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ORTHO-, META-, AND PARA-DICHLOROBENZENES

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.

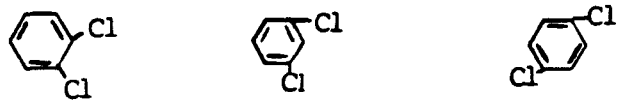
Health Advisories are developed for One-day, Ten-day, Longer-term (approximately 7 years, or 10% of an individual's lifetime) and Lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from 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 ortho-, meta-, and para-dichlorobenzenes (U.S. EPA, 1987). 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 #86-117918/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.	o-DCB	m-DCB	p-DCB
	95-50-1	541-73-1	106-46-7

Structural Formula



Synonyms

- o-DCB, m-DCB, p-DCB; 1,2-dichlorobenzene, 1,3-dichlorobenzene, 1,4-dichlorobenzene.

Uses (U.S. EPA, 1987)

- o-DCB: Solvent, chemical intermediate, deodorizer
  p-DCB: Deodorizer, insecticide
  m-DCB: None documented

Properties (U.S. EPA, 1987; 1985a)

o-DCB

Molecular Formula	$C_6H_4Cl_2$
Molecular Weight	147.01
Physical State	Colorless liquid
Boiling Point	179°C
Melting Point	-17.6°C
Density	1.3 g/mL at 20°C
Vapor Pressure	1.56 mm Hg at 25°C
Water Solubility	145 mg/L
Log Olive Oil/Water Partition Coefficient	3.65
Odor Threshold (water)	0.01-0.03 mg/L
Taste Threshold	--
Conversion Factor (air)	1 ppm = 6.01 mg/L

m-DCB

Molecular Formula	$C_6H_4Cl_2$
Molecular Weight	147.01
Physical State	Colorless liquid
Boiling Point	172°C
Melting Point	-24.2°C
Density	1.29 g/mL at 20°C
Vapor Pressure	5 mm Hg at 39°C
Water Solubility	1.23 mg/L
Log Olive Oil/Water Partition Coefficient	3.69
Odor Threshold (water)	0.01-0.03 mg/L
Taste Threshold	--
Conversion Factor	--

p-DCB

Molecular Formula	$C_6H_4Cl_2$
Molecular Weight	147.01
Physical State	Colorless crystals
Boiling Point	174°C
Melting Point	53°C
Density	1.46 g/mL at 20°C
Vapor Pressure	0.4 mm Hg at 25°C
Log Olive Oil/Water Partition Coefficient	3.65
Water Solubility	79 mg/L
Odor Threshold (water)	0.01-0.03 mg/L
Taste Threshold	--
Conversion Factor (air)	1 ppm = 6.01 mg/m^3

Occurrence

- There are no natural sources for the three isomers of dichlorobenzene (DCB).

- Production of the DCB isomers in 1981 was 11 million lbs for the ortho isomer and 15 million for the para isomer. Production of the meta isomer was not reported and is believed to be small.

- Releases of the ortho and meta isomers to the environment are believed to be small. The majority of the para isomer produced is released to the environment during its use as a deodorant and moth repellent. Dichlorobenzenes, while they have a low vapor pressure, are released to the environment largely by evaporation. Dichlorobenzenes in air are expected to degrade within a few days or weeks. Dichlorobenzenes released to surface waters would tend to be removed either by volatilization or adsorption onto soil and sediments. Dichlorobenzenes are biodegraded poorly in the environment. When released to the ground the compounds are expected to bind to soil and only slowly migrate to ground water. Dichlorobenzenes have been reported to bioaccumulate in fish, aquatic invertebrates and algae.

- The DCBs rarely occur as environmental contaminants (U.S. EPA, 1983). Based upon Federal surveys of drinking water, it is estimated that the ortho and para isomers occur at detectable levels in approximately 0.2 and 1.1 percent of all ground water supplies and 0.3 and 0.1 of all surface water supplies, respectively. No levels have been detected greater than 5 ug/L. Federal surveys of drinking waters have not reported finding the meta isomer. No information on the occurrence of DCB in food has been identified. Dichlorobenzenes have been identified as contaminants of air at very low levels (< 40 ppt) in urban and suburban areas. There are insufficient data on the DCBs to identify the major route of environmental exposure.

