TABLE OF CONTENTS

Appendix B
Section A

BENZENE
HEALTH-BASED MAXIMUM CONTAMINANT LEVEL
SUPPORT DOCUMENT

Office of Science and Research

New Jersey Department of Environmental Protection

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EXECUTIVE SUMMARY

Benzene is a natural component of crude oil. Industry uses benzene in the production of rubber, styrene, and pesticides. Benzene's volatility and water solubility provideS the potential for environmental migration. Exposure to benzene has been associated with aplastic anemia and acute myelogenous leukemia; benzene is listed as a human carcinogen (U.S.EPA Group A). A quantitative estimation of human leukemia hazard has been performed for benzene exposure via drinking water. The level of benzene in drinking water associated with a lifetime excess cancer risk (upper bound) of one in a million has been determined to be 0.15 ug benzene per liter.

TABLE OF CONTENTS

BACKGROUND INFORMATION AND PROPERTIES

Chemical properties

Chemical Name	Benzene
Synonyms	Benzol cyclohexatriene pyrobenzol
CAS #	71-43-2
Chemical formula	C_6H_6
Chemical structure	
Molecular weight	78.11
Physical state (room temperature)	clear, colorless liquid
Melting point	5.56 °C
Boiling point	80.1 °C at 760 torr
Vapor pressure, volatility	95.2 torr at 25 °C
Specific gravity, density	0.8737 at 25 °C
Water Solubility	1.78 g/L at 25 °C
Log octanol/water partition coefficient	2.13
Taste threshold (water)	not available
Odor threshold (water)	2 mg/L
Odor threshold (air)	1 ppm
Conversion factors	1 ppm=3.19 mg/m^3

Production and Use

Benzene is a natural component of crude oil and natural gas. Benzene production by the petrochemical and petroleum refining industries ranks 16th on the list of the top 50 chemicals produced in the United States (Weber, 1985). Industry utilizes benzene as an intermediate in the manufacture of polystyrene, nylon, rubber, and pesticides. At present there is no known intentional use of benzene in consumer products for home use. Gasoline in the United States contains an average of 0.8% benzene (IARC, 1982a).

Guidelines, Regulations, and Standards

In 1971 without formal rulemaking, the present Occupational Safety and Health Administration (OSHA) standard was adopted; it allows an 8-hour time-weighted-average (TWA) of 10 ppm with a ceiling limit of 25 ppm and a maximum peak concentration of 50 ppm for a ten minute period. The OSHA standard was based on concern for the development of aplastic anemia and depression of various cellular blood elements; it did not address benzene's potential to induce leukemia.

An Ambient Water Quality Criteria Document was published by the U.S. Environmental Protection Agency (U.S.EPA, 1980). Assuming that a 70-kg adult consumes 2 L of water and 6.5 of fish per day, a benzene level of 0.7 ug/L in ambient water was estimated to limit excess lifetime cancer risk (upper bound) to one in a million.

The Office of Drinking Water has developed a drinking water Health Advisory, for benzene based on data describing non-carcinogenic endpoints of toxicity (U.S.EPA, 1985a). Assuming that a 10 kg child consumes one liter of water per day, the ten-day Health Advisory is 233 ug/L.

Under the Safe Drinking Water Act the U.S.EPA promulgated final recommended maximum contaminant levels (RMCLs), and proposed maximum contaminant levels (MCLs) (U.S.EPA, 1985b). The RMCL and MCL for benzene are zero and 5 ug/L, respectively.

The World Health Organization recommended a benzene guideline value of 10 ug/L for drinking water (WHO, 1984). A linear multistage extrapolation model was used to derive a level that should give rise to less than one additional cancer per 100,000 population, assuming a daily drinking water consumption of two liters.

ENVIRONMENTAL EXPOSURE

Fate and Transport

Benzene's volatility and water solubility provide the potential for environmental migration. The half-life of benzene in water is about 37 minutes (U.S.EPA, 1984).

Ambient Levels

The Federal Reporting Data Systems data on United States populations served by primary water supply systems, were used to estimate exposure to benzene through drinking water (U.S.EPA, 1984). An estimated 4,829,000 individuals are exposed to levels of benzene in drinking water at or above 0.5 ug/L (Table I) (U.S.EPA, 1984).

Table I
Estimated Drinking Water Intake of Benzene

Exposure level (ug/L)	Population	Intake* (ug/kg/day)
0.5	4,829,000	0.014
5.0	155,000	0.14
10.0	49,000	0.29
40.0	500	1.1

* Intake estimates assume that a 70 kg man consumes 2 L of water per day.

