

## **PUBLIC NOTICE: INITIATION OF RISK ASSESSMENTS FOR CHEMICALS IN DRINKING WATER**

### **A. Requirements**

The Calderon-Sher California Safe Drinking Water Act of 1996 (the Act, as amended in 1999 by Senate Bill 635) requires the Office of Environmental Health Hazard Assessment (OEHHA) to post notices on its Web site of water contaminants for which it is initiating a risk assessment in connection with the development of a public health goal (PHG) for the chemical in drinking water. The law also describes the purpose and general context of the PHGs. PHGs are concentrations of chemicals in drinking water that are not anticipated to produce adverse health effects following long-term exposures. These goals are non-regulatory in nature but are to be used as the health basis to update the state primary drinking water standards (maximum contaminant levels, or MCLs) established by the California Department of Health Services (DHS) for chemicals in drinking water subject to regulation.

The Act requires PHGs to be developed for the approximately 85 chemicals for which MCLs are presently available, and review and update of the risk assessments at least every five years. Other chemicals may be added to the list by legislative or interdepartmental request. Opportunities for public comment and peer review are provided.

### **B. Implementation**

OEHHA has published 54 PHGs as of April 2001. The technical support documents for the published PHGs are posted on the OEHHA Web site at [www.oehha.ca.gov](http://www.oehha.ca.gov), along with draft documents for proposed PHGs for five other chemicals that have gone through public reviews to be published this year.

Twelve (12) PHGs are undergoing internal preparation and will be released for public review this year. A 45-day public comment period will be provided after posting, followed by a public workshop. Scientific peer reviews are arranged through the University of California. The overall process will include allotting time for revisions, further public comment, and preparing responses to comments. They are planned for publication in 2003.

We are now announcing initiation of the risk assessment process for an additional set of 15 PHGs. The first drafts for public review are planned for 2002. This will complete the entire list of chemicals with MCLs, plus a few other chemicals which have been added, i.e., methyl tertiary-butyl ether (MTBE), perchlorate and, most recently, hexavalent chromium. The present plan is for this final set of PHGs to be published in 2003.

### **C. PHGs soon to be released for public review**

Draft documents for the following chemicals are undergoing preparation, and are planned for release for public review as soon as possible (starting fourth quarter, 2001):

Arsenic	Chlorobenzene	Perchlorate
Asbestos	Diethylhexyl adipate	Silvex
Barium	Ethylene dibromide	1,1,2,2-Tetrachloroethane
Beryllium	Hexachlorobenzene	Toxaphene

### **D. Risk assessments under development**

Risk assessments are commencing for the following contaminants:

1,1-Dichloroethane	Polychlorinated biphenyls (PCBs)	Styrene
cis-1,2-Dichloroethylene	Radionuclides (gross alpha, beta)	1,1,1-Trichloroethane
trans-1,2-Dichloroethylene	Radium (-226 & -228)	1,1,2-Trichloroethane
dioxin (2,3,7,8-TCDD)	Selenium	Trihalomethanes
Molinate	Strontium	Tritium

A brief description of each contaminant, as well as a bibliography of references identified by OEHHA, is provided below. OEHHA hereby solicits the submission of pertinent information on these contaminants identified under Item D that could assist our office in preparing the risk assessments and deriving a PHG.

Information submitted to OEHHA in response to this request should not be proprietary in nature, because all information submitted is a matter of public record. In order for information to be considered by OEHHA as it prepares risk assessments, it must be submitted by December 31, 2001 to:

Edna Hernandez  
Office of Environmental Health Hazard Assessment  
1515 Clay St., 16<sup>th</sup> floor  
Oakland, California 94612

All relevant data submitted will be considered in the development of PHGs for the list of chemicals identified above in Item D. Draft documents will be available for discussion in a public workshop and public comment will be solicited as described above in Section B. The final risk assessments will be utilized by DHS in potential revisions to the MCLs for chemicals in drinking water, as described in more detail on the DHS Web site at [www.dhs.ca.gov/ps/ddwem/chemicals](http://www.dhs.ca.gov/ps/ddwem/chemicals).

