Advisory Opinion for Benzene
Office of Drinking Water
U.S. Environmental Protection Agency
Washington, D.C. 20460
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AN OFFICE OF DRINKING WATER HEALTH EFFECTS ADVISORY

The Office of Drinking Water provides advice on health effects upon request, concerning unregulated contaminants found in drinking water supplies. This information suggests the level of a contaminant in drinking water at which adverse health effects would not be anticipated. A margin of safety is factored in so as to protect the most sensitive members of the general population. The advisories are called Suggested No Adverse Response Levels (SNARLs). SNARLs have been calculated by EPA and by the National Academy of Sciences (NAS) for selected contaminants in drinking water. An EPA-SNARL and a NAS-SNARL may well differ due to the possible selection of different experimental studies for use as the basis for the calculations. Furthermore, NAS-SNARLs are calculated for adults while the EPA-SNARLs are established for a 10 kg body weight child. Normally EPA-SNARLs are provided for one-day, ten-day and longer-term exposure periods where available data exist. A SNARL does not condone the presence of a contaminant in drinking water, but rather provides useful information to assist in the setting of control priorities in cases where contamination occurs. EPA-SNARLs are provided on a case-by-case basis in emergency situations such as spills and accidents.

In the absence of a formal drinking water standard for an identified drinking water contaminant, the Office of Drinking Water develops EPA-SNARLs following the state-of-the-art concepts in toxicology for non-carcinogenic risk for short and longer term exposures. In cases where a substance has been identified as having carcinogenic potential, a range of estimates for carcinogenic risk based upon lifetime exposure as developed by the NAS (1977 or 1980) and/or EPA's Carcinogen Assessment Group (EPA, 1980a) is presented. However, the EPA-SNARL calculations for all exposures ignore the possible carcinogenic risk that may result from these exposures. In addition, EPA-SNARLs usually do not consider the health risk resulting from possible synergistic effects of other chemicals in drinking water, food, and air.

EPA-SNARLs are not legally enforceable standards; they are not issued as an official regulation, and they may or may not lead ultimately to the issuance of national standards or Maximum Contaminant Levels (MCLs). The latter must take into account occurrence, relative source contribution factors, treatment, technology, monitoring capability, and costs, in addition to health effects. It is quite conceivable that the concentration

set for EPA-SNARL purposes might differ from an eventeual MCL. The EPA-SNARLs may also change as additional information becomes available. In short, EPA-SNARLs are offered as advice to assist those such as Regional and State environmental and health officials, local public officials and water treatment facility personnel who are responsible for the protection of public health when dealing with specific contamination situations.

General Information and Properties

Benzene is an aromatic hydrocarbon, has the molecular formula C_6H_6 and a molecular weight of 78.1 (Weast et al. 1965). Under standard conditions, benzene is a colorless liquid with a very characteristic odor. It is highly flammable (limits of flammability in air of 1.5-8.0% by volume) and volatile (vapor pressure of 100 mm Hg at 26° C). Benzene is relatively soluble in water (1.8 g/l at 25° C) and miscible with a variety of organic solvents. Its density, 0.8737 g/ml at 25° C, is lower than that of water so that undissolved benzene floats on top of water. The pure liquid freezes at -5.553° C and boils at 80.100° C (Ayers and Muder, 1964). The vapors of benzene are nearly three times heavier than air (Lange and Forker, 1961), causing them to settle in low places if the ambient air is relatively still.

Benzene forms a two-phase, minimum boiling azeotrope with water at a benzene concentration of 91% by weight, boiling at 69° C. It also forms ternary azeotropes with other organic compounds and water (Horesly, 1947). This factor must be considered if evaporative purification systems are used to remove benzene from water. A concentration of 1 part per million in air is equivalent to 3.2 mg/m^3. It is noteworthy that the American Conference of Governmental Industrial Hygienists (ACGIH), Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) recommend threshold limit values for benzene as follows: 32 mg/m^3 (10 ppm), 3.2 mg/m^3 (1 ppm) and 32 mg/m^3 (10 ppm), respectively.

