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HEXACHLOROBENZENE

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

I. INTRODUCTION

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

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

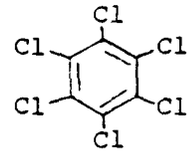
Health Advisories are developed for One-day, Ten-day, Longer-term (approximately 7 years, or 10% of an individual's lifetime) and Lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from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

This Health Advisory (HA) is based on information presented in the Office of Drinking Water's Health Effects Criteria Document (CD) for hexachlorobenzene (U.S. EPA, 1985a). The HA and CD formats are similar for easy reference. Individuals desiring further information on the toxicological data base or rationale for risk characterization should consult the CD. The CD is available for review at each EPA Regional Office of Drinking Water counterpart (e.g., Water Supply Branch or Drinking Water Branch), or for a fee from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Rd., Springfield, VA 22161, PB # 86-117777/AS. The toll-free number is (800) 336-4700; in the Washington, D.C. area: (703) 487-4650.

II. GENERAL INFORMATION AND PROPERTIES

CAS No. 118-74-1

Structural formula



Synonyms

- HCB, HEXA C.B., Perchlorobenzene

Uses

- Hexachlorobenzene is not manufactured as a commercial product in the United States, but an estimated 2-5 million pounds were produced each year during the synthesis of several chlorinated chemicals as of 1979 (Mumma and Lawless, 1975). Hexachlorobenzene also is an ingredient of a fungicide of which 200,000 pounds were imported each year as of 1979 (IARC, 1979).

Properties (U.S. EPA, 1985a)

Chemical Formula	C_6Cl_6
Molecular Weight	284.79
Boiling Point	322.9°C
Melting Point	230°C
Density	1.57 g/mL at 23°C
Vapor Pressure (mm Hg)	1 at 144.4°C
	1.68×10^{-5} at 25°C
	1.089×10^{-5} at 20°C
Water Solubility	0.005 mg/L at 25°C
Henry's Law Constant	0.12 atm m^3 mol^{-1}
Odor Threshold	Not available
Taste Threshold	Not available
Conversion Factor	--

Occurrence

- Hexachlorobenzene (HCB) is a synthetic organic compound with no natural sources. HCB is no longer directly produced but occurs as a byproduct during the manufacture of other chlorinated compounds. HCB has been used as a fungicide, but this use has been discontinued. HCB can occur as a contaminant in a number of chemically similar compounds, which are used as pesticides (U.S. EPA, 1984a).

- Because HCB has an extremely low solublity in water, releases to the environment rapidly partition to soil. HCB is resistant to hydrolysis and biodegradation and has a reported half life in soil of approximately 3-6 years. HCB has been demonstrated to bioaccumulate in fresh water fish (Lu and Metcalf, 1975).

- HCB has been included in one Federal Survey of drinking water supplies. HCB was analyzed for in 104 surface water and 12 ground water supplies. No supply contained HCB above the detection limit of 0.1 ug/L. HCB has been detected at levels of 0.005 ug/L in two drinking water supplies in the midwest. HCB has been reported to occur in some surface water samples at less than ug/L levels (U.S. EPA, 1984a).

- HCB has been reported to occur in some foods at the ppb level. Due to HCB's physical properties, diet is probably the major route of exposure (U.S. EPA, 1984a).

III. PHARMACOKINETICS

Absorption

- Absorption of HCB from the gut has been studied in detail; however, no information has been found in the available literature on HCB absorption through the lungs or skin (U.S. EPA, 1985a).

- Absorption of HCB from the intestinal tract appears to depend on the solvent vehicle used during test material administration. When HCB is administered in olive oil, approximately 80% of the dose is absorbed; when it is administered in an aqueous suspension, in 1% methyl cellulose, or in a solid crystalline form, relatively little (<20%) is absorbed (U.S. EPA, 1985a).

- Intestinal absorption of HCB occurs primarily through lymphatic channels with only a minor portion being absorbed into the portal circulation (U.S. EPA, 1985a).

Distribution

- Following intestinal absorption, HCB, which is lipophilic, distributes to tissues that are rich in lipid content (U.S. EPA, 1985a). The adipose tissue accumulates the greatest concentrations of HCB in all species studied, although bone marrow and skin, which contain large amounts of lipids, also accumulate HCB. The adrenal cortex accumulates

HCB at concentrations approaching those of fat. Other tissues (e.g., liver, kidneys, lungs, heart, spleen and blood) generally contain lower amounts of HCB.