III. PHARMACOKINETICS

Absorption

- No studies have been reported which determine the percentage of a dose of DCB absorbed following oral or inhalation exposure. However, it will be assumed that 100% of an oral dose of any of the isomers of DCB is absorbed and that 60% of an inhalation dose is absorbed when exposure persists for longer than one to three hours (Astrand, 1975; Dallas et al., 1983).

Distribution

- The ortho- and para- isomers are lipophilic and can be expected to bioaccumulate to some extent, particularly in tissues with high fat content, during prolonged, continuous exposures. Para-DCB has been detected in human adipose tissue and all three isomers have been detected in blood (Dowty et al., 1975; Morita et al., 1975; Morita and Ohi, 1975).

Metabolism

- After oral administration to rabbits, the DCBs are oxidized principally to phenols. Ortho- and meta-DCB also form catechols (Azouz et al., 1955; Williams, 1959). Although small amounts of the metabolites are excreted as free phenols or catechols, the overwhelming percentage are eliminated as conjugates of glucuronic or sulfuric acids. Ortho- and meta-DCB form mercapturic acids as well, but p-DCB does not (Williams, 1959). The conjugated dichlorophenols appear to be the principal metabolic products of the DCB isomers in humans (Hallowell, 1959; Pagnatto and Walkley, 1965).

Excretion

- Hawkins et al. (1980) found that, after exposure of female CFY rats to ^{14}C p-DCB, more than 90% of the ^{14}C was eliminated in urine within five days post-treatment, with the remainder in feces and expired air. During the first two days following treatment, 50 to 60% of the ^{14}C was excreted in bile, thus indicating reabsorption in the enterohepatic circulation.

IV. HEALTH EFFECTS

Humans

- Cases have been reported in which individuals suffered moderate to severe anemia following exposure to DCBs (concentrations not estimated) (U.S. EPA, 1987). Several instances of skin lesions (e.g., pigmentation and allergic dermatitis) developing after contact also have been reported. Exposure levels were not estimated in these reports.

- In other reported cases, patients complained of vomiting, headaches, irritation of the eyes and upper respiratory tract and profuse rhinitis and periorbital swelling (U.S. EPA, 1987). Anorexia, nausea, vomiting, weight loss, yellow atrophy of the liver and blood dyscrasias also were reported for higher exposure concentrations. Liver damage was sometimes accompanied by porphyria (Hallowell, 1959). Exposure levels were not estimated in these reports.

- Zapata-Gayon (1982) reported headache, dizziness, nausea, and chromosomal breaks in blood samples from men and women exposed to o-DCB (exposures not given) 8 hours per day for 4 days with reduced chromosomal breaks by 6 months after exposure.

Animals

Short-term Exposure

- The DCBs produce sedation and anesthesia in animals after acute oral or parenteral administration (U.S. EPA, 1987). Relatively high doses are needed to produce acute effects. Acute poisoning is characterized by signs of disturbance of the central nervous system including hyperexcitability, restlessness and muscle spasms or tremors. The most frequent cause of death is respiratory depression. Acute and subchronic exposures also may result in kidney and/or liver damage. Liver alterations may be manifested as necrosis/degeneration, perhaps coincident with porphyria.

- Fourteen-day repeated dose gavage studies in mice (30 to 4,000 mg/kg) and rats (60 to 1,000 mg/kg) were conducted with both o- and p-DCB in the prechronic testing phase of the National Toxicology Program (NTP) bioassay on these two substances (Battelle-Columbus, 1978a,b,d,e,f,g,h). In addition to early deaths and lack of body weight gain at the higher doses, animals exhibited histopathological changes indicative of hepatic centrolobular necrosis and degeneration, occasionally with cyto- and karyomegaly, as well as lymphoid depletion of the spleen and thymus. The NOAEL for o-DCB in mice cannot be determined since degeneration and necrosis in liver found at 250 and 500 mg/kg were not assessed at lower doses. In rats given o-DCB, the NOAEL was 250 mg/kg with the LOAEL being 500 mg/kg for decreased body weights in males. For animals given p-DCB, the LOAEL in mice was 250 mg/kg (lowest dose tested) for tissue lesions and in rats the NOAEL was 250 mg/kg and the LOAEL 500 mg/kg (lower body weight in males).

