Public Health Goal for 1,2-Dichloropropane In Drinking Water

Prepared by

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PREFACE

Drinking Water Public Health Goals

Pesticide and Environmental Toxicology Section

Office of Environmental Health Hazard Assessment

California Environmental Protection Agency

This Public Health Goal (PHG) technical support document provides information on health effects from contaminants in drinking water. PHGs are developed for chemical contaminants based on the best available toxicological data in the scientific literature. These documents and the analyses contained in them provide estimates of the levels of contaminants in drinking water that would pose no significant health risk to individuals consuming the water on a daily basis over a lifetime.

The California Safe Drinking Water Act of 1996 (amended Health and Safety Code, Section 116365) requires the Office of Environmental Health Hazard Assessment (OEHHA) to perform risk assessments and adopt PHGs for contaminants in drinking water based exclusively on public health considerations. The Act requires that PHGs be set in accordance with the following criteria:

1. PHGs for acutely toxic substances shall be set at levels at which no known or anticipated adverse effects on health will occur, with an adequate margin of safety.
2. PHGs for carcinogens or other substances which can cause chronic disease shall be based solely on health effects without regard to cost impacts and shall be set at levels which OEHHA has determined do not pose any significant risk to health.
3. To the extent the information is available, OEHHA shall consider possible synergistic effects resulting from exposure to two or more contaminants.
4. OEHHA shall consider the existence of groups in the population that are more susceptible to adverse effects of the contaminants than a normal healthy adult.
5. OEHHA shall consider the contaminant exposure and body burden levels that alter physiological function or structure in a manner that may significantly increase the risk of illness.
6. In cases of insufficient data to determine a level of no anticipated risk, OEHHA shall set the PHG at a level that is protective of public health with an adequate margin of safety.
7. In cases where scientific evidence demonstrates that a safe dose-response threshold for a contaminant exists, then the PHG should be set at that threshold.
8. The PHG may be set at zero if necessary to satisfy the requirements listed above.
9. OEHHA shall consider exposure to contaminants in media other than drinking water, including food and air and the resulting body burden.
10. PHGs adopted by OEHHA shall be reviewed every five years and revised as necessary based on the availability of new scientific data.

PHGs adopted by OEHHA are for use by the California Department of Health Services (DHS) in establishing primary drinking water standards (State Maximum Contaminant Levels, or MCLs). Whereas PHGs are to be based solely on scientific and public health considerations without

regard to economic cost considerations, drinking water standards adopted by DHS are to consider economic factors and technical feasibility. Each standard adopted shall be set at a level that is as close as feasible to the corresponding PHG, placing emphasis on the protection of public health. PHGs established by OEHHA are not regulatory in nature and represent only non-mandatory goals. By federal law, MCLs established by DHS must be at least as stringent as the federal MCL if one exists.

PHG documents are used to provide technical assistance to DHS, and they are also informative reference materials for federal, state and local public health officials and the public. While the PHGs are calculated for single chemicals only, they may, if the information is available, address hazards associated with the interactions of contaminants in mixtures. Further, PHGs are derived for drinking water only and are not to be utilized as target levels for the contamination of other environmental media.

Additional information on PHGs can be obtained at the OEHHA web site at www.oehha.ca.gov.

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PUBLIC HEALTH GOAL FOR 1,2-DICHLOROPROPANE IN DRINKING WATER

SUMMARY

The Office of Environmental Health Hazard Assessment (OEHHA) has developed a Public Health Goal (PHG) of 0.5 μg/L (or ppb) for 1,2-dichloropropane (1,2-DCP) in drinking water. The PHG is based on carcinogenic effects observed in experimental animals. Cancer potency estimates were made by fitting the linearized multistage model to the experimental data to establish the lower 95% confidence bound on the dose associated with a 10% increased risk of cancer (LED_{10}). The most sensitive site, gender, and species for tumor development was the combined incidence of hepatocellular adenomas and carcinomas observed in male mice in a two-year oral gavage study conducted by the National Toxicology Program (NTP, 1986). For the PHG calculation, a cancer potency estimate of 3.6×10^{-2} $(mg/kg\text{-}day)^{-1}$ was selected and a *de minimis* theoretical excess individual cancer risk level of 10^{-6} was used. In addition to calculating a PHG for 1,2-DCP based on carcinogenic effects, a health-protective level was calculated based on noncancer effects. The key study selected for the noncancer calculation was a two-year oral gavage study conducted in rats (NTP, 1986). In this study, the lowest dose of 1,2-DCP administered to female rats resulted in increased incidence of mammary gland hyperplasia. Based on a LOAEL of 89.3 mg/kg-day, and a cumulative uncertainty factor of 1,000, a PHG of 0.63 mg/L (ppm; 630 ppb) was calculated. OEHHA concludes that the most sensitive endpoint for assessing potential human health risks from chronic low level exposure to 1,2-DCP in drinking water is the carcinogenic endpoint. OEHHA therefore derived a PHG of 0.5 ppb for 1,2-DCP in drinking water based on its carcinogenic potential. A PHG of 0.5 ppb is also considered to contain an adequate margin of safety to protect against potential noncancer adverse effects.

INTRODUCTION

The purpose of this document is to develop a PHG for 1,2-DCP in drinking water. California's current drinking water standard for 1,2-DCP is 5 μg/L (ppb). This standard, referred to as the State Maximum Contaminant Level (or State MCL) was adopted by California's Department of Health Services (DHS) in 1994 (California Code of Regulations, 22 CCR 64444). The state and federal MCLs are based on the carcinogenic potential of 1,2-DCP. The U.S. Environmental Protection Agency U.S. EPA has classified 1,2-DCP as a [B2] carcinogen. In California, 1,2-DCP is listed under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) as a chemical known to the state to cause cancer.

In this document, the available data on the toxicity of 1,2-DCP are evaluated, with the primary focus on the literature related to oral exposures which may be most appropriate for the establishment of a PHG for drinking water. The studies which can be used to identify

public health-protective levels are reviewed and summarized. The results of this evaluation are described below.

CHEMICAL PROFILE

Chemical Identity

Chemical name:	1,2-dichloropropane
Molecular formula:	$C_3H_6Cl_2$
Synonyms:	dichloro-1,2-propane propylene chloride; propylene dichloride
CAS registry number:	78-87-5
RTECS registry number:	TX9625000

Physical and Chemical Properties

1,2-Dichloropropane is a colorless liquid with a chloroform-like odor (HSDB, 1998). It has a molecular weight of 112.99, a melting point of -100.4°C, and a boiling point of 96.4°C. It has a vapor pressure of 42 mm Hg at 20°C. Its solubility is 2.7 g/kg water at 20°C. It is soluble in alcohol, ether, benzene and chloroform, and it is miscible with organic solvents. When heated to decomposition, it emits highly toxic fumes of phosgene (WHO, 1993).