Source: U.S.EPA, 1984

The Office of Science and Research, New Jersey Department of Environmental Protection, sampled public water supplies statewide for over 100 substances during the period 1978 through 1981. Benzene was detected in 6% of the samples at a mean level of 7 ug/L. Chemicals listed in the A-280 amendments were recently monitored by New Jersey potable water purveyors. Benzene was found in 1% of the samples at concentrations ranging from 1.4 to 5.0 ug/L.

METABOLISM AND PHARMACOKINETICS

Absorption

Quantitative data defining the extent or rate of benzene absorption from the gastrointestinal tract are not available. Inhaled benzene rapidly diffuses through the lungs and is quickly absorbed into the blood. In human volunteers, approximately 50% of the benzene was retained (Docter and Zielhuis, 1967; Nomiyama and Nomiyama, 1974).

Distribution

The benzene absorbed by the circulating blood is distributed throughout the body. Benzene tends to accumulate in the bone marrow, liver, nervous tissue and body fat. Hydroquinone and catechol are found in the bone marrow and lymphoid tissue (U.S.EPA, 1984).

Metabolism

Benzene is metabolized in the liver. The primary oxidation occurs via the cytochrome P-450 dependent monoxygenase system and the principal metabolites are phenol, catechol and hydroquinone. Metabolites undergo sulfate and glucuronide conjugation (Irons and Pfeiffer, 1982).

Excretion

The major route of elimination is the exhalation of unchanged benzene. Urinary excretion products include phenol, hydroquinone, catechol, hydroxyhydroquinone, trans-transmuconic acid, and L-phenylmercapturic acid (U.S.EPA, 1984).

Human Exposure and Body Burden

The excretion of phenol and the ratio of inorganic sulfate to organic sulfate in urine can be used as an index of benzene exposure (IARC, 1982a; U.S. EPA, 1984).

HEALTH EFFECTS

Overview

Benzene exposure has been causally linked to aplastic anemia, suppression of various peripheral blood cellular elements (white cells, red cells, and platelets), and acute myelogenous leukemia and its variants. The basic mechanism by which benzene affects bone marrow precursor cells remains to be determined. The toxicity of benzene on the hematopoietic system has been adequately reviewed (Goldstein, 1977; IARC, 1982a).

Human

In cases of acute benzene poisoning, respiratory tract inflammation, lung hemorrhage, kidney congestion, and cerebral edema have been observed at autopsy (Winek and Collom, 1971).

Animal

The LC_{50} for a seven hour inhalation exposure is 10,000 ppm for mice (Svirbely et al., 1943). The oral LD_{50} of reagent-grade benzene in male Sprague-Dawley rats was reported to be 0.93 g/kg body weight (Cornish and Ryan, 1965).

The depression of bone marrow function was observed in AKR/J mice exposed to benzene (300 ppm, 6 hours per day for 28 weeks) (Snyder et al., 1978).

Behavioral and Central Nervous System

Benzene itself can induce acute toxicity on the central nervous system. Reversible effects include dizziness, nausea, vomiting, headache, drowsiness, and loss of balance. Exposure in the region of 25,000 ppm in air is rapidly fatal (IARC, 1982a; U.S.EPA, 1985a).

Reproductive, Embryotoxic, and Teratogenic

No teratogenic effects were observed in offspring following 6-hour daily exposure of pregnant Sprague-Dawley rats to benzene vapor at 0, 1, 10, 40, or 100 ppm, on days 6-15 of gestation (API, 1982). Both sexes of offspring of the mothers that were exposed to benzene at 100 ppm had reduced mean body weights.

Genetic

Studies examining the genetic toxicology of benzene are summarized in Table II.

Benzene is not mutagenic in bacterial systems. Benzene was tested in four Salmonella typhimurium tester strains (NTP, unpublished results). Each test consisted of a concurrent positive control, solvent control, and five dose concentrations. Exogenous metabolic activation was provided by S-9 fractions from Arochlor 1254-induced rats and hamsters. Benzene failed to induce base-pair substitution or frameshift mutations.

Benzene has been shown to cause cytogenetic damage in vivo. Tice et al. (1980) demonstrated the approximate doubling of the frequency of sister chromatid exchanges (SCE) in DBA/2 mice exposed to 3100 ppm benzene by inhalation for 4 hours. SCE lesions persisted in successive cultured bone marrow cell generations.