Long-term Exposure

- Gavage doses of o-DCB at 250 and 500 mg/kg given to rats and mice over a thirteen-week schedule of five days/week resulted in hepatic necrosis as well as porphyria (Battelle-Columbus, 1978c,i). Serum GPT levels were increased in mice exhibiting liver histopathology at the highest dose level. Some mice also exhibited myocardial and skeletal muscle mineralization and lymphoid depletion of the thymus and spleen and necrosis of the spleen. Rats also showed pathological changes in their kidneys, characterized by tubular degeneration. No treatment-related effects were observed with doses of 30, 60 and 125 mg/kg.

- Hollingsworth et al. (1958) gave rats a series of 138 doses of o-DCB over a period of 192 days (18.8, 188 or 376 mg/kg/day, five days a week) by gastric intubation. No adverse effects were noted at the lowest dose. With the intermediate dose, slight increases in the weights of the liver and kidney were noted. At the highest dose, there was a moderate increase in the weight of the spleen and swelling and cloudy appearance of the liver.

- Hollingsworth et al. (1958) also assessed the effects of multiple inhalation exposures to o-DCB in rats, guinea pigs, mice, rabbits and monkeys. The animals were exposed seven hours a day, five days a week, for six to seven months. No adverse effects were observed in rats, guinea pigs or mice exposed to 49 ppm (0.29 mg/L), or in rats, guinea pigs, rabbits and monkeys exposed to 93 ppm (0.56 mg/L).

- Twenty oral doses of 10, 100 or 500 mg/kg p-DCB given five days/week to rats produced marked hepatic effects including cloudiness, swelling and centrilobular necrosis at only the highest dose (Hollingsworth et al., 1958). No adverse effects were observed at the other doses.

- Thirteen-week exposures to p-DCB by gavage resulted in histopathological alterations in the liver similar to those observed with o-DCB, but at somewhat higher doses (675 and 800 mg/kg in the mouse, 300 and 600 mg/kg in the rat) (Battelle-Columbus, 1978a,b, 1980a,b). Hepatic necrosis, degeneration and porphyria were found in both species. The spleen and thymus also exhibited histopathological changes similar to those observed with o-DCB. In mice and rats, hematopoietic hypoplasia of the bone marrow occurred in survivors at the highest dose (1,500 mg/kg/day). Rats at the two highest dose levels (1,000 and 1,500 mg/kg) also exhibited epithelial necrosis of the nasal turbinates and small intestine as well as villar bridging of the mucosa of the latter tissue. Again, the rats exhibited multifocal degeneration or necrosis of the cortical tubular epithelium of the kidney. A NOAEL of 150 mg/kg/day for rats and 337.5 mg/kg for mice was identified.

- Oral doses of 188 or 376 mg p-DCB/kg given five days a week, for 192 days (138 doses) to rats produced an increase in the weights of the liver and kidneys (Hollingsworth et al., 1956). At 376 mg/kg, increased splenic weight and slight cirrhosis and focal necrosis of the liver were observed. No adverse effects were seen with the 18.8 mg/kg dose.

- Inhalation studies also were carried out by Hollingsworth et al. (1956) with p-DCB in rats, rabbits, mice and monkeys. The concentrations used were 96, 158, 173, 314 and 798 ppm (0.58, 0.95, 1.04, 2.05 and 4.8 mg/L, respectively). Exposures were conducted seven hours/day, five days/week for six to seven months. Adverse effects observed included liver and kidney lesions with increased organ weights, pulmonary edema and congestion, splenic weight changes and reversible, non-specific eye changes. The NOAELs were 96 ppm in rats and 158 ppm in the other species.

- Because available studies with lifetime exposures were conducted to assess carcinogenicity, they are discussed in the Carcinogenicity section.

Reproductive Effects

- Data on reproductive effects were not found in available literature.