Sources of Exposure

Since benzene is broken down rapidly by bacteria in non-chlorinated water, the levels reported in individual samples may grossly underestimate the actual amount present as a result of decomposition due to sunlight or storage (Brass, 1981). Benzene concentrations in U.S. drinking water have not been surveyed in detail. In the National Organics Monitoring Survey (NOMS), which was conducted from March 1976 through January

1977, benzene analyses were performed on three samplings from community water supplies, which were representative of various types of sources and treatment processes. The numbers of positive benzene analyses per numbers of cities sampled were 0/111, 7/113 (with a mean of 0.4 ug/liter) and 4/16 (with a mean of 0.95 ug/liter) (USEPA, 1978). Four of ten water supplies surveyed by the EPA utilizing volatile organic analysis contained benzene at concentrations of 0.1-0.3 ug/liter (USEPA, 1975). Benzene analyses were performed on samples collected during the National Organics Monitoring Survey (USEPA, 1977). Samples from some of the larger cities using surface waters as their primary water source contained low levels of benzene. The Community Water Supply Survey reported finding that eleven samples out of 230 water supplies analyzed were positive for benzene; the average concentration ranged from 0.4 ug/l in phase 2, to 0.95 ug/l in phase 3 (Brass, 1981). Of the 100 ground water supplies examined, only one was found to contain benzene; the concentration was 0.6 ug/l (ibid).

Benzene can move into surface water from landfills or industrial disposal sites. Three hundred and seven community water supplies using ground water were included in the Community Water Supply Survey. Five of these communities were found to be providing water that contained benzene; the concentration ranged from < 0.5 - 44 ug/l. Since benzene is a major commodity chemical, the potential for exposure to benzene from accidental spills, landfill and industrial leachate remains high.

A review of benzene sampling data by Howard and Durkin (1974) found that only trace levels of benzene had been detected in a few fresh-water samples at that time. For example, a 1972 EPA study cited in the report (USEPA, 1972) identified 53 organic chemicals in the finished waters and organic waste effluents from 11 plants (of 60 sampled) discharging into the Mississippi River. Benzene was not detected in the effluents, but the trace detected in the finished waters suggested another source other than effluent discharge. Dowty et al. (1975) detected benzene in both the raw water (Mississippi River) and finished water at a New Orleans area water treatment plant. It should be noted that these authors also detected benzene and other organics in some commercially bottled artesian waters and deionized charcoal-filtered water. A sampling of five benzene production or consumption plants by Battelle Research Institute found benzene concentrations in water ranging from less than 1 to 179 ppb (plant effluent). The concentrations at 13 upstream and downstream sample locations in nearby receiving waters, however, ranged from less than 1 to 13 ppb, with an average of 4 ppb (Fentiman et al. 1979).

Benzene has been detected in various food categories: fruit, nuts, vegetables, dairy products, meat, fish, poultry, eggs and several beverages. The NCI reported that an individual

could ingest as much as 250 ug/day from these foods (NCI, 1977).

The respiratory route is the primary source of human exposure to benzene. Much of this exposure is to the general population by way of gasoline vapors and automotive emissions. American gasolines contain an average of < 1% (by volume) benzene, e.g. 0.8% (Runion, 1975). Benzene comprises approximately 2.15% (by volume) of the total hydrocarbon emissions from a gasoline engine (Schofield, 1974). Ambient air concentrations of benzene in the vicinity of European gas stations were found to range from 0.8 to 3.2 ppm for gasoline having contents of 3.7% (by volume) (Parkinson, 1971). Assuming U.S. gasolines to be 1% by volume, one would expect atmospheric concentrations ranging from 0.2 ppm to 0.9 ppm at U.S. gas stations. Production, chemical conversion and industrial user emissions constitute another major source of exposure. Lonneman et al. (1968) measured an average benzene concentration of 15 ppb in Los Angeles air, with a maximum of 57 ppb.

Indoor air concentrations of benzene also may represent a significant exposure source for specific segments of the population. Young et al. (1978) stated that consumers may be exposed unknowingly to benzene in the home in the form of paint strippers, carburetor cleaners, denatured alcohol, rubber cememt and art and craft supplies, as well as through use of gasoline as a cleaning solvent.