° Intravenous injection of HCB results in a tissue distribution similar to the following oral administration (U.S. EPA, 1985a).

° Hexachlorobenzene is transported via the placenta and is distributed in fetal tissue (U.S. EPA, 1985a).

Metabolism

° The metabolism of HCB has been studied in male and female rats following oral administration, in Rhesus monkeys and beagles following intravenous injection and in rabbits following intraperitoneal injection (Renner, 1981).

° Hexachlorobenzene is metabolized slowly into other lower chlorinated benzenes, chlorinated phenols and other minor metabolites, and forms glucuronide and glutathione conjugates (Renner, 1981).

° Tissues were found to contain mainly unchanged HCB together with small amounts of metabolites (Renner, 1981).

° Only small amounts of HCB metabolites were detected in feces. Most of the HCB metabolites were excreted in the urine together with small amounts of unchanged HCB (U.S. EPA, 1985a).

Excretion

° The excretion of HCB from treated animals is slow and occurs mainly as the parent compound through the feces, with relatively little being excreted in the urine. It is characterized by an initial rapid phase followed by a very slow phase. This slow phase of excretion can be enhanced by the administration of mineral oil, paraffin and n-hexadecane (U.S. EPA, 1985a).

° Both biliary and intestinal excretion contribute to fecal excretion (U.S. EPA, 1985a).

° A three-compartment mammalian model has been reported for the behavior of HCB in beagles and Rhesus monkeys following intravenous injection of a single dose. Radioactivity was not detected in exhaled air following intraperitoneal injection of ^{14}C-HCB. Hexachlorobenzene has been detected in the milk of nursing mammals (U.S. EPA, 1985a).

IV. HEALTH EFFECTS

Humans

° The exposure of humans to seed wheat contaminated with HCB in Turkey from 1955-1959 caused an epidemic of HCB-induced PCT, also known as

porphyria turcica, which is manifested by disturbed porphyrin metabolism, cutaneous lesions and hyperpigmentation. Two investigators (Cam and Nigogosyan, 1963) estimated that 0.05 to 0.2 g/day were ingested. In children under 1 year of age, pink sores were observed as well as 95% mortality (U.S. EPA, 1985a).

- Follow-up studies conducted with patients 20 to 25 years after the onset of porphyria showed that a few patients (10%) still had active porphyria, whereas >50% exhibited hyperpigmentation (78%) and scarring (83%) as well as other dermatologic, neurologic and skeletal features of HCB toxicity. Enlarged thyroids were diagnosed in 60% of the female patients. Hexachlorobenzene residues also were found in the blood, fat or breast milk of some patients (U.S. EPA, 1985a).

Animals

Short-term Exposure

- Information on the acute toxicity of HCB is limited to oral LD_{50} values determined with a few mammalian species. The following LD_{50} values were reported in the available literature: rats, 3,500-10,000 mg/kg; rabbits, 2,600 mg/kg; cats, 1,700 mg/kg; and mice, 4,000 mg/kg (NAS, 1977; IARC, 1979; Sax, 1979).

Long-term Exposure

- Subchronic oral toxicity studies with a number of mammalian species indicated statistically significant increases in liver and kidney (rats only) weights in hexachlorobenzene-treated animals. Some studies have shown increases in the weights of other organs as well. Chronic oral toxicity studies revealed similar effects to those seen in the subchronic studies plus HCB-associated mortality and various hepatic and renal lesions. These subchronic and chronic effects were usually dose-related with effect levels as low as 2 mg/kg/day in subchronic studies and 0.29 to 0.4 mg/kg/day in chronic studies. Other effects included multiple alopecia and scabbing, together with neurologic effects in rats, mice and dogs (U.S. EPA, 1985a).

- Dose-related histopathologic changes in the ovaries of monkeys given 8 to 128 mg/kg/day by gavage for 60 days also have been reported (U.S. EPA, 1985a).

- The livers of HCB-exposed animals have shown histologic changes such as irregular shaped and moderately enlarged liver mitochondria and increases in the size of the centrilobular hepatocytes (U.S. EPA, 1985a).