Developmental Effects

- Several teratogenicity studies have been conducted on two of the three isomers of DCB. Hayes et al. (1985) observed no teratogenic or fetotoxic effects in rat or rabbit fetuses whose dams were exposed by inhalation to doses of o-DCB at levels up to 400 ppm. Similarly, no fetotoxic or teratogenic effects were noted in rabbits subjected to exposures of p-DCB at levels up to 500 ppm. In addition, the results of a study by Hodge et al. (1977, summarized in Loeser and Litchfield, 1983), support the conclusions of the Hayes et al. (1985) study in showing that maternal exposure to atmospheric levels of p-DCB up to 500 ppm on days 6 through 15 of pregnancy in the rat does not result in any embryotoxic, fetotoxic or teratogenic effects in the offspring.

Mutagenicity

- Para-dichlorobenzene induces abnormal mitotic division in higher plants. Observed effects include shortening and thickening of chromosomes, precocious separation of chromatids, tetraploid cells, binucleate cells and chromosome bridges (c-mitosis) (Sharma and Battacharya, 1956; Sharma and Sarkar, 1957; Srivastava, 1966; Gupta, 1972). Ortho-DCB was shown to produce abnormal mitotic division in the onion Allium cepa (Ostergren and Levan, 1943).

- Ortho- and para-dichlorobenzene were not mutagenic when tested in a culture of histidine-requiring mutants of Salmonella typhimurium or in the E. coli WP2 system (Anderson et al., 1972; Anderson, 1976; Simmon et al., 1979; Shimizu et al., 1983; NTP, 1985; NTP, 1986). However, all three isomers increased the frequency of back mutation of the methionine-requiring locus in the fungus Aspergillus nidulans (Prasad and Pramer, 1968; Prasad, 1970). In addition, the meta isomer was shown to increase mitotic recombination in the Saccharomyces cerevisiae C3 yeast system (Simmon et al., 1979). The results with the para isomer were ambiguous. These investigators also showed that

both o- and m-DCB interacted with and damaged bacterial DNA in the E. coli W3110 polA$^+$/p3478 polA$^-$ differential toxicity assay system. Treatment with p-DCB did not induce forward mutations in mouse lymphoma cells (NTP, 1986), sister-chromatid exchange in Chinese hamster ovary cells (NTP, 1986), and unscheduled DNA synthesis in human lymphocytes (Perocco et al., 1983).

- DCB has not been found to be mutagenic in animals. Guerin et al. (1971) showed that DCB (unspecified isomer) did not produce a significantly different number of mitoses in rat lung cell cultures. Cytogenetic studies with rat bone marrow cells and a dominant lethal study in CD-1 mice following exposure to p-DCB were all negative (Anderson and Hodge, 1976; Anderson and Richardson, 1976; NTP, 1986).

Carcinogenicity

- Hollingsworth et al. (1956, 1958) exposed several species of animals to various oral and inhalation exposures of ortho- and para-dichlorobenzene for six to seven months. No evidence of carcinogenicity was observed; however, the exposure duration was too short to allow conclusions on carcinogenicity to be drawn.

- An assessment of the data from an NTP bioassay using o-DCB administered by gavage indicates that, under the conditions of the study, this substance is not carcinogenic in Fischer 344 rats or B6C3F$_1$ mice (NTP, 1985). The NTP Board of Scientific Counselors added that no non-neoplastic lesions were noted in either the mice or the rats, suggesting that the maximum tolerated dose was not achieved. Both rats and mice (50/sex/dose) were given o-DCB in corn oil by gavage 5 days/week for 103 weeks at doses of 0, 60 or 120 mg/kg. No effect on survival, body weight, and pathology was noted except for lower ($p < 0.001$) survival in high-dose male rats and increased tubular regeneration in kidney of high-dose male mice.

- In an NTP (1986) bioassay on p-DCB in F344 rats and B6C3F$_1$ mice, treatment-related neoplastic effects include renal adenocarcinomas in male rats (1/50, controls; 3/50, low dose, $p > 0.05$; 7/50, high dose, $p < 0.05$) and carcinomas and adenomas in liver of high-dose male and female mice ($P < 0.001$). Rats and mice (50/sex/group) were given p-DCB in corn oil by gavage 5 days/week for 103 weeks at 0, 150 or 300 mg/kg (male rats) and 0, 300 or 600 mg/kg (remaining groups). Other treatment-related effects include kidney lesions in male and female rats at both doses, kidney and liver lesions in male and female mice at both doses, and reduced survival ($p < 0.05$) in high-dose male rats.