Smoking may be a very significant benzene exposure source for a portion of the population. Newsome et al. (1965) found that a 40 ml draw of cigarette smoke contained 6.1 ug of benzene. Assuming 15 draws per cigarette, one pack of 20 cigarettes smoked per day and a daily air intake of 20 m^3 (Diem, 1962), the equivalent annual average atmospheric exposure would be 92 ug/m^3 (28 ppb).

Pharmacokinetics

Benzene is absorbed readily through the lungs of humans and has an absorption rate of about 50% after five hours at a dose level of 340 mg/m^3 (Srobova et al. 1950, Teisinger et al. 1952). Inhalation at 166.4 mg/m^3 to 198.4 mg/m^3 for four hours resulted in 30% retention after three hours (Nomiyama and Nomiyama, 1974). Hunter and Blair (1972) reported that humans retained 230 mg after exposure to 80 to 100 mg/m^3 for 6 hours.

Retained benzene is distributed in tissues according to their fat content. Bone marrow, which, in toto, is an organ about two-thirds of the size of the liver, has a high tissue/blood partition co-efficient for benzene. Metabolites are believed to be important in the development of hematotoxicity, partly because of the effect of altered liver metabolism upon leuko-

penia and other hematopoietic responses. But little is known of the metabolite fate of benzene in the bone marrow (Snyder and Kocsis, 1975).

Whether administered by inhalation, orally, or by another route, benzene is eliminated rapidly by expiration and excretion in the urine. Parke and Williams (1953) administered ^{14}C-labeled benzene orally to rabbits (0.34-0.5 g/kg) and collected samples over three days. Benzene expired in air accounted for 43% of the dose; 34.5% was excreted in the urine as glucuronide or ethereal sulfate conjugates of metabolic oxidation products phenol, quinol, catechol and hydroxyquinol together with small amounts of other products; and 5% to 10% remained in the tissues. Benzene is metabolized similarly in humans (Laskin and Goldstein, 1977).

Health Effects

Short-term exposure to relatively high levels of benzene produces central nervous system effects. Such effects include dizziness, giddiness, exhilaration, nausea, vomiting, headache, drowsiness, staggering, loss of balance, narcosis, coma and death.

It has been known since the 19th century that long-term low-level exposure to benzene produces adverse hematological effects; Santesson (1897) described cases of aplastic anemia in workers fabricating bicycle tires. The original association of acute leukemia with benzene exposure was made in 1928 (Delore and Borgomano, 1928) and it has been postulated that benzene may be a cause of acute myeloblastic leukemia (Goldstein, 1981; OSHA, 1978b; NAS, 1980). Other hematological diseases also have been reported to be associated with benzene exposure (Goldstein, 1977).

Short-Term Exposure

Gerarde (1960) provides a table summarizing acute effects in which it is stated that 19,000-20,000 ppm for 5-10 minutes is a fatal benzene level; "7,500 ppm for 30 minutes is dangerous to life; 1,500 ppm for 60 minutes produces serious symptoms; 500 ppm for 60 minutes leads to symptoms of illness; 50-150 ppm for five hours produces headache, lassitude and weakness."

Mild central nervous system effects appear to be rapidly reversible following cessation of exposure. There is no evidence that they result in chronic brain damage. Also of importance is that these effects appear to be concentration-dependent. Lower levels of benzene do not seem to elicit these responses

no matter how long the exposure (at 480 mg/m^3) (Goldstein, 1977). Therefore, for acute (single dose or one day) exposures, a study that evaluates acute effects is required.

In animal studies, effects similar to those described for humans have been noted. Six rabbits exposed by inhalation to 112,000 to 144,000 mg/m^3 underwent anesthesia after 3.7 minutes and showed other effects in the central nervous system until death, which ensued after 22.5 to 71 minutes (Carpenter et al. 1944).