- Increased porphyrin levels in the liver and in urine have been reported for all species studied except the dog. Hexachlorobenzene was found to cause the accumulation of δ-H-steroids which induce porphyrin biosynthesis and to inhibit uroporphyrinogen decarboxylases (U.S. EPA, 1985a).

- The inhibition of uroporphyrinogen decarboxylases appears to be due to pentachlorophenol, a HCB metabolite (U.S. EPA, 1985a).

- Indications are that females are more susceptible to HCB-induced porphyria than are males, which may be related to higher estrogen levels and greater HCB metabolism in females (U.S. EPA, 1985a).

- Hexachlorobenzene was reported to produce a mixed-type induction of cytochromes resembling that produced by a combination of phenobarbital (P-450) and 3,4-benzpyrene (P-448). In addition, the activities of several hepatic microsomal enzymes were found to be induced by HCB (U.S. EPA, 1985a).

Reproductive Effects

- Hexachlorobenzene has been shown to cross the placenta into fetal tissues and to be present in the milk of nursing dams (U.S. EPA, 1985a).

- The NOAEL in a four-generation reproduction study with rats was reported to be 20 ppm of HCB in the diet (Grant et al., 1977). Pups from treated dams receiving diets containing 80 ppm HCB recovered from elevated liver weights when nursed by untested foster dams (Mendoza et al., 1978).

- Hepatomegaly and reduced survival were reported in kittens from cats receiving 263 ppm of HCB in their diets (8.7 mg/day/cat (Hansen et al., 1979).

- Three infant Rhesus monkeys nursed by mothers given HCB by gavage at 64 mg/kg/day for 60 days developed clinical signs of toxicity, and 2 infants which died while nursing had severely congested lungs or bilateral hemorrhagic pneumonia (Bailey et al., 1980).

- Feeding female minks with dietary HCB at doses as low as 1 ppm during gestation and lactation resulted in increased mortality of kits (Rush et al., 1983).

Developmental Effects

- Fetal mice from dams treated with 100 mg HCB/kg/day by gavage during days 7 through 16 of gestation exhibited teratogenic responses, e.g., cleft palate, and decreased fetal weight. Maternal liver:body weights were also increased (Courtney et al., 1976).

- Hexachlorobenzene was not teratogenic in Wistar rats with gavage doses of 10, 20, 40, 60, 80 or 120 mg HCB/kg/day in corn oil or 0.25% aqueous gum tragacanth given during gestation days 6-21. Maternal toxicity (body weight loss, central nervous system effects) and reduced fetal body weight occurred at the two highest doses (Khera, 1974).

Mutagenicity

- Hexachlorobenzene was not found to be mutagenic in 5 strains of S. typhimurium, with or without metabolic activation (Lawlor et al., 1979).

- Hexachlorobenzene was mutagenic in the yeast, S. cerevisiae, at a minimum concentration of 100 ppm (Guerzoni et al., 1976).

- Hexachlorobenzene was negative in dominant lethal mutation studies with rats (Khera, 1974; Simon et al., 1979).

Carcinogenicity

- In a lifetime study with HCB administration to hamsters, hepatoma was induced in both males and females (Cabral et al., 1977). The response at a dose of 4 to 5 mg/kg/day dissolved in corn oil and mixed in the feed was 47% for both sexes; controls had no hepatomas. In addition to hepatomas, hamsters responded to HCB treatment with malignant liver haemangioendotheliomas and thyroid adenomas. The incidence of haemangioendotheliomas was 20% in males (versus 0% in controls) at 8 mg/kg/day and 12% in females (versus 0% in controls) at 16 mg/kg/day. Thyroid adenomas occurred at 14% incidence in males treated with 16 mg/kg HCB (versus 0% in controls).

- Liver cell tumors, described as hepatomas, also were produced in both sexes of Swiss mice (Cabral et al., 1979). At 24 mg/kg/day, the incidence was 34% for females and 16% for males, and the response showed a dose-dependency not only in the number of tumor-bearing animals but also in the latent period, and multiplicity and size of tumors. In ICR mice, HCB administered concurrently with polychlorinated terphenyl induced hepatocellular carcinomas (Shirai et al., 1978).