Benzene inhalation induced an increase in chromosomal aberrations in DBA/2 mice only when the animals had been pretreated with phenobarbital (Tice et al., 1982). There was no increase in chromosomal rearrangements as the aberrations were all of the chromatid-type.

Benzene is one of the few agents whose cytogenic effects have been studied in humans. In many of these studies, significant increases in chromosomal aberrations were observed (IARC, 1982a). The data indicate an association between benzene-associated hemopathies and chromosomal aberrations.

In summary, benzene is a clastogen (an agent that breaks chromosomes). Benzene metabolites are responsible for the observed cytogenic changes (IARC, 1982a).

Carcinogenicity

The carcinogenic potential of benzene has been adequately reviewed (IARC, 1982a; U.S EPA, 1985c). Benzene is classified as a human carcinogen (IARC Category 1; EPA Group A). The International Agency for Research on Cancer (IARC, 1982a) stated the following:

> A series of epidemiological studies, both cohort and case-control, showed statistically significant associations between leukemia (predominantly myelogenous) and occupational exposure to benzene and benzene-containing solvents. These results were replicated in a number of countries and different industries. In the epidemiological studies of people exposed to benzene, statistically significant excesses of leukemia were observed.

Table II

Genetic Toxicology of Benzene

Process	End Point	Test System	Conclusions	References
Gene Mutation	Base-pair substitution, Frameshift	Ames *Salmonella* battery with and without metabolic activation	Negative	NTP unpublished results
Chromosomal Rearrangement Homologous recombination	Sister chromatid exchange	Chinese hamster ovary cells *in vitro* with and without metabolic activation	Negative	NTP unpublished results
	Sister chromatid exchange	Mice *in vivo*	Positive	Tice et al., 1980 Tice et al., 1982
Chromosomal Rearrangement Non-homologous recombination	Chromosomal aberrations	Chinese hamster ovary cells *in vitro* with and without metabolic activation	Negative	NTP unpublished results
		Mice *in vivo*	Positive	Tice et al., 1980 Tice et al., 1982
		Human occupational studies	Positive	Reviewed by IARC, 1982a

There is sufficient evidence that benzene is carcinogenic to man.

Human Epidemiology. An historical prospective mortality study of chemical workers with occupational benzene exposure was conducted by Environmental Health Associates, Inc. for the Chemical Manufacturers Association (CMA) (Wong, 1983). The cohort was comprised of 7,676 male chemical workers who were employed by any of seven chemical manufacturing plants for at least six months between 1946 and the end of 1975. Cohort members were classified according to benzene exposure: 3,074 were not exposed, 1,066 were only intermittently exposed, and 3,536 were continuously exposed. Cumulative benzene exposure was calculated for each member of the continuous exposure group.

Vital status for the entire cohort was determined via company and governmental records through 31 December 1977, giving 1,036 (13.50%) deaths and 177 (2.31%) untraced subjects. Death certificates were obtained for 1,013 (97.78%) of the deceased. Among those not exposed to benzene, 53 cancer deaths were observed, whereas 82.5 were expected, based on age-cause-race-calendar adjusted U.S. national mortality rates. One hundred twenty-three (123) cancer deaths occurred in the continuous exposure group with 117.7 expected. No leukemia deaths were recorded in the unexposed group, representing a substantial deficit compared to 3.40 expected deaths. An excess of leukemia (6 observed versus 4.43 expected) was noted in the continuous exposure group. Three of the six leukemia deaths were lymphatic (1 acute, 1 chronic, and 1 unspecified), two were chronic myeloid, and one was acute (unspecified). The acute myeloid cell type, frequently associated with benzene exposure (Aksoy, 1985; Rinsky et al., 1981), was not found in this study.

Statistically significant dose-response relationships were demonstrated between cumulative benzene exposure and leukemia ($p=0.011$) (Table III), as well as the broader category of all lymphatic and hematopoietic cancers ($p=0.020$). However, the dose-response for all lymphatic and hematopoietic cancers was due primarily to the leukemia increase.

The National Institute for Occupational Safety and Health (NIOSH) conducted a retrospective cohort mortality study of the employees of three facilities manufacturing rubber hydrochloride (Pilofilm) at two locations in Ohio (Infante et al., 1977; Rinsky et al., 1981). Rinsky examined job histories and mortality experience for 1,006 nonsalaried white males who worked at least one day between 1940 and 1959 in a department with benzene exposure. Vital status follow-up of the cohort was 98% complete through 30 June 1975. Among the 748 workers with benzene exposure prior to 1950, 180 deaths from all causes occurred, whereas 161.32 were expected. Seven (7) leukemia deaths were observed with 1.25 expected (standardized mortality ratio (SMR) = 560, p 0.001). Among the 258 individuals first exposed after 1950, there were 49 deaths observed from all causes compared to 56 expected. One (1) leukemia death was noted in the latter group with 0.46 expected (SMR = 217). All leukemia deaths were of the myeloid or monocytic cell types.