Kimura et al. (1971) studied acute oral toxicity in Sprague-Dawley rats. They used 6 to 12 rats of both sexes per group in testing newborn and 14-day old rats, and 6 male rats per group for the other older ages. Single dose LD_{50} values for 14-day old, young adult, and old adult rats were 3.0, 3.3 and 4.9 g/kg body weight, respectively. Withey and Hall (1975) performed an initial range finding study of ten male Sprague-Dawley rats (150-200 gm) using five dose levels: 2.00, 2.99, 4.47, 6.69 and 10.0 gm/kg. The benzene was administered via gavage. A separate study then was initiated on 20 male rats at each of five dose levels (3.00, 4.25, 6.00, 8.46 and 11.92 g/kg). The LD_{50} in both experiments was the same: 5.96 g/kg. Three of the dose levels used (2.00, 2.99 and 3.0) had no deaths.

Longer-Term Exposure

The toxicity of benzene to the hematopoietic system of humans experiencing chronic exposure to benzene is well documented. Reported effects include myelocytic anemia, thrombocytopenia, or leukopenia (occurring either separately or in cases of pancytopenia) and leukemia, particularly acute myelogenous and monocytic leukemia. In many of these studies, humans were exposed to benzene along with other solvents at relatively high concentrations. Data on the level and duration of exposure are inadequate for deriving dose-response relationships of chronic benzene toxicity (Vigliani and Forni, 1976). While it is impossible to determine a no-effect dose, it is highly probable that continuous exposure to benzene at low levels will result in the above noted effects. Infante et al. (1977) reported a retrospective cohort study of two populations of workers who were involved in production of rubber sheeting (Pliofilm). Benzene was the only material in their work environment that was known to be associated with blood disorders. In both plants during 1940-1949, the occupational exposure of 561 workers to benzene was apparently well within the maximum allowable concentration of 100 ppm that was usually recommended. Vital status to 1975, which was obtained for 75% of the workers, showed a significant excess of leukemia in those exposed to benzene, indicating a 10-fold increase in risk of death from

myeloid and monocytic leukemia.

The onset of leukemia is usually preceded by many observable effects on the hematopoietic system (Snyder and Kocsis, 1975). It is not known whether benzene causes leukemia as one aspect of its hematotoxic effects, whether the leukemia is a consequence of benzene-induced damage to immunological components of the bone marrow, or whether the leukemic effects are unrelated to the other hematopoietic manifestations (Laskin and Goldstein, 1977).

Benzene mixed with equal parts of olive oil was administered to rats by subcutaneous injection (Latta and Davies, 1941); Gerarde, 1956). Weight loss and leukopenia resulted from doses of 880 mg benzene/kg body weight, which were given daily for 14 days (Gerarde, 1956), and from doses of 1.32 g benzene/kg body weight, which were given daily for 3 to 60 days (Latta and Davies, 1941). In Latta and Davies' study, a rat that died after 10 days had hyperplastic bone marrow, and one that died at 21 days had acute leucopenia and hypoplastic bone marrow. Oral administration of benzene to rats in daily doses of 1, 10, 50 and 100 mg/kg body weight during 132 days over 6 months resulted in leucopenia and erythrocytopenia at the lowest minimal effect level of 10 mg/kg and above (Wolf et al. 1956).

Leucopenia is the most commonly observed effect of chronic benzene intoxication in laboratory animals. Deichmann et al. (1963) exposed 40 male and 40 female Sprague-Dawley rats by inhalation to six different levels of benzene for 5 hours to 7 hours per day, four days a week for six to 31 weeks. Tail blood was collected weekly or biweekly and analyzed for total peripheral white blood cell count, red blood cell count and benzene concentrations. All rats were examined for gross pathologic tissue changes and, in a few instances, the nucleated cell populations of femoral bone marrow were determined. The dose levels were 0, 50, 96, 103, 146, 156 and 2760 mg/m^3. The most significant and constant pathological changes were found in the lung (chronic bronchopneumonia) and spleen (hemosiderosis). The splenic hemosiderosis was more severe and occurred more frequently in females when compared to controls, but was not dose related. Leucopenia developed at 146 mg/m^3 and above. This effect was dose related and occurred with greater severity and at earlier times in females. In addition, there was some indication, also in females, that the circulating white blood cell count was depressed at 103 mg/m^3. However, at lower exposures, a fall in leukocyte causes cyclical fluctuations. Moreover, there is normally wide variation among cell counts during diurnal cycles and among individual animals.