- A long-term (76 weeks exposure, 36 weeks further observation) inhalation study revealed no increase in tumor incidence or type after exposure to p-DCB in Alderley Park Wistar rats (Riley et al., 1980, summarized in Loeser and Litchfield, 1983). At the high exposure level (500 ppm), observed effects included increases in liver, kidney, heart and lung weights (both sexes) and an increase in urinary protein and coproporphyrin output (males). The low exposure level of 75 ppm was a NOAEL. The 500 and 75 ppm levels equal 3,005 and 451 mg/m3, respectively.

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:

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

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).

o-Dichlorobenzene (and/or m-Dichlorobenzene)

One-day and Ten-day Health Advisories

No satisfactory dose-response data are available from which to derive a One-day HA or Ten-day HA for the 10-kg child. It is recommended, that for this duration of exposure, the Longer-term HA for the 10-kg child (8.93 mg/L) be applied (see below).

Longer-term Health Advisory

Subchronic treatment studies with o-DCB in rats and mice were conducted in which daily doses were administered in corn oil by gavage at dose levels of 30, 60, 125, 250 and 500 mg/kg/day five days/week for 13 weeks (Battelle Columbus, 1978c,i). The NOAEL in these studies was 125 mg/kg. Renal and hepatic lesions, lower body weights and increased uro- and coproporphyrin levels were found with higher doses.

The Longer-term HA for a 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(125 \text{ mg/kg/day}) \ (10 \text{ kg}) \ (5)}{(100) \ (1 \text{ L/day}) \quad (7)} = 8.93 \text{ mg/L } (8{,}930 \text{ ug/L})$$

where:

125 mg/kg/day = NOAEL based on absence of renal and hepatic effects in rats and mice exposed to o-DCB for 13 weeks.

10 kg = assumed body weight of a child.

5/7 = conversion of 5 day/week dosing regimen to 7 day/week exposure pattern.

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 consuming 2 L of water per day, the Longer-term HA is calculated as follows:

$$\text{Longer-term HA} = \frac{(125 \text{ mg/kg/day})\ (70 \text{ kg})\ (5)}{(100)\ (2 \text{ L/day})\ \ (7)} = 31.25 \text{ mg/L } (31{,}250 \text{ ug/L})$$

125 mg/kg/day = NOAEL based on absence of renal and hepatic effects in rats and mice exposed to o-DCB for 13 weeks.

70 kg = assumed body weight of an adult.

5/7 = conversion of 5 day/week dosing regimen to 7 day/week exposure pattern.

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, 1986a), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

The fact that the HAs generated from the chronic studies in the NTP bioassay with a NOAEL of 120 mg/kg/day would be larger than those derived from the subchronic studies preceding them with a NOAEL of 125 mg/kg/day would suggest that the extra 10-fold uncertainty factor used with the subchronic data to estimate a Lifetime HA from subchronic data may not be necessary for this compound. However, the chronic studies offer a narrower evaluation of toxicity in that urinalysis, clinical chemistry and hematology were not included in the chronic study protocols. In view of this consideration, the extra 10-fold uncertainty factor may be appropriate.

The results of Hollingsworth et al. (1958) suggest a safe daily level of 0.94 mg/day to be used in the calculation of a lifetime HA, while those of the subchronic studies preceding the NTP bioassay suggest a level of 6.25 mg/day. Each of these levels was derived from a NOAEL (18.8 mg/kg and 125 mg/kg, respectively). Since the highest NOAEL should be used to derive a Lifetime HA, it is more appropriate to use the NOAEL established in the NTP subchronic studies than the NOAEL from the Hollingsworth study. Furthermore, the minimal effect dose identified in the Hollingsworth study (188 mg/kg) is somewhat higher than the NOAEL established in the NTP subchronic studies.

The Lifetime HA is, therefore, calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(125\ mg/kg/day)\ (5)}{(1{,}000)\quad (7)} = 0.089\ mg/kg/day\ (89\ ug/kg/day)$$

where:

125 mg/kg/day = NOAEL used for Longer-term HA.

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

5/7 = conversion of 5 day/week dosing to 7 day/week.