Table III

Observed and Expected Leukemias as a Function of Cumulative Dose[a] in the Wong Cohort

Cumulative Dose in ppm-years (average)[b]	Observed	Expected	SMR
0	0	3.40	0
15 (7.5)	2	2.07	97
15 - 60 (37.5)	1	1.28	78
60 (79.2)	3	1.09	276

[a] Person-years of observation were not available for each dose group.

[b] The averages shown were not presented in Wong (1983). They have been estimated as the midpoints of the intervals. The average for the last group is derived assuming a maximum cumulative exposure of 98.4 ppm-years.

Adapted from Crump (1986a).

The Infante-Rinsky cohort was updated to include 1,713 white male nonsalaried workers who were exposed to benzene between 1940 and plant closure (Crump and Allen, 1984). The Goodyear Tire and Rubber plants were closed in 1965 at Akron and in 1976 at St. Mary's. Survival follow-up was completed through 1978. Crump and Allen (1984) constructed a complete benzene exposure profile for each worker with industrial hygiene and job category information provided by Rinsky. The 73 malignant neoplasm deaths ascertained were very close to the 70.1 expected. In contrast, 8 leukemia deaths occurred, whereas 2.98 were expected (SMR = 268, p = 0.01). The dose-response relationship between cumulative benzene exposure and leukemia was statistically significant ($p \leq 0.0001$) (Table IV).

The Michigan division of the Dow Chemical Company reported the occupational, health, and vital status of chemical workers with exposure to benzene (Townsend et al., 1978; Ott et al., 1978). Benzene was used as a feedstock consumed in the production of chlorobenzenes and alkylbenzenes, and as a solvent in the fabrication of ethyl cellulose resins. The cohort consisted of 594 white males who were assigned to these production areas on or after January 1, 1940. Mortality experience follow-up proceeded through 1973. Cumulative benzene exposure for each worker was estimated from work histories and industrial hygiene measurements supplied by Mr. Ott (Crump and Allen, 1984). Non-significant excess mortality from total malignancies was found (30 observed; 22.8 expected). Two acute myelocytic leukemia deaths were noted versus 1.0 expected. The cumulative benzene exposures calculated for these two leukemia decedents were 1.5 and 45.4 ppm-years (Table V).

Aksoy (1985) has focused attention to the incidence of aplastic anemia and leukemia among 28,500 handbag, shoe, and leather workers in Istanbul, Turkey. The concentration of benzene in the working environment was estimated to be between 150 and 210 ppm when benzene-containing glue adhesives were being used, and between 15 and 30 ppm during nonworking hours. Thirty-four cases of leukemia were admitted to the hematology departments of medical schools in Istanbul during the period 1967 and 1975. The predominant histology was acute leukemia (myeloblastic and erythroleukemia). The Carcinogen Assessment Group of the EPA (U.S.EPA 1979) used the Aksoy series of case reports to calculate a relative risk of 20 for non-lymphoblastic leukemia among workers exposed to average benzene levels which ranged from 15 to 250 ppm. The International Agency for Research on Cancer (IARC, 1982a) determined that the relative risk of acute non-lymphocytic leukemia among Istanbul shoeworkers was 24.

Animal Laboratory Bioassays. The experimental induction of cancer by benzene has been demonstrated in rats and mice (NTP, 1985; Maltoni, 1985; Goldstein et al., 1982; Cronkite et al., 1985). These studies complement the epidemiological evidence that benzene is a human carcinogen. This document will only discuss bioassays using the oral route of benzene exposure.

Table IV

Observed and Expected Leukemias as a Function of Cumulative Dose in the Rinsky et al. Cohort

Cumulative Dose in ppm-years (average)	Observed	Expected	SMR	Person-Years
5 (1.29)	2	1.11	180	16890
5 - 20 (11.0)	0	0.52	0	7092
20 - 80 (42.2)	0	0.50	0	6591
80 - 200 (129)	0	0.31	0	3557
200 - 1000 (421)	5	0.32	1560	3075
1000 (1489)	1	0.049	2040	396

Adapted from Crump (1986a).