- In rats, the target organs for HCB-induced tumors in various studies included the liver, kidney, adrenal gland and parathyroid gland. Liver tumors were found in three studies which included three different strains of rat: Agus, Wistar and Sprague-Dawley. These tumors were induced with doses between 1.5 and 8 mg/kg/day. The incidence was as high as 100% in Agus rats but lower for the other strains. Renal cell tumors were found in one study on Sprague-Dawley rats. In two studies with Sprague-Dawley rats, significant increases in adrenal pheochromocytoma in females were found. In one of these studies the incidence of parathyroid tumors in males was increased significantly as well (Smith and Cabral, 1980; Lambrecht, et al., 1983a, 1983b; Arnold, 1983, 1984; Arnold et al., 1985).

- Lambrecht et al. (1983a, 1983b) fed male and female Sprague-Dawley rats HCB in the diet for up to two years at estimated doses of 4-5 mg/kg/day and 8-9.5 mg/kg/day. By 48 weeks, females had gross liver tumors. Significant increases in tumor incidence included hepatoma in both sexes at both doses, hepatocellular carcinomas in females at both doses, renal cell adenomas in females at both doses, and adrenal pheochromocytoma in females at both doses. Hepatocellular carcinoma was slightly higher in males at both doses.

° The data on HCB provide sufficient evidence of the carcinogenicity of HCB since there were increased incidences of malignant tumors of the liver in two species (haemangioendothelioma in hamsters and hepatocellular carcinoma in rats) as well as reports of hepatoma in mice, rats and hamsters.

V. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

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

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

where:

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

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

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

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

The following Health Advisories, which are based on toxicological effects, are above the solubility of hexachlorobenzene in water (0.005 mg/L at 25°C).

One-day and Ten-day Health Advisories

Available evidence for the acute toxicity of hexachlorobenzene is considered to be insufficient for calculation of One-day and Ten-day Health Advisory (HAs). Therefore, the Longer-term HA (0.05 mg/L) for a 10-kg child is proposed as a conservative estimate for One-day and Ten-day HAs for the 10-kg child.

Longer-term Health Advisory

In the Kuiper-Goodman et al. (1977) study, groups of 70 male and 70 female Charles River (COBS) rats were fed diets with hexachlorobenzene at 0.5, 2.0, 8.0 or 32.0 mg/kg bw/day dissolved in corn oil for as long as 15 weeks. Female rats were found to be more susceptible to hexachlorobenzene, as indicated by all parameters studied, and an "apparent" NOAEL of 0.5 mg/kg/day was concluded by the authors. Increased liver porphyrin levels in females and increases in the size of centrilobular hepatocytes along with the depletion of hepatocellular marker enzymes were noted with higher doses.

Using the NOAEL of 0.5 mg/kg bw/day reported by Kuiper-Goodman et al. (1977), the Longer-term HA for a 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(0.5 \text{ mg/kg/day})\ (10 \text{ kg})}{(100)\ (1 \text{ L/day})} = 0.050 \text{ mg/L (50 ug/L)}$$

where:

0.5 mg/kg/day = NOAEL based on absence of liver effects.

10 kg = assumed body weight of a child.

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

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

For a 70 kg-adult:

$$\text{Longer-term HA} = \frac{(0.5 \text{ mg/kg/day})\ (70 \text{ kg})}{(100)\ (2 \text{ L/day})} = 0.175 \text{ mg/L (175 ug/L)}$$

where:

0.5 mg/kg/day = NOAEL based on absence of liver effects.

70 kg = assumed body weight of an adult.

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

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

Lifetime Health Advisory

The Lifetime HA represents that portion of an individual's total exposure that is attributed to drinking water and is considered protective of noncarcinogenic adverse health effects over a lifetime exposure. The Lifetime HA is derived in a three step process. Step 1 determines the Reference Dose (RfD), formerly called the Acceptable Daily Intake (ADI). The RfD is an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, and is derived from the NOAEL (or LOAEL), identified from a chronic (or subchronic) study, divided by an uncertainty factor(s). From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined (Step 2). A DWEL is a medium-specific (i.e., drinking water) lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived from the multiplication of the RfD by the assumed body weight of an adult and divided by the assumed daily water consumption of an adult. The Lifetime HA is determined in Step 3 by factoring in other sources of exposure, the relative source contribution (RSC). The RSC from drinking water is based on actual exposure data or, if data are not available, a value of 20% is assumed for synthetic organic chemicals and a value of 10%

is assumed for inorganic chemicals. If the contaminant is classified as a Group A or B carcinogen, according to the Agency's classification scheme of carcinogenic potential (U.S. EPA, 1986), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