Production and Uses

1,2-Dichloropropane is produced by the chlorination of propylene. In the United States, annual production was approximately 41 million pounds in 1972, 84 million pounds in 1975, and 77 million pounds in 1980 (HSDB, 1998). Since that time, domestic production of isolated 1,2-DCP has been discontinued, although the compound is still in use.

1,2-DCP has been used alone as an insecticide for stored grain, and as a component of several insecticidal and nematocidal soil fumigants including Dowfume EB-5, Telone II, D-D Mixture, Nematox, Vidden D and Dow-421 (HSDB, 1998). In 1981, approximately 4 million pounds of 1,2-DCP were used in soil fumigant applications in California . The average 1,2-DCP content of the applied fumigant mixtures was 25%. In 1985, the California Department of Food and Agriculture adopted a regulation limiting the 1,2-DCP content of pesticides to 0.5% of the total formulation, potentially decreasing usage of this chemical in California (Reed et al., 1988). 1,2-DCP is no longer registered for use as a soil fumigant in the United States (DPR, 1997; HSDB, 1998). Currently, 1,2-DCP is used primarily as a chemical intermediate in the production of carbon tetrachloride and the dry-cleaning agent, perchloroethylene. It also has use as an industrial solvent for fats, oils, resins, waxes and rubber (IARC, 1986; HSDB, 1998). 1,2-DCP is found as a trace impurity

in the production of 1,3-dichloropropene (Telone). The current maximum amount of 1,2-DCP found in Telone has been reported to be no greater than 100 ppm (0.01%) (Brinkmeyer, 1998).

ENVIRONMENTAL OCCURRENCE AND HUMAN EXPOSURE

The general population is primarily exposed to 1,2-DCP from inhalation of contaminated ambient air and from consumption of contaminated drinking water. Workers may be exposed to 1,2-DCP via inhalation and dermal contact during use and/or production (HSDB, 1998).

Air

Releases into air occur during 1,2-DCP production and its many industrial uses (HSDB, 1998). In addition, releases to air occur from volatilization during wastewater treatment and incomplete incineration (ATSDR, 1989). As a component of fumigants, 1,2-DCP is released into the air as fugitive emissions. Following its application, it volatilizes and diffuses into ambient air.

In a report of 7 selected cities in the United States, mean concentrations of 1,2-DCP ranged from 0.11 to 0.37 $\mu g/m^3$ (Singh et al., 1982). At 7 of 11 sample sites in the United States where industrial activity included the production, use, or storage of halogenated hydrocarbons, estimated concentrations of 1,2-DCP ranged from trace amounts to 2.2 $\mu g/m^3$ (IARC, 1986, citing Pellizzari, 1982). In a study of Philadelphia, Pennsylvania, mean concentrations were reported to be 1.3 $\mu g/m^3$ in areas in which 1,2-DCP was detected (Versar, 1986).

Soil

If released on soil (e.g., as a fumigant, or from landfill and spills), 1,2-DCP will partially volatilize. The remainder will leach into the subsurface soil and groundwater (ATSDR, 1989; HSDB, 1998).

The California State Water Resources Control Board measured 1,2-DCP in soil samples from an agricultural field adjacent to contaminated wells in central California (Reed et al., 1988; citing Cohen et al., 1983). 1,2-DCP was found at depths of 1.5 to 9 feet with concentrations ranging from 3 to 11 ppb.

Water

1,2-DCP has been identified as a contaminant in groundwater, surface water and drinking water in numerous places in the United States (HSDB, 1998).

Studies of groundwater in California conducted in 1982 and 1983 showed that 1,2-DCP was detected in 56 wells in the Central Valley and North Coast (Reed et al., 1988; citing Cohen et al., 1983). Since that time, agricultural use of 1,2-DCP has been restricted and its

occurrence in California groundwater has decreased. During the period from July 1995 through June 1996, 3564 wells were sampled for pesticide residues in 48 counties across the State. 1,2-DCP was detected in 8 wells from 6 counties at concentrations ranging from 0.5-3.2 ppb. California's Department of Pesticide Regulation (DPR) has determined that the residues of 1,2-DCP that were detected in the wells are due to historical non-point source, legal agricultural use of the compound (DPR, 1997).

Toxic Release Inventory (TRI) data for California indicate that from 1988 through 1994, reported releases of 1,2-DCP into water were approximately 200 pounds per year.

Food

No information was located on 1,2-DCP and food products.

METABOLISM AND PHARMACOKINETICS

Absorption

1,2-DCP is readily and almost completely absorbed from the gastrointestinal tract and lungs in rats. In a retention and excretion study (Hutson et al., 1971), rats were administered a single dose of radiolabeled 1,2-DCP by gavage. Within 24 hours, 80-90% of the administered dose was recovered in urine, expired air, and feces. Within 96 hours, the total radioactivity of the administered dose was recovered. Only 5% was measured in feces, which could have resulted from biliary excretion or unabsorbed dose. Similarly, 48 hours following oral administration of single or multiple doses of [^{14}C]-1,2-DCP in rats, 91-107% of the administered dose was recovered, with 5.5-7.9% measured in feces (Timchalk et al., 1991). In an inhalation study, rats were exposed to [^{14}C]-1,2-DCP vapors for 6 hours. After 48 hours the total radioactivity was recovered with 6.3-9.7% measured in feces (Timchalk et al., 1991).

Due to the physical properties of this compound (i.e., nonpolar, highly lipophilic, low molecular weight), 1,2-DCP is also likely to be readily absorbed from dermal contact.

Distribution

1,2-DCP diffuses rapidly into the bloodstream and distributes to tissues. When rats were administered multiple oral doses of [^{14}C]-1,2-DCP, peak concentrations were found in blood 4 hours after treatment. Forty-eight hours after treatment, radioactivity was well distributed among the 13 organs and tissues analyzed. The highest concentrations of ^{14}C-activity were found in liver (0.2-0.4% of the dose/g wet weight). Similar results were obtained in rats following inhalation of [^{14}C]-1,2-DCP vapors; peak blood concentrations were found at 4 hours, radioactivity was well distributed among analyzed tissues, and highest concentrations were found in liver and kidney (Timchalk et al., 1989 as cited by WHO, 1993).

Four days after rats were administered a single oral dose of radiolabeled 1,2-DCP, radioactivity was measured: 0.5% of the administered dose was recovered from gut, 1.6%

was recovered from skin, and 3.6% recovered in carcass (Hutson et al., 1971). Forty-eight hours after oral or inhalation exposure in rats, 6-11% of the dose was recovered in tissues and carcass, combined (Timchalk et al., 1991).