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

$$DWEL = \frac{(0.089\ mg/kg/day)\ (70\ kg)}{(2\ L/day)} = 3.13\ mg/L\ (3{,}125\ ug/L)$$

where:

0.089 mg/kg/day = RfD.

70 kg = assumed body weight of an adult.

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

Step 3: Determination of the Lifetime Health Advisory

Lifetime HA = 3.13 mg/L x 20% = 0.62 mg/L (620 ug/L)

where:

3.13 mg/L = DWEL.

20% = assumed relative source contribution from water.

m-Dichlorobenzene

There are no toxicity studies on m-DCB on which to base Health Advisories; however, because certain properties of o-DCB and m-DCB are similar, the HAs for o-DCB are recommended for m-DCB (U.S. EPA, 1987).

p-Dichlorobenzene

One-day and Ten-day Health Advisories

No satisfactory dose-response data are available from which to derive a One-day HA or a Ten-day HA for p-DCB for the 10-kg child. It is recommended that for this duration of exposure, the Longer-term HA for the 10-kg child (10.7 mg/L) be applied (see below).

Longer-term Health Advisory

The 90-day treatment study with p-DCB by Battelle-Columbus (1979a) is selected for calculation of a Longer-term HA; results in rats were used since they indicated a lower NOAEL compared to that in mice (Battelle-Columbus, 1979b). In addition, a 90-day study is considered to provide a stronger evaluation of toxicity than 14-day treatment studies which preceded the 90-day studies. The rats were given p-DCB in corn oil by gavage, 5 days/week, for 13 weeks. The NOAEL was 150 mg/kg/day since renal lesions were observed in males at higher doses.

The Longer-term HA for the 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(150 \text{ mg/kg/day})\ (10 \text{ kg})\ (5)}{(100)\ (1 \text{ L/day})\ \ (7)} = 10.7 \text{ mg/L } (10{,}700 \text{ ug/L})$$

where:

150 mg/kg/day = NOAEL, based on absence of renal lesions.

10 kg = assumed body weight of a child.

5/7 = conversion of 5 day/week dosing regimen to 7 day/week exposure pattern.

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, the Longer-term HA is calculated as follows:

$$\text{Longer-term HA} = \frac{(150 \text{ mg/kg/day})\ (70 \text{ kg})\ (5)}{(100)\ (2 \text{ L/day})\ \ \ (7)} = 37.5 \text{ mg/L } (37{,}500 \text{ ug/L})$$

where:

150 mg/kg/day = NOAEL, based on absence of renal lesions.

70 kg = assumed body weight of an adult.

5/7 = conversion of 5 day/week dosing regimen to 7 day/week exposure pattern.

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

p-Dichlorobenzene

The EPA has developed for comparison with cancer-based criteria, a presumed safe daily intake level based on non-carcinogenic effects as indicated in U.S. EPA (1987). For consistency, the rationale used by EPA for the calculation of this value by U.S. EPA (1987) is used here for the DWEL calculation. The rationale as presented in U.S. EPA (1987) is as follows:

The results of the Hollingsworth et al. (1956) study and the subchronic studies preceding the NTP bioassay, as well as the acute toxicity studies described earlier, indicate that the rat is somewhat more sensitive to p-DCB toxicity than is the mouse. Therefore, when estimating potential risk to the human, the data from the experiments in the rat should be used in deriving a Lifetime HA.

The NOAEL derived from the Hollingsworth study was 18.8 mg/kg; the NOAEL from the NTP subchronic study in the rat was 150 mg/kg. Since the highest NOAEL should be used to calculate a daily level of intake, the NOAEL established in the NTP subchronic study will be used. In addition, it should be noted that the minimal effect level identified in the Hollingsworth study (188 mg/kg) was somewhat higher than the NOAEL established in the NTP subchronic study.

As with o-DCB (and m-DCB), any Lifetime Health Advisories derived from the NTP chronic studies might be higher than those derived from the subchronic studies preceding them because the 10-fold uncertainty factor applied to accommodate for the difference in duration of exposure may be unnecessarily large. However, as mentioned for o-DCB, the lack of certain parameters in the chronic study (urinalysis, clinical chemistry and hematology) may make the use of a 10-fold uncertainty factor appropriate. Also, the finding of renal lesions with 150 mg/kg/day in the NTP (1986) chronic study in rats further supports use of an extra 10-fold uncertainty factor.