## **E. Descriptions of chemicals or substances under review**

### **1,1-DICHLOROETHANE**

1,1-Dichloroethane (1,1-DCA) is an organic solvent used as a chemical intermediate in the synthesis of vinyl chloride and 1,1,1-trichloroethane (ATSDR, 1990). Vinyl chloride is used in the production of vinyl plastics and 1,1,1-trichloroethane is used extensively as a solvent and degreaser. 1,1-DCA is not manufactured in California (ATSDR, 1990), and the U.S. Environmental Protection Agency's (U.S. EPA) Toxic Release Inventory (U.S. EPA, 1999) for data extracted on May 4, 1999, showed no reported releases in California.

Analyses of 13,347 California groundwater sources of drinking water found 1,1-DCA in 68 samples at levels ranging from 0.51 to 30 ppb. No 1,1-DCA was found in any of the 754 surface water sources of drinking water sampled (DHS, 1999). Populations experiencing the highest exposures would likely be workers in occupations where 1,1-DCA is present in workplace air (ATSDR, 1990).

1,1-DCA has been used as a volatile anesthetic (Miller et al., 1965), but is not currently applied for that purpose. The toxicology data identified so far is very limited. No birth defects or teratogenic effects have been reported, although adverse developmental effects were observed at high doses (Schwetz et al., 1974). Only one chronic toxicity/carcinogenesis study was found (NCI, 1978). Both mice and rats were studied. Male mice had hepatocellular carcinomas in control and treatment groups. Female rats had significant evidence of two types of neoplasms, circulatory system hemangiosarcomas and mammary adenocarcinomas, but their low survival rate weakened the conclusions. The survival rate of male rats was too poor to assess carcinogenic potential of 1,1-DCA. The National Toxicology Program (NTP) concluded that the overall data provide limited evidence of carcinogenicity in animals. U.S. EPA concluded that this bioassay "provides limited evidence of the carcinogenicity of 1,1-DCA in Osborne-Mendel rats and B6C3F<sub>1</sub> mice...based on significant dose-related increases in the incidence of hemangiosarcomas at various sites and mammary carcinomas in female rats and statistically significant increases in the incidence of liver carcinoma in male mice and benign uterine polyps in female mice" (U.S. EPA, 2001). The *in vitro* genotoxicity data is contradictory and somewhat inconclusive. OEHHA considered the data strong enough to list 1,1-DCA as a chemical known to cause cancer under Proposition 65 (OEHHA, 1994), which was reviewed and sustained by the State's Scientific Review Panel (Portale and Associates, 1999).

U.S. EPA has not set a federal MCL or Maximum Contaminant Level Goal (MCLG) for 1,1-DCA. The California DHS established an MCL of 0.005 mg/L, or 5 parts per billion (ppb), in 1988 (DHS, 1988). The California MCL was computed using the lowest dose level to which male rats were exposed in the National Cancer Institute bioassay of 1,1-DCA (NCI, 1978). The reported effects used in the calculation were non-cancer endpoints, stated as "increased mortality, clinical signs of intoxication and depressed body weight gain"

## References

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## CIS- AND TRANS-1,2-DICHLOROETHYLENE

There are two isomeric forms of 1,2-dichloroethylene (1,2-DCE): cis-1,2 DCE (CASRN 156-59-2) and trans-1,2 DCE (CASRN 156-60-5). The two isomers are very similar; both are highly flammable, colorless liquids with a sharp, harsh odor. They are fairly volatile with a vapor pressure of 180 Torr (cis) and 265 Torr (trans) at 20° C and the vapors are heavier

than air. These chemicals are slightly soluble in water with a solubility of 3.5 g/L (cis) and 6.3 g/L (trans) (ATSDR, 1996).

1,2-DCE is used as a chemical intermediate in the synthesis of chlorinated solvents and compounds. It has also been used as a solvent for waxes, resins, perfumes, dyes, lacquers, thermoplastics, fats, and phenols. It is used in the extraction of oils and fats from fish and meat, and has been used as an extraction solvent for organic materials such as decaffeinated coffee. The trans isomer is more widely used in industry than the cis isomer or the commercial mixture (ATSDR, 1996).