Metabolism

Metabolism of 1,2-DCP has been reported to occur mainly in the liver (Reed et al., 1988). Three mercapturic acids have been identified as major urinary metabolites in rats following both oral and inhalation exposures (Jones and Gibson, 1980, Timchalk et al., 1991). The three mercapturates are: N-acetyl-S-(2-hydroxypropyl)-L-cysteine, N-acetyl-S-(2-oxopropyl)-L-cysteine, and N-acetyl-S-(1-carboxyethyl)-L-cysteine. It has been suggested that 1,2-DCP undergoes direct oxidation either prior to, or following, conjugation with glutathione, forming N-acetyl-S-(2-hydroxypropyl)-L-cysteine. Both 1-chloro-2-hydroxypropane and 1,2-epoxypropane are proposed intermediary metabolites in the metabolism of 1,2-DCP to the 2-hydroxypropyl-mercapturic acid (Jones and Gibson, 1980; Bartels and Timchalk, 1990).

In addition to forming the 2-hydroxypropyl-mercapturic acid, 1,2-epoxypropane may also undergo hydrolysis to propanediol, which may be further metabolized to pyruvate and converted through the tricarboxylic acid cycle to carbon dioxide. 1,2-epoxypropane may also be conjugated with glutathione and excreted in urine (Jones and Gibson, 1980).

Two minor urinary metabolites have been identified: β-chlorolactate and N-acetyl-S-(2,3-dihydroxy-propyl)cysteine (Jones and Gibson, 1980). In expired air, both $^{14}CO_2$ and the parent compound have been identified following oral and inhalation exposure in rats (Hutson et al., 1971; Jones and Gibson, 1980, Timchalk et al., 1991).

Excretion

1,2-DCP is rapidly eliminated in rats following oral or inhalation exposure (80-90% in 24 hours) (Hutson et al., 1971; Timchalk et al., 1991). Urine is the primary route of elimination, with measurements of up to 65% of an administered dose being eliminated by this route within 48 hours. Less than 10% is eliminated in feces. Approximately 20-40% is eliminated in expired air as both carbon dioxide and a mixture of volatile materials, including the parent compound.

TOXICOLOGY

Toxicological Effects in Animals

Acute Toxicity

Lethal oral doses, or LD_{50}s, have been reported for rats (2000-2200 mg/kg), mice (860 mg/kg) and guinea pigs (2000-4000 mg/kg) exposed to 1,2-DCP (Windholz et al., 1976;

Pozzani et al., 1959; Smyth et al., 1962; Smyth et al., 1969; Farm Chemicals Handbook, 1988). Lethal inhalation concentrations (LC_{50}s) of 2000-3000 ppm have been reported for rats (Smyth et al., 1962, Smyth et al., 1969; Pozzani et al., 1959) and 480 ppm for mice (Dow Chemical Co., 1988a). Signs of acute toxicity include depression of the central nervous system and irritation of the respiratory tract and eyes.

Single oral doses of 1,2-DCP administered to dogs (230-5800 mg/kg) resulted in adverse effects on the central nervous system (marked incoordination, loss of balance, unsteady gait), gross and microscopic changes in liver (congestion, hemorrhage, cloudy swelling, fatty degeneration, parenchymatous degeneration), and renal effects (congestion of the cortex, fatty infiltration, gross discoloration) (Wright and Schaffer, 1932; summarized by U.S. EPA, 1990, and Reed et al., 1988).

Male Sprague-Dawley rats were administered 1,2-DCP by gavage once a day for one, five or ten consecutive days at doses of 0, 100, 250, 500, or 1000 mg/kg (Bruckner et al., 1989). Single oral doses of 1,2-DCP resulted in central nervous system depression and decreased body weight at the lower dose levels (100-250 mg/kg) and liver toxicity at the higher dose levels (500-1000 mg/kg). Oral administration of 100 mg/kg for 10 days resulted in significantly increased levels of hepatic cytochrome P450 levels, and nucleolar enlargement of hepatocytes. Doses of 500-1000 mg/kg for 10 days lead to more significant liver injury (toxic hepatitis, periportal vacuolization, changes in liver enzyme concentrations) as well as hemolytic anemia. "Resistance" to 1,2-DCP-induced hepatotoxicity developed over the 10 days of exposure, as evidenced by decreased incidence and severity of toxic hepatitis and periportal vacuolization, and by progressively lower serum enzyme levels. Nucleolar enlargement of hepatocytes, however, was observed at all dose levels at both 5 and 10 days.

Female New Zealand white rabbits (two/dose) were administered 1,2-DCP by gavage for up to 13 consecutive days at doses of 0, 250, 500 or 1000 mg/kg (Dow Chemical Co., 1988b). Five of six treated animals died during the exposure period or were submitted to necropsy in a moribund condition. General signs of toxicity included lethargy and slight-to-moderate ataxia. Animals receiving 500 or 1000 mg/kg had hepatic necrosis with minor hepatocellular alterations in the remaining viable hepatocytes. One rabbit receiving 250 mg/kg had minor hepatic lesions similar to those seen at higher dose levels, although hepatic necrosis was not present. Some treated rabbits also exhibited signs of renal toxicity (i.e., pale kidneys, dilation of the renal collecting ducts or the entire tubular system).

Fischer 344/N rats and $B6C3F_1$ mice (five/sex/group) were administered 1,2-DCP by gavage at doses of 0, 125, 250, 500, 1000 or 2000 mg/kg for 14 days. Among rats, all animals in the highest dose group died during the study and final mean body weights were 14-15% lower in the 1000 mg/kg group compared to controls. Among mice, all males receiving 1000 or 2000 mg/kg died during the study, as well as 3/5 males in the 500 mg/kg group. All female mice receiving 2000 mg/kg died during the study, as well as 4/5 receiving 1000 mg/kg. Mean body weights of surviving mice were not affected by 1,2-DCP exposure. At necropsy, the only compound-related effect observed was redness of the renal medullae. This effect was seen in both rats and mice in the higher dose groups. Histopathology was not performed (NTP, 1986).

Fischer rats (10/sex/dose) were administered 1,2-DCP by gavage at doses of 0, 300, or 500 mg/kg-day for 14 consecutive days. Among male and female treated rats, transient clinical effects (tearing, blinking, and lethargy) were observed, and body weights were significantly

decreased. A dose-related increase in liver and kidney weights was observed in both sexes. Histopathologic changes (prominent nucleoli of hepatocytes, degeneration and necrosis of liver cells) were found in males and females at both dose levels. No microscopic effects were noted in kidneys (Dow Chemical Co., 1989).

A number of studies have been conducted evaluating the effects of acute inhalation exposure to 1,2-DCP. These studies are summarized in U.S. EPA, 1990, and Reed et al., 1988. Concentrations of 1000-2200 ppm 1,2-DCP for one or multiple seven-hour exposures resulted in toxicity to liver (fatty degeneration, necrosis, congestion) and kidney (fatty degeneration) in rats, guinea pigs and rabbits (Heppel et al., 1946; Heppel et al., 1946). Other toxic endpoints found include adrenal glands, central nervous system, spleen, bladder and lungs. Continuous exposure to lower concentrations of 1,2-DCP (200-450 ppm) for seven days resulted in similar liver and kidney changes in rats (Sidorenko et al., 1976). Liver toxicity (including visible lesions, extensive acute hemorrhagic coagulation necrosis, and regenerative changes) has also been found in mice exposed to 500 ppm for a single six-hour period (Dow Chemical Co., 1983).