The Lifetime HA is, therefore, calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(150\ mg/kg/day)\ (5)}{(1{,}000)\quad (7)} = 0.1\ mg/kg/day\ (100\ ug/kg/day)$$

where:

150 mg/kg/day = NOAEL used for Longer-term HA.

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

5/7 = conversion of 5 day/week dosing to 7 day/week.

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

$$DWEL = \frac{(0.1\ mg/kg/day)\ (70\ kg)}{(2\ L/day)} = 3.75\ mg/L\ (3{,}750\ ug/L)$$

where:

0.1 mg/kg/day = RfD.

70 kg = assumed body weight of an adult.

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

Step 3: Determination of the Lifetime Health Advisory

$$Lifetime\ HA = \frac{(3.75\ mg/L)\ (20\%)}{10} = 0.075\ mg/L\ (75\ ug/L)$$

where:

3.75 mg/L = DWEL.

20% = assumed relative source contribution from water.

10 = additional uncertainty factor for Group C carcinogens per Office of Drinking Water policy.

Evaluation of Carcinogenic Potential

- Assessment of the NTP bioassay on o-DCB suggests that it was not carcinogenic under the conditions of the experiment.
- No adequate data are available to assess the potential cancer risk associated with exposure to m-DCB.

- The IARC (1982) classified both p-DCB and o-DCB as Group 3 chemicals with inadequate evidence for carcinogenicity in animals and humans.

- Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986a), o-DCB and m-DCB may be classified in Group D: Not classified. This category is for agents with inadequate animal evidence of carcinogenicity.

- Because of positive evidence in two animal species, p-DCB may be placed in category B2 (sufficient animal evidence, inadequate human evidence) by these guidelines. However, consideration of the overall weight of evidence could suggest the alternative view that p-DCB be placed in Group C (limited animal evidence) by these guidelines, with respect to uncertainties with high doses and corn oil gavage and diminished toxicological significance of the mouse liver tumor results. The EPA has concluded that the overall weight of evidence favors classification of p-DCB in Group C (U.S. EPA, 1987).

- Because p-DCB is considered a Group C agent, the DWEL would be divided by an extra uncertainty factor of 10 to yield 0.375 mg/L.

- Provisional cancer potency estimates for p-DCB were derived using the multistage model and the liver tumor data on male mice in the chronic feeding study by NTP (1986).

- The 95% upper-limit carcinogenic potency factor for humans, q_1^*, is 2×10^{-2} $(mg/kg/day)^{-1}$ by the multistage model (U.S. EPA, 1986b). For a 70 kg human drinking 2 L water/day, the water concentration should be 17.5 ug/L in order to keep the upper-limit individual lifetime cancer risk at 10^{-5}. Water concentrations corresponding to excess cancer risk of 10^{-4} and 10^{-6} are, therefore, 175 and 1.8 ug/L, respectively. Maximum likelihood estimates by the multistage model associate risks of 10^{-5} and 10^{-6} with exposures to 20.7 and 6.3 mg/L, respectively. There are not enough distinct data points to allow fits to other models tried (Weibull, logit, probit). 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.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- The OSHA standard for 1,2-dichlorobenzene is 50 ppm (300 mg/m^3) (U.S. EPA, 1985a).

- The 1982 ACGIH TLV is 50 ppm (U.S. EPA, 1985a).

- The OSHA standard for 1,4-dichlorobenzene is 75 ppm (450 mg/m^3) (U.S. EPA, 1985a).

- The dichlorobenzene isomers are designated as hazardous wastes under the Resource Conservation and Recovery Act (RCRA) (U.S. EPA, 1985a).

- Under the Federal Water Pollution Control Act, 1,2-di- and 1,4-dichlorobenzenes are hazardous substances with reportable quantities of 100 lbs.

- The ambient water quality criterion for dichlorobenzenes is 400 ug/L, using a NOAEL of 13.4 mg/kg/day and an uncertainty factor of 1,000 (U.S. EPA, 1980).

- The WHO (1984) recommended an acceptable drinking water level of 1 ug/L for 1,2- and 1,4-dichlorobenzenes based on odor threshold.