Teratogenicity

Only one study of teratogenicity has been noted. In this study, Watanabe and Yoshida (1970) gave subcutaneous injections of acute toxic doses of benzene (2.62 mg/kg body weight) to pregnant mice on days 11 through 15 of gestation. Malformations were most prevalent in the group that was treated on the 13th day. Four of 15 litters, involving 10 of 127 fetuses, had cleft palate, agnathia, or micrognathia. Decreased white cell count and weight gain in the benzene-treated mice were the same whether the litters were normal or included malformed fetuses. As an indication of the toxicity of the dose used in this experiment, five male mice that received benzene at 2.62 mg/kg body weight survived, while four of five male mice that had been injected with 3.49 mg/kg died within 3 days. Therefore, teratogenicity occurs in mice exposed to benzene, though at doses very close to lethal.

Mutagenicity

Toxic effects on bone marrow cells of rats and other laboratory animals include changes in chromosome number and chromosome breakage that resemble those in humans. There is no clear evidence for dose-dependent response (Laskin and Goldstein, 1977). Lyon (1975) used the Ames assay with Salmonella typhimurium strains TA98 and TA100 to test benzene for mutagenicity in doses ranging from 0.1 to 1.0 ul/plate, both without and with microsomal fractions at concentrations from 1 to 50 ul/plate. Postmitochondrial supernatant suspensions of microsomes were prepared from liver homogenates from normal rats and from rats that had been treated with phenobarbital and 3-methylcholanthrene (MCA), and from the bone marrow of normal and MCA-treated rats. Benzene was uniformly negative in all of these assays and was also inactive in the dominant lethal assay in rats.

Carcinogenicity

Maltoni and Scarnato (1979) administered by gavage benzene dissolved in virgin olive oil to 13 week old Sprague-Dawley rats. The material was administered at doses of 50 and 250 mg/kg for 4-5 days a week for 52 weeks. The animals then were allowed to live until spontaneous death. Each high dose group consisted of 35 male and 35 female rats and controls and low dose groups were composed of 30 male and 30 female rats. After 20 weeks of exposure, Maltoni and Scarnato corrected the denominators (number of animals surviving) to reflect "nonexperimentally" caused deaths. The 250 mg/kg dose level group then consisted of 33 male and 32 female rats; the 50 mg/kg and olive oil control

group then consisted of 28 male and 30 female rats. The authors reported their results after 144 weeks. At the 250 mg/kg dose level, 25% (8/32) of the female rats and Zymbal gland tumors, 6.2% (2/32) had skin carcinomas, 21.9% (7/32) had mammary carcinomas, 3.1% (1/32) had leukemias. The male rats in the 250 mg/kg dose group had no Zymbal gland tumors, no skin carcinomas and no mammary gland tumors; however, they had 12.1% leukemias (4/33), one subcutaneous angiosarcoma (3.0%) and one hematoma (3.0%). In the rats remaining after the 20 week adjustments, the following carcinogenic effects were noted. At the 50 mg/kg dose level, only female rats had tumors which were Zymbal gland carcinoma, 6.7% (2/25) and mammary carcinoma, 13.3% (4/25). The control group had tumors only in female rats, which were: mammary carcinoma 10.0% (3/30), leukemias 3.3% (1/30). The authors concluded that benzene "appears to cause Zymbal gland carcinomas, at the two studied dose levels with a dose response relationship. Moreover, a dose correlated increase of hemato-lympho reticular neoplasias (leukemias) and mammary carcinomas has also been observed."

Ward et al. (1975) subcutaneously injected male C57BL/6N mice repeatedly with benzene dissolved in corn oil. Eighty benzene treated mice, while initially divided into four dose groups ranging from 0.5-2.0 mg/kg, were eventually combined and reported as a single experimental group. Three control groups were used with twenty male mice per group: a no treatment control, a corn oil only control, and a positive control using butylnitrosourea. The animals were injected twice weekly for 44 weeks, then once weekly until 54 weeks. At 104 weeks after the first injection, all surviving mice were sacrificed (108 weeks of age) and a complete necropsy was performed, as had been done with all the mice that died. The toxic lesions included a bone marrow depleted of hematopoietic cells and hepatonecrosis. A granulocytic leukemia was also noted. After reviewing the data from that study, the National Academy of Sciences Safe Drinking Water Committee concluded that the increase in pathology was not statistically significant, even when time to response was incorporated into the analysis (National Academy of Sciences, 1977).

