities in the U.S. Finished drinking water from New Orleans contained up to 11 ppb of toluene. In a nationwide survey of 10 cities surface water supplies, 6 were found to contain toluene. In another similar survey, toluene was detected in 1 of 111 finished drinking water supplies. A screening program sponsored by the National Screening Program found 15% of 132 urban public water supplies contaminated with toluene at concentrations ranging from 0.1-1.0 ppb (average concentration=0.24 ppb). The Community Water Survey took 423 samples from the water supplies of small urban areas and found 1.4% of them to have toluene in their finished water supplies at concentrations ranging from 0.5-6.1 ppb. Of 65 groundwater samples taken by 5 states (CA, DE, IN, NJ, and NY), 21.5% proved positive for toluene contamination at concentrations ranging from 0.2-2,500 ppb (average concentration=180.6 ppb). Toluene has been detected in private and public groundwater supplies in Wisconsin.[1] In summary, 6.5% of 620 finished drinking water samples taken by federal and state survey showed toluene contamination ranging from 0.1-2,500 ppb (average concentration = 63.6 ppb).

Human Exposure Routes:

Human exposure to toluene usually involves inhalation in experimental or occupational settings or during episodes of intentional abuse. Little data exists on human exposure to toluene in foodstuffs.

Acute Toxicity:

The following values have been reported in the literature:

*Oral LD_{50} (rats): 4.3-7.5 g/kg
*Dermal LD_{50} (rabbit): 14.1 ml/kg

Acute inhalation studies agree that toluene concentrations of 200 ppm or above produce undesirable effects on the nervous system including central nervous system depression.

Chronic Toxicity:

No chronic ingestion studies using humans or animals have been reported in the literature. Chronic occupational exposures to toluene vapors at approximately 200 ppm have yielded inconsistent findings on central nervous system effects.

Some researchers report no adverse responses to years of toluene exposure while others report psychological disturbances in exposed individuals. All these studies can be faulted due to multiple chemical exposures to the people under study. Rats inhaling toluene at concentrations of 0-300 ppm for 2 years were examined for changes in hematology, clinical chemistry, body weights, and histopathology. Except for reduced hematocrits (100 and 300 ppm) and increased mean corpuscular hemoglobin concentration (300 ppm), all other parameters were normal.

Human Health Effects:

Effects of toluene exposure in humans include adverse mental changes such as altered psychomotor performance, irritability, disorientation, and unconsciousness. Toluene abuse has been reported to yield cardiac arrhythmias and liver and kidney dysfunction.[2]

Mutagenicity:

Toluene was not mutagenic in a battery of microbial, mammalian cell, and whole organism test systems including reverse mutation testing, mitotic gene conversion/crossing over, differential toxicity/DNA repair assays, thymidine kinase assays, sister-chromatid exchange, and micronucleus test. Russian literature reports of chromosome aberrations in rats exposed to toluene subcutaneously and by inhalation have not been corroborated by U.S. studies.

Carcinogenicity:

Rats exposed to concentrations of toluene up to 300 ppm for 24 months showed no increases in neoplastic, proliferative, inflammatory, or degenerative lesions. Other studies suggest that toluene is not carcinogenic when topically applied to the shaved skin of mice.

Teratogenicity/Reproductive Effects:

The majority of studies reviewed indicate no teratogenic effects from exposure to toluene. Teratogenic effects noted in a few tests include increased incidence of cleft palate in offspring of mice fed 0.1 ml/kg toluene during gestation and irregular sternebrae and extra ribs in the offspring of mice inhaling 1,500 mg/m^3 of toluene from days 9-14 of gestation.

Environmental Fate:

No reports were found for review.

Risk Assessment:

The weight of evidence to date does not support toluene as a mutagen or teratogen. In a long-term study, CIIT concluded that toluene did not produce carcinogenicity in F-344 rats. Other studies also suggest that toluene is not carcinogenic.

Utilizing the results from the CIIT study and converting the inhalation minimal effective dose into a dose expressed as mg/kg/day, the EPA has determined:

NOEL: 34.3 mg/kg/day
Safety Factor: 1,000
ADI: .0343 mg/kg/day

Recommendations and Conclusions:

Utilizing the federally-provided (EPA) numbers above and the procedures outlined in ss 160.07(4) and 160.13, the calculations for the Department of Health and Social Services recommended groundwater standard are as follows:

$$\frac{34.3 \text{ mg/kg/day} \times 10 \text{ kg} \times 100\%}{1{,}000 \times 1 \text{ liter}} = 0.343 \text{ mg/liter} = 343 \text{ µg/liter} = 343 \text{ ppb}$$

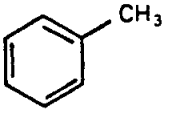
Recommended Enforcement Standard: 343 µg/liter (343 ppb)
Recommended Preventive Action Limit factor: 20%

References:

1. DNR Groundwater Volatile Organic Water Chemistry Sampling Program. November 28, 1984

2. National Research Council, 1980. Drinking Water and Health. National Academy Press. Washington, D.C. Vol. 3, p. 168-173

General: USEPA, 1982. Advisory Opinion for Toluene. Office of Drinking Water

COMMON SYNONYMS:	CAS REG. NO.:	FORMULA:	AIR W/V CONVERSION FACTORS at 25°C (12)
Methyl benzene Toluol Phenyl methane Methyl benzol	108-88-3 NIOSH NO.: XS5250000	C_7H_8	3.77 mg/m³ ≅ 1 ppm 0.2652 ppm ≅ 1 mg/m³
	STRUCTURE: 		MOLECULAR WEIGHT: 92.14

REACTIVITY	Toluene may generate heat, react vigorously, and possibly ignite or explode in contact with oxidizing mineral acids or other strong oxidizing agents (507,38,511,505).