Subchronic Toxicity

Fischer 344/N rats (10/sex/dose) were administered 1,2-DCP by gavage five days/week for 13 weeks, at doses of 0, 60, 125, 250, 500, or 1000 mg/kg. All males and females receiving 1000 mg/kg and half of the males receiving 500 mg/kg died before the end of the exposure period. Final mean body weights for animals receiving 500 mg/kg were 16% lower in males and 8% lower in females relative to control animals. Administration of 1,2-DCP at the highest dose level resulted in centrilobular congestion of the liver in male and female rats. In addition, hepatic fatty changes and centrilobular necrosis were observed in females (NTP, 1986).

$B6C3F_1$ mice (10/sex/dose) were administered 1,2-DCP by gavage five days/week for 13 weeks at concentrations of 0, 30, 60, 125, 250 or 500 mg/kg. No DCP-related effects were observed in either sex (NTP, 1986).

Male Sprague-Dawley rats (15-16/group) were administered 1,2-DCP by gavage at doses of 0, 100, 250, 500 or 750 mg/kg, five days per week for up to 13 weeks (Bruckner et al., 1989). Over half of the animals in the high-dose group died within 10 days, and in the 500 mg/kg group within 13 weeks. Doses of 500 and 750 mg/kg resulted in pronounced CNS depression with substantially lower water and food intake. Significantly lower and dose-dependent body weight gain was observed at all dose levels compared to controls. Histological examination of high-dose animals showed mild hepatitis, splenic hemosiderosis, adrenal medullary vacuolization and cortical lipidosis, as well as adverse testicular effects (see Developmental and Reproductive Toxicity). Evidence of hepatotoxicity was also seen with 500 mg/kg (periportal vacuolization, active fibrosis and increased liver/body weight ratios). Manifestations of hemolytic anemia (increased bilirubin, decreased hematocrit and hemoglobin, hemosiderosis and hyperplasia of erythropoietic elements of the spleen, renal tubular cell hemosiderosis and hepatic Kupffer cell hemosiderosis) were found in response to 100-500 mg/kg, with increased serum bilirubin levels and hemosiderosis of erythropoietic elements of the spleen observed at the lowest dose. Morphologic changes in spleen were dose-dependent ranging from slight to

moderately severe. Effects observed at 100 and 250 mg/kg largely disappeared during the one-week recovery period following the 13-weeks of exposure. A LOAEL of 100 mg/kg was identified.

In a series of inhalation studies (Nitschke et al., 1988; summarized by WHO, 1993), $B6C3F_1$ mice and Fischer rats were exposed to 1,2-DCP six hours/day, five days/week for 13 weeks. The mean exposure concentrations of the compound were 0, 74.5, 233, or 694 mg/m^3. Among treated mice, there were no effects of 1,2-DCP observed on gross pathology, hematology, and histopathology at any of the dose levels. Among rats, body weights were significantly lower in animals of the two highest exposure groups compared to controls. In addition, microscopic examination revealed 'minimal effects' in nasal tissues of animals exposed to 233 and 694 mg 1,2-DCP/m^3, while a few rats from the low-dose group had slight thickening of a small portion of the respiratory nasal mucosa. A NOEL of 74.5 mg/m^3 was identified for rats. New Zealand white rabbits were also exposed to 1,2-DCP via inhalation for six hours/day, five days/week for 13 weeks. The mean exposure concentrations were 0, 694, 2204, or 4436 mg/m^3. 'Minimal effects' on nasal tissues were found in males exposed to 4436 mg/m^3. The primary effects observed from 1,2-DCP exposure was in blood (i.e., decreased red cell count, hemoglobin, and packed cell volume), occurring in males at all exposure concentrations, and in females exposed to 2204-4436 mg/m^3.

Genetic Toxicity

Data on the mutagenicity and genotoxicity of 1,2-DCP have been reviewed and summarized in WHO (1993). 1,2-DCP has been tested for its mutagenic activity in *Salmonella typhimurium*, *Saccharomyces cervisiae*, and *Streptomyces coelicolor* (De Lorenzo et al., 1977; Priston et al., 1983; Stolzenberg and Hine, 1980; Carere and Morpurgo, 1981; Haworth et al., 1983; NTP, 1986). Results in most studies on *S. typhimurium* TA100 and TA1535 were positive, with and without metabolic activation, but negative results were obtained with TA98, TA1537, TA1538, *S. cerevisiae*, and *S. coelicolor*.

1,2-DCP did not induce crossing-over, mitotic nondisjunction or haploidization in *Aspergillus nidulans* in a plate incorporation assay using a single dose of 154 mM (Crebelli et al., 1984; HSDB, 1998).

1,2-DCP induced sister chromatid exchanges and chromosome aberrations in Chinese hamster ovary cells, both with and without metabolic activation (NTP, 1986; Von Der Hude et al., 1987).

1,2-DCP was tested by injection in germ cells and inhalation in *Drosophila melanogaster*, using the sex-linked mutation for their mutagenicity (Woodruff et al., 1985). The results were negative.

1,2-DCP was not mutagenic in a dominant lethal assay in male Sprague-Dawley rats (WHO, 1993; citing Hanley et al., 1989). Rats were exposed continuously to concentrations of 1,2-DCP ranging up to 2.4 g/L in drinking water.

Developmental and Reproductive Toxicity

Groups of Sprague-Dawley rats (30/sex/dose) were given 1,2-DCP in drinking water at concentrations of 0, 0.24, 1, or 2.4 g/L (w/v), over two generations. [These concentrations of 1,2-DCP are equivalent to 0, 33.6, 140, or 336 mg/kg-day (WHO, 1993).] Decreased water palatability resulted in reduced water consumption at all dose levels in both the F_0 and F_1 generations, causing dose-related decreases in parental body weight at the two highest doses levels. Body weights were significantly reduced in both generations exposed to 2.4 g/L compared to controls. These differences in water intake and body weights were also evident among females during gestation and/or lactation. The 0.24 g/L dose level resulted in a minor effect on water consumption and body weights, but no adverse effects on the animals in this group. There were no treatment-related gross pathological changes reported in any dose group. Histological changes were limited to increased hepatocellular granularity in both sexes in both generations at all dose levels. Reproductive function and morphology were unaffected in males and females of either generation. Significantly lower neonatal body weight and slightly increased neonatal mortality in litters of dams of the high-dose group were considered by the study authors to be secondary to the decreased maternal water intake, rather than a direct effect of 1,2-DCP exposure. There were no neonatal effects at the two lower concentrations. In addition, no evidence of dominant lethal toxicity was observed in males exposed continuously to concentrations of 1,2-DCP of up to 2.4 g/L in drinking water. A NOAEL of 0.24 g/L (33.6 mg/kg-day) was identified for adults, while the reproductive NOAEL is 1 g/L (140 mg/kg-day) (Kirk et al., 1990; as summarized by WHO, 1993 and Sullivan et al., 1993; Hanley et al., 1992).