EPA-SNARL Development

The Office previously released an emergency SNARL for kerosene and fuel oil #2 based, in part, on their benzene content. The present document supercedes all previous ODW benzene guidances. The Office of Drinking Water will, from time to time, as data and other relevant information become available, update these guidances to reflect the most recent scientific reports.

The available data suggest that the EPA-SNARL for benzene

should be based on the potential of this compound to produce hematopoietic damage. This decision is justified by the following factors:

1. The hematopoietic system appears to be the most sensitive indicator of benzene toxicity.

2. Benzene-induced leukopenia and fatal anemia develop in days; rabbits, guinea pigs, rats and mice sometimes develop anemia within 12-15 days (Hough and Freeman, 1944; Petrini, 1941; Wolf et al. 1956).

The ten-day and longer-term SNARL values calculated for benzene do not take into account the suggested carcinogenicity of benzene and are based on data from papers in which benzene toxicity was evaluated. In some of the studies, dose-response information is available, whereas, in others a single dose was chosen to produce a toxic effect. In the cases reported here, the effects were related to bone marrow toxicity. Where possible, studies were selected where benzene was administered orally.

One-Day EPA-SNARL

The EPA determined that there were insufficient data to compute a one-day SNARL. Similarly, the National Academy of Sciences (1981) stated that there are insufficient data to determine a one-day SNARL.

Ten-day SNARL

Calculation of the ten-day SNARL is based on the study of Deichman et al. (1963) who exposed rats to benzene four days a week by inhalation and monitored their hematology weekly. By the second week of treatment, there was definite hematological impairment at the 2659 mg/m^3 exposure concentration and some indication, especially in females, that white blood cells were depressed at the 103 mg/m^3 exposure concentration. No effect was seen, however, at 96 mg/m^3. The following equation was applied to provide a ten-day SNARL of 0.23 mg/l.

Step 1

$$\frac{(96\ mg/m^3)(6\ m^3)(0.5)(4)(10\ kg)}{(100)(1/day)\ x\ 7\ (70\ kg)} = 0.23\ mg/l$$

where: $(96\ mg/m^3)$ = 29 ppm exposure
$6\ m^3$ = volume of air inhaled over 6 hours exposure based upon equivalent lung/whole body ratios for adult humans and rats (Olson and Gehring, 1976)
0.5 = absorption factor
4/7 = conversion of total weekly dose to equivalent daily dose
$\frac{10}{70}$ = child/adult body weight ratio
1 l = liter of water consumed per day by 10 kg child
100 = safety factor

Longer-term SNARL

Longer-term SNARLs are not for lifetime exposures. These SNARLs apply only to contamination levels during interim periods of exposure.

A longer-term SNARL can be calculated using data from Wolf et al. (1956) who gavaged female rats at doses of 1, 10, 50 and 100 mg/kg over a 187 day period. No effects were seen at 1 mg/kg but a slight leucopenia was observed at 10 mg/kg given 132 times over the 187 days. The no-effect level would appear to lie between these values.

$$\frac{(1\ mg/kg)(10\ kg)(100\%)(5)}{(100)(7)} = 0.07\ mg/liter$$

where: 1 mg/kg = assumed no effect dose
10 kg = 10 kilogram child
100% = absorption factor
1 l = 1 liter of water consumed per day by 10 kg child
100 = safety factor
5/7 = factor to correct from 5 days/week to 7 days

The National Academy of Sciences derived its 10-day SNARL using the Wolf data. They chose the 50 mg/kg as the no effect dose, five times the 10 mg/kg dose which showed a slight leucopenia.

No chronic SNARL was calculated for benzene by the National Academy of Sciences because, in their opinion, benzene is a suspect human carcinogen.