Table V

Observed and Expected Leukemias as a Function of Cumulative Dose in the Ott et al. Cohort

Cumulative Dose in ppm-years (average)	Observed	Expected	SMR	Person-Years
5 (1.48)	1	0.18	556	3533
5 - 20 (10.9)	0	0.202	0	2961
20 - 80 (44.8)	1	0.31	323	3758
80 - 200 (125.9)	0	0.14	0	1790
200 (352.9)	0	0.13	0	1229

Adapted from Crump (1986a).

In a two-year study conducted by the National Toxicology Program (NTP), (1985), 8-week-old F344/N rats and B6C3F$_1$ mice of both sexes were given benzene by gavage. The benzene was dissolved in 5 mL/kg of corn oil and administered as a single daily dose for 5 days per week for 103 weeks. Dosages were (in mg benzene/kg body weight): 0, 50, 100, 200 for male rats and 0, 25, 50, 100 for female rats and for mice of both sexes. Both rats and mice were randomly distributed so that there were 50 animals/sex/treatment group. Food and water were freely available.

Animals were killed when moribund or at the conclusion of the study (104 weeks). A complete necropsy was performed on all animals. Selected results are presented in Table VI. The National Toxicology Program concluded the following:

Under the conditions of these studies, there was clear evidence of carcinogenicity of benzene for male F344/N rats, for female F344/N rats, for male B6C3F$_1$ mice, and for female B6C3F$_1$ mice. For male rats, benzene caused increased incidences of Zymbal gland carcinomas, squamous cell papillomas and squamous cell carcinomas of the oral cavity, and squamous cell papillomas and squamous cell carcinomas of the skin. For female rats, benzene caused increased incidences of Zymbal gland carcinomas and squamous cell papillomas, and squamous cell carcinomas of the oral cavity. For male mice, benzene caused increased incidences of Zymbal gland squamous cell carcinomas, malignant lymphomas, alveolar/bronchiolar carcinomas and alveolar/bronchiolar adenomas or carcinomas (combined), harderian gland adenomas, and squamous cell carcinomas of the preputial gland. For female mice, benzene caused increased incidences of malignant lymphomas, ovarian granulosa cell tumors, ovarian benign mixed tumors, carcinomas and carcinosarcomas of the mammary gland, alveolar/bronchiolar adenomas, alveolar/bronchiolar carcinomas, and Zymbal gland squamous cell carcinomas. Dose-related lymphocytopenia was observed for male and female F344/N rats and male and female B6C3F$_1$ mice.

In an experiment coded BT902 by Maltoni et al. (1985), 7-week-old Sprague-Dawley rats of both sexes were given benzene by gavage. A single dose of 500 mg/kg in olive oil was administered daily, 4-5 days per week for 104 weeks. Controls received only olive oil. Food and water were freely available. Animals were under observation for 141 weeks or until spontaneous death.

A complete autopsy was performed on each animal and histological examination made of organs and tissues. The rat organs that showed statistically significant increases in carcinogenic tumors were as follows: Zymbal glands in males and females; oral cavity in males and females; and skin of males.

Table VI

Incidence of Tumors in Mice and Rats Induced by Benzene[a]

Dose Levels[b]		Responses	
		(# animals with tumor/# animals at risk)	
Experimental mg/kg	Adjusted mg/kg/day	Male	Female
		Mouse Squamous Cell Carcinoma	
0	0	0/50	0/48
25	17.9	4/47	0/45
50	35.7	20/49	1/50
100	71.4	37/47	5/49
		Mouse Lung Carcinoma	
0	0	5/50	0/48
25	17.9	11/47	3/45
50	35.7	12/49	6/50
100	71.4	14/47	6/49
		Mouse Malignant Lymphoma	
0	0	4/49	
25	17.9	9/47	
50	35.7	9/49	
100	71.4	15/47	
		Mouse Lymphoma or Leukemia	
0	0	4/50	
25	17.9	10/47	
50	35.7	10/49	
100	71.4	15/47	
		Mouse Mammary Gland	
0	0		0/48
25	17.9		2/45
50	35.7		5/50
100	71.4		10/49

[a] Data are taken from National Toxicology Program (NTP) gavage studies (1985).

[b] Dose levels are converted from mg/kg to mg/kg/day by multiplying by factors of 5/7 to account for the fact that benzene was administered 5 days per week for NTP studies.