In a more recent study (Kirk et al., 1995), 1,2-DCP was administered by oral gavage to pregnant Sprague-Dawley rats (30/group) on gestation days 6-15 at doses of 0, 10, 30, or 125 mg/kg-day. Maternal toxicity was observed at the highest dose level, as evidenced by transient central nervous system depression (decreased movement, muscle tone, and extensor thrust reflex), decreased maternal body weight gain, and decreased feed consumption. Significant increases in the incidence of delayed ossification of skull bones were observed in fetuses from the highest dose group; however, Kirk et al. (1995) considered the effects to be secondary to maternal toxicity. No maternal or fetal effects were observed at 10 or 30 mg/kg-day. Based on these results, the authors identified a NOEL of 30 mg/kg-day.

In a parallel study by the same authors (Kirk et al., 1995), pregnant New Zealand white rabbits (18/group) were administered 1,2-DCP by oral gavage (0, 15, 50, or 150 mg/kg-day) on days 7-19 of gestation. Maternal toxicity was observed at the highest dose level, as evidenced by decreased food consumption (with intermittent episodes of anorexia), significantly lower weight gain, and anemia. Consistent with the results from the rat study described above, the only fetal effect reported was a significant increase in the incidence of delayed ossification of skull bones observed at the highest dose level. Again, this effect was considered by Kirk et al. (1995) to be secondary to maternal toxicity. Based on these results, a NOEL of 50 mg/kg-day is identified.

Male Sprague-Dawley rats (15-16/group) were administered 1,2-DCP by gavage five days/week at doses of 0, 100, 250, 500 or 1000 mg/kg for up to 13 weeks. In addition to increased mortality, lower body weight gain, and other endpoints of toxicity (see

Subchronic Toxicity), adverse reproductive effects were reported. Specifically, testicular degeneration, reduction in sperm density, and increased numbers of degenerate spermatogonia in the epididymis were detected within 10 days in animals of the highest dose group, and within 13 weeks in animals of the 500 mg/kg group. Lower doses caused manifestations of hemolytic anemia, but did not affect testes (Bruckner et al., 1989).

Noncancer Chronic Toxicity

1,2-DCP was administered to F344/N rats and B6C3F$_1$ mice (50/sex/dose) by gavage five days/week at doses of 0, 62 or 125 mg/kg (male rats) and 0, 125, or 250 mg/kg (female rats, and mice of both sexes) for two years (NTP, 1986). Among rats, throughout most of the study mean body weights of treated animals were lower than those of controls. Final body weights were 14% lower than controls for high-dose males, and 24% lower for high-dose females. In addition, survival was adversely affected in high-dose females, with only 16/50 animals surviving to the end of the study. The high-dose female rats had increased incidences of non-neoplastic liver lesions (i.e., clear-cell changes and necrosis), although there was no increase in the incidence of liver tumors in the female rats (see carcinogenicity section). Mammary gland hyperplasia was increased in the low-dose females, but not in the high-dose group. It was suggested that this finding might be due to the poor survival as well as an increased incidence of adenocarcinomas in the high-dose females. There were no treatment-related non-neoplastic effects observed in male rats.

Among mice in the NTP (1986) studies, no influence of growth was observed; however, survival of high-dose females was significantly decreased relative to controls. Decreased survival in high-dose females was due, in part, to reproductive tract infections. 1,2-DCP caused dose-related increases in non-neoplastic liver lesions (hepatocytomegaly and necrosis) in male mice, which were significantly higher at the highest dose level compared with controls. These effects did not occur at increased incidences in dosed female mice.

Carcinogenicity

In an inhalation study, 80 C3H mice were exposed to 400 ppm 1,2-DCP four to seven hours/day, five days/week for a total of 37 exposures (Heppel et al., 1948, as cited by U.S. EPA, 1990 and Reed et al., 1988). Only three mice survived the exposure period and subsequent seven month observation period. Histopathological examination of the three mice revealed multiple hepatomas; however, the significance of these data is uncertain due to the high mortality.

In a carcinogenicity study conducted by NTP, 1,2-DCP was administered to F344/N rats (50/sex/group) in corn oil by gavage five days/week for 103 weeks (NTP, 1986). Male rats received 0, 62 or 125 mg/kg (averaged over seven days/week these doses equal 0, 44.3 and 89.3 mg/kg-day, respectively). Female rats received 0, 125 or 250 mg/kg (0, 89.3 and 178.6 mg/kg-day, respectively). There were no treatment-related tumor incidences observed in males. Among female rats, a dose-related increase in the incidence of mammary gland adenocarcinomas was observed (1/50, 2/50 and 5/50). The overall incidence rate was not statistically significant; however, the incidence in the high-dose group was significantly higher than that of controls after adjustment for survival ($p<0.05$, Life Table Test and

Incidental Tumor Test). The majority of these tumors were found at the end of the study, and it was noted that mammary gland adenocarcinomas are relatively uncommon in female F344/N rats. Although the incidence of mammary gland adenocarcinomas was statistically significant, NTP concluded that the evidence of carcinogenicity in female rats was *equivocal*, based on the marginal increase in tumors that occurred along with decreased survival and weight gain.

In the same NTP study (NTP, 1986), 1,2-DCP was administered to $B6C3F_1$ mice (50/sex/group) in corn oil by gavage five days/week for 103 weeks at doses of 0, 125 or 250 mg/kg (0, 89.3 and 178.6 mg/kg-day, respectively). Survival was adversely affected in female mice, due in part to an increased incidence of reproductive tract infections. Liver tumors were increased among both male and female treated mice (Table 1). A significant dose-related trend was observed for liver adenomas in both sexes ($p<0.05$, Life Table Test), with the overall incidence statistically significant in high-dose males ($p<0.05$, Fisher Exact Test). There was an increase in the frequency of liver carcinomas in both sexes, but the incidences were not statistically significant. The overall incidences of combined liver tumors in high-dose males, and in low- and high-dose females, were significantly higher than those in controls. NTP concluded that there was *some evidence of carcinogenicity* for male and female $B6C3F_1$ mice exposed to 1,2-DCP.

Table 1. Tumor Incidence in 1,2-DCP-Treated $B6C3F_1$ Mice (NTP, 1986).

Dose (mg/kg)	Hepatocellular Adenomas		Hepatocellular Carcinomas		Combined Hepatocellular Adenoma or Carcinoma	
	Male[1]	Female[2]	Male[1]	Female[2]	Male[1]	Female[2]
0	7/50	1/47	11/50	1/47	18/50	2/47
125	10/47	5/43	17/47	3/43	26/47*	8/43*
250	17/50*	5/41	16/50	4/41	33/50*	9/41*

[1] Tumor incidence based on the effective number of animals (i.e., the number of animals with the tumor / number of animals alive at week 54, the week the first liver tumor was identified in male mice).
[2] Tumor incidence based on the effective number of animals (i.e., the number of animals with the tumor / number of animals alive at week 82, the week the first liver tumor was identified in female mice).
* Statistically significant increase in tumor incidence ($p<0.05$, Fisher Exact Test).