Carcinogenic Risk Estimate

The National Academy of Sciences, in Drinking Water and Health,

Volume 3, 1980) states:

> There are no data from animal models for use in extrapolation. Occupational studies on human exposure (Aksoy et al. 1972, 1974 a, b, 1976; Ishimaru et al. 1971; Thorpe, 1974) do not contain adequate information on degree of exposure or size of population at risk. In addition, the workers in benzene-related occupations typically were exposed to other chemicals, as in the study reported by Ott et al. 1978. Consequently, extrapolation of benzene-induced cancer risk from such data as these would be tenuous.
>
> In a study by Infante et al. 1977, workers were exposed to benzene as the sole chemical suspected of affecting the hematopoietic system. In these cases, benzene concentrations apparently were high during the first years of exposure and were lower thereafter. There are no data indicating how often short exposures at elevated levels may have occurred. Estimates of actual exposure are inadequate for extrapolation for risk of benzene-induced leukemia.

The EPA's Carcinogen Assessment Group (CAG) has determined a carcinogenic risk estimate by using the following considerations.

> Three epidemiology studies of workers exposed to benzene vapors on their jobs, performed by Infante, Ott and Aksoy, were reviewed by the CAG for the Office of Air Quality Planning and Standards (USEPA, 1979). Their result was that the potency for humans breathing benzene continuously is B = 0.02407. This means that the lifetime risk of getting leukemia, R, equals 0.024074 times the lifetime average continuous exposure, X, measured as ppm of benzene by volume in air, or R = BX. Therefore, the air concentration, X, resulting in a risk of 10^{-5} is X = R/B = $10^{-5}/0.024074$ = 4.1539×10^{-4} ppm.
>
> Since the air concentration corresponding to 1 ppm of benzene is 3.25 mg/m^3 and assuming a respiratory rate of 20 m^3/day and a respiratory absorption coefficient of 0.50, the daily intake that would result in a risk of 10^{-5} is:
>
> 4.154×10^{-4} ppm x 3.25×10^3 ug/m^3 per ppm x 20 m^3/day x 0.5 = 13.5 ug/day

If it is assumed that the fraction of benzene absorbed is the same between inhalation and ingestion of water and fish, a daily benzene intake of 13.5 ug through drinking water would cause a leukemia risk of 10-5. The water concentration given

this intake is:

$$C = (13.5 \text{ ug/day})/(2)$$

$$= 6.75 \text{ ug/l}$$

$$= 6.8 \text{ ug/l}$$

Exposure Assumptions (per day)	Risk Levels	Corresponding Criteria
2 liters of drinking water	10^{-7}	0.068
	10^{-6}	0.68
	10^{-5}	6.8

Analysis

Benzene and other related aromatic compounds can be analyzed by a purge-and-trap gas chromatographic procedure developed by EPA's Environmental Monitoring and Support Laboratory (USEPA, 1980b). Volatile compounds are transferred from aqueous solution to the gas phase by an inert gas which is bubbled through the aqueous sample. The compounds are swept from the purging device and are trapped in a short column containing a sorbent material. The trapped components are then thermally desorbed and backflushed onto the head of a gas chromatographic column where they are separated under programmed temperature conditions.

The following specifications are recommended for benzene analysis:

Primary Column: Six feet long x 0.082 inch ID#304 stainless steel or glass tubing. Packed with 5% SP-1200 + 1.75 Bentone 34 on 100/120 mesh Supelcoport.

Temperature: 50° isothermal for 2 minutes, then program at 6°/minute to 90° C.

Carrier gas: Helium at a flow rate of 30 ml/minute.

Detector: A high temperature photoionization detection equipped with a 10.2 eV lamp. The unit is operated with an electrometer/lamp power supply. The electrometer must be capable of stable, noise-free operation at 1×10^{-12} amps with a full scale response time of 1 second.

Sample size: 5 ml.

Confirmatory analysis by GC-MS or a secondary chromatographic column is recommended. With the recommended primary column the

retention time for benzene is 199 seconds and the lower limit of detection is 0.02 ug/l.

Treatment

(Forthcoming from STB)

Conclusions and Recommendations

Benzene at high levels is extremely toxic to the central nervous system. Its toxicity at lower levels is the result of bone marrow effects which may result in pancytopenia with fatal outcomes. As stated above, the recommended guidance levels for benzene are:

Ten-Day - 0.23 mg/l
Longer-term - 0.07 mg/l

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