The derivation of the DWEL is based on a 130-week study by Arnold et al. (1985). This study involved feeding male and female Sprague-Dawley rats (the F_0 generation) diets containing 0, 0.32, 1.6, 8.0 or 40 ppm of hexachlorobenzene (analytical grade) for 90 days before mating and until 32 days after parturition (at weaning).

The number of offspring (F_1 generation) from these matings was reduced to 50 males and 50 females per dose group at 28 days of age and fed their respective parents' diets. Thus, the F_1 animals were exposed to hexachlorobenzene and metabolites in utero, from maternal nursing and from their diets for the remainder of their lifetime (130 weeks). No hexachlorobenzene-induced effects were reported in the 0.32 ppm hexachlorobenzene F_1 group, indicating this level is a NOAEL. Although a significant ($p<0.05$) increase in the incidence of periportal glycogen depletion was found in F_1 male rats fed 1.6 ppm hexachlorobenzene, the 1.6 ppm level of hexachlorobenzene also is concluded to be a NOAEL in that this result was not evident in other treated groups of male rats. The 8.0 ppm hexachlorobenzene F_1 groups were reported to have an increase ($p<0.05$) in the incidence of hepatic centrilobular basophilic chromogenesis. The 40 ppm hexachlorobenzene F_1 groups were reported to have increases ($p<0.05$) in pup mortality, hepatic centrilobular basophilic chromogenesis, peribiliary lymphocytosis and fibrosis, severe chronic nephrosis in males, adrenal pheochromocytomas in females and parathyroid tumors in males. It is difficult to estimate lifetime doses on a mg/kg bw basis in this study because of the initial exposure of the animals to hexachlorobenzene and its metabolites in utero and during lactation. However, in an attempt to estimate the lifetime hexachlorobenzene doses on a mg/kg bw basis, the 1.6 mg/kg hexachlorobenzene dietary level, interpreted from this study as the highest NOAEL level, was converted to a daily intake dose of 0.08 mg/kg bw/day by averaging the dosage data provided by Arnold (1984).

Using this NOAEL, the DWEL is derived as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(0.08 \text{ mg/kg/day})\ (1{,}000 \text{ ug/mg})}{(100)} = 0.8 \text{ ug/kg/day}$$

where:

0.08 mg/kg/day = NOAEL.

1,000 ug/mg = Conversion of NOAEL in mg to ug.

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

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

$$DWEL = \frac{(0.8 \text{ ug/kg/day})\ (70 \text{ kg})}{(2 \text{ L/day})} = 28 \text{ ug/L}$$

where:

0.8 ug/kg/day = RfD.

70 kg = assumed body weight of an adult.

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

Hexachlorobenzene may be classified as Group B: probable human carcinogen. The estimated excess cancer risk associated with lifetime exposure to drinking water containing hexachlorobenzene at 28 ug/L is approximately 1×10^{-3}. This estimate represents the upper 95% confidence limit from extrapolations prepared by EPA's Carcinogen Assessment Group using the linearized, multistage model. The actual risk is unlikely to exceed this value, but there is considerable uncertainty as to the accuracy of risks calculated by this methodology.

Evaluation of Carcinogenic Potential

- Data on hepatocellular carcinomas in female rats after oral ingestion from the study by Lambrecht et al. (1983) have been used by the U.S. EPA Carcinogenic Assessment Group to estimate the carcinogenic potency of hexachlorobenzene and the risks associated with one unit of the compound in drinking water (U.S. EPA, 1984b). This particular data set was selected because it is a malignant tumor in the primary target organ and results in the highest potency estimate. The 95% upper bound cancer risks associated with 1 ug/L of hexachlorobenzene in drinking water is estimated to be 4.9×10^{-5}. Accordingly, upper bound cancer risks of 10^{-6}, 10^{-5} and 10^{-4} would be associated with 0.02, 0.2 and 2 ug/L, respectively, of hexachlorobenzene in drinking water.