Toxicological Effects in Humans

Acute Toxicity

A 46-year-old male ingested 50 ml of a cleaning solvent containing 1,2-DCP (other components not specified) which resulted in coma followed by delirium, irreversible shock,

hepatic cytolysis, cardiac failure, and death within 36 hours. Histological examination revealed centrilobular and mediolobular hepatic necrosis (Larcan et al., 1977).

Two cases of disseminated intravascular coagulation syndrome (DIC) have been described in association with acute 1,2-DCP poisoning (Perbellini et al., 1985, as summarized by WHO, 1993). Adverse effects on the central nervous system, liver, and kidney functions were also noted; however, details were not provided.

Clinical observations have been described for three additional people hospitalized for 1,2-DCP poisoning (two poisoned by ingestion, one by inhalation). All three patients exhibited acute renal and hepatic damage, hemolytic anemia, and disseminated intravascular coagulation. Kidney biopsy of one of the patients showed acute tubular necrosis. Clinical observations were similar in all three patients, despite the different routes of exposure (Pozzi et al., 1985).

Ingestion of 1,2-DCP by a 49-year-old man in an attempted suicide resulted in toxic hepatitis with portal hypertension (Thorel et al., 1986, as summarized by WHO, 1993).

Subchronic Toxicity

No information was located.

Genetic Toxicity

No information was located.

Developmental and Reproductive Toxicity

No information was located.

Noncancer Chronic Toxicity

In a study of occupational exposure, 10 cases of contact dermatitis resulting from 1,2-DCP were studied (Baruffini et al., 1989). The patients (painters or metalworkers in the engineering industry) all had known contact with mixtures of solvents containing 10-40% 1,2-DCP. Patch tests were carried out with multiple concentrations of 1,2-DCP, as well as with other constituents of products used at work. All subjects showed a positive response (allergic contact dermatitis) to concentrations of 2% 1,2-DCP or more. The results in 120 control patients were negative.

Carcinogenicity

No information was located.

DOSE-RESPONSE ASSESSMENT

Noncarcinogenic Effects

Numerous reports have identified adverse noncancer effects in humans resulting from 1,2-DCP exposure; however, these reports do not provide adequate quantitative exposure estimates to establish a dose-response relationship.

Of the studies conducted in experimental animals, the most appropriate for the purposes of calculating a PHG in drinking water is the study by NTP (1986). In this study, the lowest dose of 1,2-DCP administered to female rats (125 mg/kg; 5 days/week; 2 years) resulted in increased incidence of mammary gland hyperplasia. Adjusting for discontinuous exposure, a LOAEL of 89.3 mg/kg-day is identified. This study does not provide a NOAEL.

The only other data from a chronic noncancer study is provided by Kirk *et al.* (1990). In this study, rats were administered 1,2-DCP in drinking water over two generations. Decreased water palatability resulted in reduced water consumption, causing dose-related decreases in parental body weight at the two highest dose levels. In addition, the authors reported that there was significantly lower neonatal body weights and slightly increased neonatal mortality in litters of dams of the high-dose group. These litter effects were considered by Kirk *et al.* to be secondary to the decreased maternal water intake, rather than a direct effect of the 1,2-DCP exposure. Kirk *et al.* (1990) identified a NOAEL of 0.24 g/L (33.6 mg/kg-day) for adults, and a reproductive NOAEL of 1 g/L (140 mg/kg-day). While a drinking water study provides data from the most relevant route of exposure, and a study providing both a NOAEL and LOAEL is preferred for risk assessment purposes, the Kirk *et al.* (1990) study is complicated by the issue of water palatability. Since the observed effects were caused by decreased palatability, and not necessarily a toxic effect of the 1,2-DCP, this study was not used in the calculation of the PHG. Therefore, 89.3 mg/kg-day has been selected as the most appropriate value for the calculation of the PHG for drinking water for noncarcinogenic endpoints.

Carcinogenic Effects

U.S. EPA has classified 1,2-DCP as a group [B2] carcinogen based primarily on the results of the NTP (1986) bioassay. Results of the NTP study showed a statistically significant increase in the incidence of hepatocellular neoplasms, primarily adenomas, in male and female $B6C3F_1$ mice. The increases in the frequency of liver carcinomas in either male or female mice were not significant, but there was an statistically significant increase in combined hepatocellular adenomas and carcinomas in both sexes. In F344 rats, there were no statistically significant increases in tumors of any specific organ; however, there was a significant dose-related trend (by life table analysis) of mammary adenocarcinomas in females. The increased incidence in the female rats is considered significant since the F344

rat has a relatively low background occurrence of these tumors. In addition, the high mortality observed during the course of the bioassay may have precluded higher tumor incidence observations (i.e., some animals that died may have developed tumors had they survived for the duration of the study.)

In addition to the NTP (1986) bioassay, U.S. EPA considered other evidence in the overall evaluation of the carcinogenicity of 1,2-DCP. 1,2-DCP has shown positive mutagenic activity in short-term tests. It is metabolized to 1,2-epoxypropane which is thought to have carcinogenic potential since other epoxy compounds are known carcinogens. Finally, 1,2-DCP itself is structurally similar to compounds with known carcinogenic activity in animal test systems (i.e., 1,2-dichloroethane, 1,2-dibromoethane, and 1,2-dibromo-3-chloropropane).

Considering the total weight of evidence, U.S. EPA has classified 1,2-DCP as a group [B2] carcinogen. OEHHA agrees with this assessment.

For the purpose of establishing the most sensitive site of tumor formation in the most sensitive sex and strain of experimental animals, cancer potencies/slope factors were calculated for the tumor incidences reported to be statistically significantly increased ($p<0.05$) and exposure-related in the NTP (1986) bioassay.

For the generation of cancer potencies, the Tox_Risk program (Version 3.5) was used which fit the linearized multistage (LMS) model to the data on tumor incidence (ICF Kaiser International, 1993). In accordance with U.S. EPA's proposed guidelines for carcinogenic risk assessment, the LMS model was used to estimate the lower 95% confidence limit on the dose associated with a 10% increase in tumor development (LED_{10}) (U.S. EPA, 1996). At doses below this point, a linear dose-response was assumed with which a cancer slope factor (CSF) was calculated. A theoretical excess individual cancer risk from exposure to 1,2-DCP was limited to the *de minimis* level of 10^{-6}. The results of these analyses are presented in Table 2 below. For comparison purposes, estimates of cancer potency were also made using the LMS model polynomial exclusively (q_1^*).

Following U.S. EPA guidance (U.S. EPA, 1996), interspecies scaling of cancer potencies derived from experimental animals (CSF_{animal} or $q_{1\ animal}^*$) to human potencies (CSF_{human} or $q_{1\ human}^*$) was based on the following relationship:

$$CSF_{human} = CSF_{animal} \times (\text{human body weight/animal body weight})^{1/4}$$

where, the default body weight is 70 kg for humans and 0.035 kg for mice.