- The NAS (1983) calculated a chronic SNARL of 0.3 mg/L for o-DCB, using a NOAEL of 60 mg/kg, 20% relative source contribution, and a 1,000-fold uncertainty factor.

- The NAS (1977) calculated a chronic SNARL of 0.094 mg/L for p-DCB, using a NOAEL of 13.4 mg/kg/day, a relative source contribution of 20%, and an uncertainty factor of 1,000.

- The proposed RMCL for o-DCB is 0.62 mg/L (U.S. EPA, 1985b).

- The U.S. EPA Office of Drinking Water issued a final RMCL of 0.75 mg/L, a proposed MCL of 0.75 mg/L, and a practical quantitation level of 5 ug/L for p-DCB (U.S. EPA, 1985c). However, p-DCB is being considered for reproposal as a result of the recent positive NTP (1986) carcinogenicity bioassay.

VII. ANALYTICAL METHODS

- Analysis of dichlorobenzene(s) is by a purge-and-trap gas chromatographic procedure used for the determination of volatile organohalides in drinking water (U.S. EPA, 1985d). This method calls for the bubbling of an inert gas through the sample and trapping dichlorobenzene(s) on an adsorbant material. The adsorbant material is heated to drive off the dichlorobenzene(s) onto a gas chromatographic column. The gas chromatograph is temperature programmed to separate the method analytes which are then detected by a halogen specific detector. This method is applicable to the measurement of dichlorobenzene(s) over a concentration range of 0.05 to 1500 ug/L. Confirmatory analysis for dichlorobenzene(s) is by mass spectrometry (U.S. EPA, 1985e). The detection limit for confirmation by mass spectrometry is 0.3 ug/L.

VIII. TREATMENT TECHNOLOGIES

- Granular activated carbon (GAC) adsorption and aeration for the removal of ortho-, meta- and para-dichlorobenzene from water are available and have been reported to be effective. Because ortho-, meta- and para-dichlorobenzene are chemically similar, they can be considered together (U.S. EPA, 1985f).

- McCarty et al. (1979b) conducted a study at a 15-MGD advanced waste treatment (AWT) plant which examined organics removal in air stripping towers designed for ammonia removal. That study showed that 83 to 97 percent of trace quantities (ug/L range) of o-DCB, m-DCB and p-DCB were removed.

- In a laboratory study where water containing an average of 151 ug/L of o-DCB, 229 ug/L of m-DCB and 225 ug/L of p-DCB was passed through a diffused-air aerator using a 15:1 air to water ratio, there was a 74% reduction in the o-DCB concentration, a 79% reduction of m-DCB and a 77% reduction in the p-DCB (Love et al., 1983). In another study of well water contaminated with 3.0 ug/L o-DCB, 90% or more of the compound was removed with air to water ratios of 47:1.

- Carbon adsorption also can be used to remove o-DCB, m-DCB and p-DCB from contaminated water. According to Dobbs and Cohen (1980) at equilibrium concentrations of 1 mg/L and 10 mg/L, activated carbon had adsorptive capacities of 129 mg and 350 mg of o-DCB per gram of carbon, respectively. Their data for p-DCB show carbon capacities of 121 mg/gram of carbon and 470 mg/gram of carbon, respectively, at the identical equilibrium concentrations. Adsorption capacities for m-DCB are slightly less than those for o-DCB and p-DCB (Love et al., 1983).

- Data from a GAC system containing Filtrasorb® 300 at an AWT Plant demonstrated significant removals of o-DCB and p-DCB at trace concentrations (McCarty et al., 1979a).

- A column study by EPA/ESE (ESE, 1981) examined removal of benzene, monochlorobenzene, o-DCB and p-DCB from a wastewater stream by regenerated GAC. With influent concentrations of each in the mg/L range, o-DCB and p-DCB did not break through during the study. Estimated carbon usage rates for each could be expected to be less than those obtained for benzene (10 lb/1,000 gallons). Although experimental data from drinking water and wastewater experimentation are markedly different, some comparisons can be made. Another ESE field study (1978) at North Miami Beach using powdered activated carbon addition to potable water demonstrated up to 97 percent removal of dichlorobenzenes by 52 mg/L (434 lb/10^6 gallons) of PAC. This concentration of PAC is much greater than that normally used.

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