PHYSICO-CHEMICAL DATA	• Physical State (at 20°C): liquid	(23)
	• Color: colorless	(23)
	• Odor: benzene-like	(23)
	• Odor Threshold: 2.9 ppm	(384)
	• Liquid Density (g/ml at 20°C): 0.8669	(68)
	• Freezing/Melting Point (°C): -95	(68)
	• Boiling Point (°C): 110.6	(68)
	• Flash Point (°C): 4.4 (closed cup)	(23)
	• Flammable Limits in Air, % by Volume: 1.2-7.1	(51,38,506)
	• Autoignition Temperature (°C): 480-536	(510,506,504)
	• Vapor Pressure (mm Hg at 20°C): 22	(67)
	• Saturated Concentration in Air (mg/m³ at 20°C): 110,000	(67)
	• Solubility in Water (mg/L at 20°C): 515	(67)
	• Viscosity (cp at 20°C): 0.580	(ADL estim)
	• Surface Tension (dyne/cm at 20°C): 29	(59)
	• Log (Octanol-Water Partition Coefficient), log K_{ow}: 2.73	(29)
	• Soil Adsorption Coefficient, K_{oc}: 259	(652)
	• Henry's Law Constant (atm·m³/mol at 25°C): 0.00661	(74)
	• Bioconcentration Factor: 27.1 (estim), 26 (estim)	(207,659)

PERSISTENCE IN THE SOIL-WATER SYSTEM	Relatively mobile in soil-water systems, including transport of vapor through air-filled pores as well as transport in solution. Chemical is resistant to hydrolysis but will probably biodegrade easily if microbiological populations are sufficiently numerous and active. It may persist for months to years (or more) if biodegradation is not possible.

PATHWAYS OF EXPOSURE	The primary pathway of concern from a soil-water system is the migration of toluene to ground-water drinking water supplies. Data from NPL sites indicate that migration of this compound has occurred in the past, although survey data do not show extensive contamination of drinking water. Inhalation resulting from volatilization from surface soils may also be important.

HEALTH HAZARD DATA	Signs and Symptoms of Short-term Human Exposure (54): Acute exposure to toluene results in CNS depression. Symptoms include headache, dizziness, fatigue, muscular weakness, drowsiness and incoordination with staggering gait. The liquid splashed in the eyes may cause irritation and reversible corneal damage. Prolonged or repeated skin contact may cause drying and dermititis.
	Toxicity Based on Animal Studies: LD_{50} (mg/kg) oral [rat] 5000 (47); skin [rabbit] 12,124 (47); LC_{50} (ppm) inhalation [mouse] (47) 5320·8 hr
	Long-Term Effects: No adverse effects based on limited data
	Pregnancy/Neonate Data: Conflicting teratogenic data
	Mutation Data: Conflicting data in toluene-exposed workers
	Carcinogenicity Classification: IARC - none assigned; NTP - none assigned (currently under evaluation)

HANDLING PRECAUTIONS (38)	Handle chemical only with adequate ventilation • Vapor concentrations of 200-500 ppm: any supplied-air respirator, self-contained breathing apparatus or chemical cartridge respirator with an organic vapor cartridge • 500-1000 ppm: chemical cartridge respirator with full facepiece and organic vapor canister • 1000-2000 ppm: any supplied-air respirator or self-contained breathing apparatus with full facepiece • Chemical goggles if there is probability of eye contact with the liquid • Impervious clothing to prevent prolonged or repeated skin contact.

EMERGENCY FIRST AID TREATMENT (54,38)	Ingestion: Do not induce vomiting. Seek medical attention • Inhalation: Move victim to fresh air; give artificial respiration if necessary. Get medical attention • Skin: Remove contaminated clothing. Wash skin with soap and water. If irritation persists after washing, get medical attention • Eye: Irrigate with large amounts of water; get medical attention.