The most sensitive site, gender and species for tumor development from 1,2-DCP was the combined incidence of hepatocellular adenomas and carcinomas observed in male mice in the NTP (1986) bioassay. The p-value of the least squares coefficient (χ^2) indicates a reasonable fit of the model polynomial to this experimental dataset. The CSF_{human} calculated from this dataset is 3.6×10^{-2} $(mg/kg\text{-}day)^{-1}$. This value has been selected as the most appropriate for the calculation of the PHG for drinking water for carcinogenic endpoints.

Table 2. Cancer Potencies for 1,2-DCP Based on Results from the NTP (1986) Bioassay.

Data sets B6C3F1 Mice	**$q_1^*_{animal}$ $(mg/kg\text{-}d)^{-1}$**	**$q_1^*_{human}$ $(mg/kg\text{-}d)^{-1}$**	**χ^2**	**p**	**k**	**MLE_{10} (mg/kg-d)**	**LED_{10} (mg/kg-d)**	**CSF_{animal} $(mg/kg\text{-}d)^{-1}$**	**CSF_{human} $(mg/kg\text{-}d)^{-1}$**
Liver Adenomas Male	2.4E-3	1.6E-2	0	1	2	100	44	2.2E-3	1.5E-2
Combined Liver Tumors Male	5.7E-3	3.8E-2	0.05	0.83	2	29	19	5.4E-3	3.6E-2
Combined Liver Tumors Female	2.2E-3	1.5E-2	0.55	0.46	2	80	48	2.1E-3	1.4E-2

Note: The q_1^* is the carcinogenic potency determined exclusively from the polynomial by the linearized multistage (LMS) model (previous cancer risk assessment methodology). χ^2 is the value of the Chi-squared goodness of fit statistic; p is the significance of the Chi-squared value where a criterion of $p \geq 0.05$ is considered an adequate fit of the polynomial equation to a data set; k is the number of non-zero doses used in the fitting procedure. MLE_{10} is the maximum likelihood estimate of the dose that corresponds to a 10% extra tumor response. LED_{10} is the 95% lower confidence limit on the MLE_{10} dose. The CSF is the carcinogenic slope factor calculated from the LED_{10} (derived by dividing 10% or 0.1 by the LED_{10}).

CALCULATION OF PHG

Calculations of concentrations of chemical contaminants in drinking water associated with negligible risks for carcinogens or noncarcinogens must take into account the toxicity of the chemical itself, as well as the potential exposure of individuals using the water. Tap water is used directly as drinking water, for preparing foods and beverages. It is also used and for bathing or showering, and in washing, flushing toilets and other household uses resulting in potential dermal and inhalation exposures.

Noncarcinogenic Effects

Calculation of a public health-protective concentration (C, in mg/L) for 1,2-dichloropropane in drinking water for noncarcinogenic endpoints follows the general equation:

$$C = \frac{NOAEL/LOAEL \times BW \times RSC}{UF \times L/day}$$

where,

NOAEL/LOAEL	=	No-observed-adverse-effect-level or lowest-observed-adverse-effect-level
BW	=	Adult body weight (a default of 70 kg for male or 60 kg for female)
RSC	=	Relative source contribution (a default of 20% to 80%)
UF	=	Uncertainty factors (typical defaults of a 10 to account for inter-species extrapolation, a 10 for uncertainty from the subchronic nature of the principal study and a 10 for potentially sensitive human subpopulations)
L/day	=	Daily volume of water consumed by an adult (a default of 2 L/day, or 4 Leq/day for VOCs)

For 1,2-DCP, the key study selected for the calculation of a PHG based on noncarcinogenic endpoints was that of NTP (1986). In this oral gavage study, the lowest dose of 1,2-DCP administered to female rats (125 mg/kg; 5 days/week; 2 years) resulted in an increased incidence of mammary gland hyperplasia. Adjusting for discontinuous exposure, a LOAEL of 89.3 mg/kg-day was identified. This study does not provide a NOAEL.

There are two factors in the equation which make up the consideration of exposure: relative source contribution and water intake. For volatile compounds such as 1,2-DCP exposures through food are unlikely, so the relative source contribution (RSC; the estimate of the contribution of drinking water to the total exposure to a particular chemical contaminant) is set at 40% for VOCs, instead of the more commonly used default value of 20%. In addition, net exposures to VOCs in water could also be higher than estimated using the default of 2 L/day for water consumption, due to inhalation of vapors and dermal exposure during showering/bathing. U.S. EPA estimates that for VOCs, bathing/showering could add an

exposure equivalent to drinking 2 L/day, thus the total estimate for water intake in the PHG calculation is 4 liter equivalents per day (Leq/day).

Finally, the default value of 70 kg was used for the estimation of adult human body weight (BW), and a cumulative uncertainty factor (UF) of 1000 was applied (10 for the use of a LOAEL instead of a NOAEL, 10 to account for interspecies extrapolation, and 10 for potentially sensitive human subpopulations).

Therefore:

$$C = \frac{89.3 \text{ mg/kg-day} \times 70 \text{ kg} \times 0.4}{1000 \times 4 \text{ L/day}}$$

$$C = 0.63 \text{ mg/L (ppm), or } 630 \text{ µg/L (ppb)}$$

Carcinogenic Effects

The following general equation can be used to calculate the public health-protective concentration (C) for 1,2-dichloropropane in drinking water (in mg/L):

$$C = \frac{BW \times R}{q_1^* \text{ or CSF} \times L/day} = mg/L$$

where,

BW = Adult body weight (a default of 70 kg)

R = *De minimis* level for lifetime excess individual cancer risk (a default of 10^{-6})

q_1^* or CSF = q_1^* is the upper 95% confidence limit on the cancer potency slope calculated by the LMS model; CSF (cancer slope factor) is a potency derived from the lower 95% confidence limit on the 10% tumor dose (LED_{10}). CSF = 10% / LED_{10}. Both potency estimates (q_1^* and CSF) are converted to human equivalent [in $(mg/kg\text{-}day)^{-1}$] using $BW^{3/4}$ scaling.

L/day = Daily volume of water consumed by an adult (a default of 2 L/day, or 4 Leq/day for VOCs).

The purpose of calculating two potency estimates for a carcinogen is based on the fact that our current experience-base is almost wholly with the LMS model whereas the new methodology, proposed by U.S. EPA (1996) in its proposed guidelines for carcinogen risk assessment, is based on the LED_{10} which has little or no experience-base and may present problems. The LMS model focuses on the linear low-dose extrapolation, while the new method places a higher premium on fitting the observed data to estimate the ED_{10} and the 95% lower bound (LED_{10}), the point from which the low-dose extrapolation is made. In the case of 1,2-DCP, the potency estimates calculated using the two methodologies were consistent
(3.8×10^{-2} $(mg/kg\text{-}day)^{-1}$ and 3.6×10^{-2} $(mg/kg\text{-}day)^{-1}$). See Table 2.