Table VI (Cont'd)

Incidence of Tumors in Mice and Rats Induced by Benzene[a]

Dose Levels[b]		Responses	
Experimental	Adjusted	(# animals with tumor/# animals at risk)	
mg/kg	mg/kg/day	Male	Female
		Rat Squamous Cell Carcinoma	
0	0	0/48	0/50
25	7.31	--	1/50
50	14.6	10/50	4/50
100	29.3	8/50	6/48
200	58.5	16/50	--
		Rat Zymbal Gland	
0	0	2/32	0/45
25	7.31	--	5/40
50	14.6	6/46	5/44
100	29.3	10/42	14/46
200	58.5	17/42	--

a Data are taken from National Toxicology Program (NTP) gavage study (1985).

b Dose levels are converted from mg/kg to mg/kg/day by multiplying by factors of 5/7 to account for the fact that benzene was administered 5 days per week for NTP study. A factor of $(104/130)^4$ is further applied, for NTP rat study, due to termination of the experiment before the animals have lived out their full life spans. Adopted from Crump (1986b).

QUANTITATIVE RISK ASSESSMENT

Studies Useful for Risk Assessment

The evidence for classifying benzene as a human carcinogen is obtained from human epidemiologic studies. Occupational cohort epidemiology studies (Wong, 1983; Rinsky et al., 1981; Ott et al., 1978) that provide adequate exposure and response data appear most suitable for developing quantitative estimates of the carcinogenic risk of benzene (Crump and Allen, 1984; Crump and Allen, 1985; U.S. EPA, 1985c). Leukemia is the adverse response of interest in man. The best judgment risk number is obtained by using the most extensive data base available. The data source is the pooled studies of Ott et al. (1978), Rinsky et al. (1981), and Wong (1983) studies.

Calculation of the Health-Based Maximum Contaminant Level

The modeling of the epidemiological data sets was approached by using regression techniques. The relative risk (multiplicative) model assumes that the increased age-specific leukemia mortality from a specific benzene dose is proportional to the background leukemia mortality. Only linear (first order) functions of cumulative benzene exposure have been considered.

The dose and effect groups presented in Tables 3 through 5 were combined and used in the relative risk model. In mathematical terms, the relative risk model is:

$$E(Oi) = aEi\ (1+bdi),$$

where Oi is the observed number of leukemia deaths assuming a Poisson distribution, Ei is the expected number of leukemia deaths based on a comparison population, and di is the average cumulative benzene exposure. E(Oi) is the expected number of leukemias if the model adequately represents the data. Calculations were performed by K.S. Crump and Company (Crump, 1986a).

Risk has been defined as "extra risk", i.e.,

$$[P(d) - P(0)]/[1-P(0)],$$

where P(d) is the lifetime probability of dying of leukemia when exposed to benzene dose d and P(0) is the lifetime probability when not exposed to benzene. A risk level of one in a million was selected for a lifetime exposure scenario. The 95% upper confidence interval on risk is judged a plausible upper bound on risk.

Standard assumptions are that an individual in an occupational setting breathes 10 cubic meters of air in an eight-hour shift, and spends 260 days per year on the job. One-half of the inhaled benzene is absorbed. One ppm of benzene is 3.19 mg/m^3. Furthermore, let us assume that two liters of drinking water are consumed each day by a 70 kg adult.

From occupational data, the human dose expressed in units of ppm in air associated with a risk level of one in a million excess cancer for lifetime exposure is 2.64×10^{-5}. This is converted to a drinking water concentration level as follows:

human dose (ug/L) =

human dose (ppm) (3.19 mg/m^3/ppm) (1000 ug/mg) ($10 m^3$) (260 days/360 days) (0.5)/(2 liters)

human dose = 0.15 ug/L.

A drinking water concentration of 0.15 ug/L benzene is associated with a lifetime excess cancer risk of one in a million.

Assumptions and Uncertainty

The standard assumption is that a 70 kg adult drinks 2 liters of water per day for life. The following has not been quantified, but should be considered when evaluating these risk estimates:

1) Exposure measurements were not complete in any of the occupational studies. The industrial hygiene records were area samples, as opposed to personal samples, resulting in estimation of exposure concentrations.

2) The pharmacokinetics of benzene inhalation may be different enough from those of benzene ingestion to confound a straightforward mg per day conversion of risks identified from inhalation exposure to potential risks from oral ingestions benzene.

Conclusions

Benzene is a human carcinogen. The quantitative estimation of the leukemia hazard associated with benzene exposure was based on three occupational cohort studies. The drinking water level yielding a lifetime leukemia excess risk (upper bound) of one in a million has been estimated to be 0.15 ug/L.

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