ENVIRONMENTAL AND OCCUPATIONAL STANDARDS AND CRITERIA

AIR EXPOSURE LIMITS:

Standards
- OSHA PEL (8-hr TWA): 200 ppm; CL: 300 ppm; PEAK: 500 ppm/10 minutes
- AFOSH PEL (8-hr TWA): 100 ppm; STEL (15-min): 150 ppm

Criteria
- NIOSH IDLH (30-min): 2000 ppm
- ACGIH TLV® (8-hr TWA): 100 ppm (skin)
- ACGIH STEL (15-min): 150 ppm

WATER EXPOSURE LIMITS:

Drinking Water Standards
None established

EPA Health Advisories
In the absence of formal drinking water standards, the EPA (383) has developed the following Health Advisories (formerly termed SNARLs) for noncarcinogenic risk for short and long-term exposure to toluene in drinking water:

- 1 day: 21.5 mg/L
- 10 days: 2.2 mg/L
- long-term: 0.34 mg/L

EPA Ambient Water Quality Criteria (355)
- Human Health
  - Based on ingestion of contaminated water and aquatic organisms, 14.3 mg/L.
  - Based on ingestion of contaminated aquatic organisms only, 424 mg/L.
- Aquatic Life
  - Freshwater species
    acute toxicity: no criterion, but lowest effect level occurs at 17,500 µg/L.

    chronic toxicity: no criterion established due to insufficient data.
  - Saltwater species
    acute toxicity: no criterion, but lowest effect level occurs at 6300 µg/L.

    chronic toxicity: no criterion, but lowest effect level occurs at 5000 µg/L.

REGULATORY STATUS (as of October 1, 1985)

Promulgated Regulations

- Federal Programs

Clean Water Act (CWA)

Toluene is designated a hazardous substance under CWA. It has a reportable quantity (RQ) limit of 454 kg (347,556). It is also listed as a toxic pollutant (351). Water quality criteria have been set. No effluent limitations specific to this chemical have been set.

Safe Drinking Water Act (SDWA)

In states with an approved Underground Injection Control program, a permit is required for the injection of toluene-containing wastes designated as hazardous under RCRA (295).

Resource Conservation and Recovery Act (RCRA)

Toluene is identified as a toxic waste (U220) and listed as a hazardous waste constituent (328,329). Non-specific sources of toluene-containing waste are solvent use (or recovery) activities and chlorinated aliphatic hydrocarbon production (325). Waste streams from the following industries contain toluene and are listed as specific sources of hazardous wastes: organic chemicals (benzyl chloride production) and pesticides (disulfoton production) (326,327).

Toxic Substances Control Act (TSCA)

Manufacturers, processors or distributors of toluene must report production usage and disposal information to EPA. They, as well as others who possess health and safety studies on toluene, must submit them to EPA (334,335).

Comprehensive Environmental Response Compensation and Liability Act (CERCLA)

Toluene is designated a hazardous substance under CERCLA. It has a reportable quantity (RQ) limit of 454 kg. Reportable quantities have also been issued for RCRA hazardous waste streams containing toluene but these depend upon the concentration of the chemicals present in the waste stream (556).

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)

Toluene is exempt from a tolerance requirement when used as a solvent in pesticide formulations applied to growing crops (315).

Occupational Safety and Health Act (OSHA)

Employee exposure to toluene shall not exceed an 8-hour time-weighted-average (TWA) of 200 ppm. A ceiling level of 300 ppm shall not be exceeded at any time during an 8-hour work-shift except for a duration of 10 minutes when it may reach a ceiling level of 500 ppm (298).

Hazardous Materials Transportation Act (HMTA)

The Department of Transportation has designated toluene as a hazardous material which is subject to requirements for packaging, labeling and transportation (306).

Food, Drug and Cosmetic Act (FDCA)
Toluene is approved for use as an indirect food additive (362).

- State Water Programs
  California has an action level of 100 µg/L for drinking water (731).
  Connecticut has an action level of 1000 µg/L for drinking water (731).
  Iowa has an unpublished internal criterion of 148 µg/L for streams (731).

  Other states follow EPA Ambient Water Quality Criteria.

Proposed Regulations

- Federal Programs
  Clean Water Act (CWA)
  Effluent guidelines for toluene have been proposed in the pesticide chemicals category (359) and in the organic chemicals, plastics and synthetic fibers category (357).

  Resource Conservation and Recovery Act (RCRA)
  EPA has proposed listing spent solvent mixtures containing 10% of more toluene as non-specific sources of hazardous wastes (780).

  Comprehensive Environmental Response Compensation and Liability Act (CERCLA)
  EPA has proposed lowering the reportable quantity (RQ) for toluene to 45.4 kg when it is contained in RCRA hazardous waste streams from non-specific sources (557).

- State Water Programs
  Wisconsin has proposed a ground-water enforcement standard of 343 µg/L for toluene (731).

EEC Directives

Directive on Ground Water (538)
Direct discharge into ground water (i.e., without percolation through the ground or subsoil) of organohalogen compounds and substances which may form such compounds in the aquatic environment, substances which possess carcinogenic, mutagenic or teratogenic properties in or via the aquatic environment, and mineral oils and hydrocarbons is prohibited. Appropriate measures deemed necessary to prevent indirect discharge into ground water (i.e., via percolation through ground or subsoil) of these substances shall be taken by member countries.

Directive Relating to the Classification, Packaging and Labeling of Dangerous Preparations (Solvents) (544)
Toluene is listed as a Class II/c harmful substance and is subject to packaging and labeling regulations.