The cancer slope factor selected for calculating the PHG was derived using the LED_{10} methodology. Using the combined incidence of hepatocellular adenomas and carcinomas observed in male mice in the NTP (1986) bioassay, a cancer potency estimate of 3.6×10^{-2} $(mg/kg\text{-}day)^{-1}$ was determined. A risk level of 10^{-6} is generally considered *de minimis*. The default value of 70 kg was used for the estimation of adult human body weight (BW). Net exposures to VOCs in water could be higher than estimated using the default of 2 L/day for water consumption, due to inhalation of vapors and dermal exposure during showering or bathing. U.S. EPA estimates that for VOCs, bathing/showering could add an exposure equivalent to drinking 2 L/day, thus the total estimate for water intake in the PHG calculation is 4 liter equivalents per day (Leq/day).

Therefore,

$$\text{PHG} = \frac{70\ \text{kg} \times 10^{-6}}{[3.6 \times 10^{-2}\ (\text{mg/kg-day})^{-1}] \times 4\ \text{L/day}}$$

$$= 0.000486\ \text{mg/L}$$

$$= 0.0005\ \text{mg/L (rounded)}$$

$$= 0.0005\ \text{ppm}$$

$$= 0.5\ \text{ppb}$$

OEHHA concludes that the most sensitive endpoint for assessing potential human health risks from chronic low level exposure to 1,2-DCP in drinking water is the carcinogenic endpoint. OEHHA therefore derived a PHG of 0.0005 mg/L (0.5 ppb) for 1,2-DCP in drinking water based on its carcinogenic potential. A PHG of 0.5 ppb is also considered to contain an adequate margin of safety to protect against potential noncancer adverse effects.

RISK CHARACTERIZATION

The PHG of 0.5 ppb was calculated based on the carcinogenic potency of 1,2-DCP. In calculating the PHG, a *de minimis* theoretical excess individual cancer risk level of 10^{-6} was assumed. The corresponding values for cancer risk levels of 10^{-5} or 10^{-4} are 5 and 50 ppb, respectively.

The primary sources of uncertainty in the development of the PHG for 1,2-dichloropropane in drinking water are also the general issues of uncertainty in any risk assessment, particularly inter- and intra-species extrapolation and relative source contribution (RSC).

For PHGs, our use of the RSC has, with a few exceptions, followed U.S. EPA drinking water risk assessment methodology. U.S. EPA has treated carcinogens differently from noncarcinogens with respect to the use of RSCs. For noncarcinogens, RfDs (in mg/kg-day), drinking water equivalent levels (DWELs, in mg/L) and MCLGs (in mg/L) are calculated using uncertainty factors (UFs), body weights and water consumption rates (L/day) and the RSC, respectively. The RSC range is 20% to 80% (0.2 to 0.8) depending on the scientific evidence.

U.S. EPA follows a general procedure in promulgating MCLGs:

1. if Group A and B carcinogens (i.e., strong evidence of carcinogenicity) MCLGs are set to zero,
2. if Group C (i.e., limited evidence of carcinogenicity), either an RfD approach is used (as with a noncarcinogen) but an additional UF of 1 to 10 (usually 10) is applied to account for the limited evidence of carcinogenicity, or a quantitative method (potency and low-dose extrapolation) is used and the MCLG is set in the 10^{-5} to 10^{-6} cancer risk range,
3. if Group D (i.e., inadequate or no animal evidence) an RfD approach is used to promulgate the MCLG.

For approaches that use low-dose extrapolation based on quantitative risk assessment, U.S. EPA does not factor in an RSC. The use of low-dose extrapolation is considered by U.S. EPA to be adequately health-protective without the additional source contributions. In developing PHGs, we have adopted the assumption that RSCs should not be factored in for carcinogens grouped in U.S. EPA categories A and B, and for C carcinogens for which we have calculated a cancer potency based on low-dose extrapolation. This is an area of uncertainty and scientific debate and it is not clear how this assumption impacts the overall health risk assessment.

OTHER REGULATORY STANDARDS AND GUIDELINES

In California, 1,2-DCP is listed under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) as a chemical known to the state to cause cancer.

U.S. EPA has classified 1,2-DCP as a group [B2] carcinogen, or probable human carcinogen. As such, U.S. EPA adopted a Maximum Contaminant Level Goal (MCLG) of zero and a Maximum Contaminant Level (MCL) of 0.005 mg/L for 1,2-DCP. The MCL of 0.005 mg/L is based on the sensitivity of generally available laboratory methods for detecting 1,2-DCP in drinking water. In this case, the MCL is the same as the practical quantitation limit, or PQL, and has been set to reduce the risk of cancer or other adverse health effects which have been observed in laboratory animals. U.S. EPA also states that drinking water that meets this standard is associated with little to none of this risk and is considered safe with respect to 1,2-dichloropropane. [Note: In U.S. EPA's Drinking Water Criteria Document for 1,2-DCP (U.S. EPA, 1990), carcinogenic risks are quantified, even though they do not serve as the basis for the federal MCL. U.S. EPA calculated a carcinogenic potency factor for humans based on the combined incidence of hepatocellular adenomas and carcinomas observed in male mice in the NTP (1986) study. The potency calculated by OEHHA is slightly lower than that calculated by U.S. EPA due to updated methodology proposed by U.S. EPA (U.S. EPA, 1996). Specifically, a surface area scaling factor (the human to animal body weight ratio raised to the 1/4 power) is now used in the calculation to relate the experimental animal doses to equivalent human doses, instead of the 1/3 power previously used.]

In WHO (1993), there is mention of a WHO guideline in preparation with a proposed value of 20 μg/L for 1,2-DCP in drinking water, although to our knowledge this value has not yet been adopted.

Working groups of the International Agency for Research on Cancer (IARC) considered 1,2-DCP in 1986 (IARC, 1986) and 1987 (IARC, 1987). In the more recent evaluation, IARC concluded that there is no evidence of the carcinogenicity of 1,2-DCP in humans, and limited evidence in experimental animals. IARC considers 1,2-DCP as a Group 3 carcinogen, not classifiable as to its carcinogenicity to humans.

Threshold Limit Values (TLVs) have been established for 1,2-DCP by the American Congress of Governmental Hygienists (ACGIH): 8-hour time-weighted average (TWA) of 75 ppm, short-term exposure limit (STEL) of 110 ppm. The Occupational Safety and Health Administration (OSHA) has adopted an 18-hour TWA and a 215-minute STEL of 75 ppm and 110 ppm, respectively. (HSDB, 1998)

Table 3. State Drinking Water Guidelines[1]

State	Drinking Water Guideline
Maine	5 μg/L
Minnesota	5 μg/L
Arizona	0.56 μg/L
Connecticut	5 μg/L

[1]Source: HSDB, 1998

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