- Maximum likelihood estimates as well as 95% upper limits of cancer risks by the multistage model have been calculated (U.S. EPA, 1984b, 1985a). For example, at 0.01 mg/kg/day or 0.35 mg/L cancer risk estimates are 1.4×10^{-2} (MLE) and 1.7×10^{-2} (UL) and at 0.1 mg/kg/day cancer risk estimates are 1.3×10^{-1} (MLE) and 1.7×10^{-1} (UL).

- The EPA's Carcinogen Assessment Group has estimated cancer risks with other models besides the multistage (U.S. EPA, 1984b, 1985a). As an example, 0.1 mg/kg/day lifetime exposure was associated with additional risks (95% upper confidence limit) of 1.7×10^{-1} by the multistage and one-hit, 1.3×10^{-1} by the probit, and 2.9×10^{-1} by the Weibull. While recognized as statistically alternative approaches, the range of risks described by using any of these modeling approaches has little biological significance unless data can be used to support the selection of one model over another. In the interest of consistency of approach and in providing an upper bound on the potential cancer risk, the EPA has recommended use of the linearized multistage approach.

- In the absence of evidence of human carcinogenicity, hexachlorobenzene would be classed in IARC category 2B, meaning that it has been demonstrated to be carcinogenic in animals and is probably carcinogenic in humans.

- Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986), hexachlorobenzene may be classified in Group B2: Probable human carcinogen. This category is for agents for which there is inadequate evidence from human studies and sufficient evidence from animal studies.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- The U.S. EPA (1980) has set ambient water quality criteria for hexachlorobenzene of 7.2, 0.72, and 0.072 ug/L corresponding to cancer risks of 10^{-5}, 10^{-6}, and 10^{-7}, respectively, assuming 70 kg humans daily consume 2 L of water and 6.5 g of fish and shellfish.

- The National Academy of Sciences (1983) estimated a cancer risk of 1.85×10^{-6}, with lifetime consumption of 1 L of water containing 1 ug of hexachlorobenzene, based on the carcinogenicity study in mice by Cabral et al. (1979). In 1980, the NAS also calculated a 7-day SNARL (suggested-no-adverse-response-level) of 0.03 mg/L.

- The WHO (1984) guideline value for hexachlorobenzene is 0.01 ug/L.

VII. ANALYTICAL METHODS

- Determination of hexachlorobenzene is by a liquid-liquid extraction gas chromatographic procedure (U.S. EPA, 1978; Standard Methods, 1985). Specifically, the procedure involves the use of 15% methylene chloride in hexane for sample extraction, followed by drying with anhydrous sodium sulfate, concentration of the extract and identification by gas chromatography. Detection and measurement is accomplished by electron capture, microcoulometric or electrolytic conductivity gas chromatography. Identification may be corroborated through the use of two unlike columns or by gas chromatography-mass spectroscopy (GC-MS). The method sensitivity is 0.001 to 0.010 ug/L for single component pesticides and 0.050 to 1.0 ug/L for multiple component pesticides when analyzing a 1-liter sample with the electron capture detector.

VIII. TREATMENT TECHNOLOGIES

- Treatment technologies for the removal of hexachlorobenzene (HCB) from water have not been evaluated extensively. An evaluation of some of the physical and/or chemical properties of hexachlorobenzene indicates that carbon adsorption is a candidate for further investigation. Individual or combinations of technologies selected to attempt hexachlorobenzene removal must be based on a case-by-case technical evaluation, and an assessment of the economics involved.

- Based on its Freundlich constants (K = 450; 1/n = 0.6) hexachlorobenzene is a viable candidate for removal from water by activated carbon adsorption (U.S. EPA, 1985b). There are, however, limited available data to substantiate this. Home water treatment units of the line bypass faucet and pour-through type were tested by Gulf South Research Institute to determine their effectiveness in removing hexachlorobenzene from water. Six of ten units tested had initial efficiencies of 99%; however, by the end of the test the effectiveness of some units had fallen to as low as 45% (U.S. EPA, 1985b).

- Hexachlorobenzene has a Henry's Law Constant of 2.06 atm at 20°C (U.S. EPA, 1985b). This indicates that air stripping would not be effective in removing HCB from solution.

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