1,2-DCE enters the atmosphere from chemical and manufacturing industrial processes. It can also enter water supplies via wastewater from the above-mentioned processes and also by leaching from waste disposal sites.

Sources of human exposure include process and fugitive emissions from production and use, evaporation from wastewater streams, landfills, and solvents, and leaching from landfills. Human exposure may also occur from contaminated tap water through consumption, inhalation during showering and dermal contact (ATSDR, 1996).

Like other halogenated solvents, 1,2-DCE is sedative at high doses. Inhalation of trans-1,2-DCE has resulted in liver and lung toxicity in animals. Humans breathing high levels of trans-1,2-DCE have reported feeling nauseous, drowsy, and fatigued. Ingestion of cis-1,2-DCE in animal studies has been shown to result in a diminished number of red blood cells as well as liver damage (ATSDR, 1996). Neither cis- nor trans-1,2-DCE has been adequately evaluated for carcinogenicity (U.S. EPA, 2001a,b).

The federal MCL for cis-1,2-DCE is 0.07 mg/L, and for trans-1,2-DCE is 0.1 mg/L (U.S. EPA, 1991). The California MCL for cis-1,2-DCE is 0.006 mg/L, and for trans-1,2-DCE is 0.01 mg/L (DHS, 2001). U.S. EPA has defined an oral reference dose (RfD) of 0.02 mg/kg-d for trans 1,2-DCE, based on an indication of liver damage in a mouse study (Barnes et al., 1985), but no RfD has been established for cis-1,2-DCE.

## References

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### **DIOXIN (2,3,7,8-TCDD)**

Chlorinated dibenzodioxins (dioxins) are three-ring aromatic hydrocarbons that can be formed as combustion byproducts or as side-products of synthetic chemical reactions. There are many different possible isomers, and mixtures of these are normally produced. The isomer 2,3,7,8-Tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD, or TCDD) has been found to be the most toxic, possibly because of its planar structure, and is the isomer of most interest when a specific chemical among the group is discussed. A PHG will be developed for this isomer.

The chemical stability, low volatility, and high lipophilicity of dioxins give them a long residence time in the environment, high soil binding, and a great potential for bioaccumulation in animals and humans. When released to water, these chemicals adsorb strongly to sediments and suspended matter (Jackson et al., 1986). Volatilization from water is slow.

TCDD has no specific uses, but the many isomeric dioxin forms are ubiquitous in urban settings. Dioxins are formed inadvertently during the production of many chlorinated organic chemicals, such as hexachlorophene and the herbicide 2,4,5-T. U.S. EPA suspended the registration of most uses of 2,4,5-T in 1979, and banned it in 1989 partly because of its TCDD content. Other sources of dioxins are hospital and municipal waste incineration, combustion of coal, wood, chemical wastes, and improper disposal of certain chlorinated chemical wastes (ATSDR, 1988; U.S. EPA, 2000). Dioxins are also released from fires of PVC-containing materials, in sewage from municipal wastewater, and in effluents from pulp and paper mills that use chlorine bleaching of the pulp.

Exposure of the general population occurs through inhalation of contaminated air resulting from incineration processes and consumption of animal products. Direct exposure to dioxins may also occur through inhalation of cigarette smoke. Infants are exposed to dioxins through ingestion of breast milk, derived from the dioxin residues accumulated in their mother's body fat. Occupational exposures may result from workers involved with incineration operations, handling pesticides which may contain TCDD impurities, or fire fighters and cleanup workers involved with PCB transformer fires.

TCDD is extremely toxic to some animal species, as indicated by its acute oral LD<sub>50s</sub> of 0.022 and 0.045 mg/kg for male and female rats, and only 0.0006 mg/kg (0.6 µg/kg) for female guinea pigs (Klaassen et al., 1986). Industrial and accidental exposures indicate that TCDD has a relatively low acute toxicity in humans, resulting in chloracne as well as acute irritation of the eyes, skin and respiratory tract (U.S. EPA, 1985; HSDB, 2001).

TCDD is a multi-site carcinogen in experimental animals (NTP, 1998). Several epidemiological studies have shown increased cancer risks after industrial exposures to TCDD and other dioxins (IARC, 1997; Steenland et al., 1999).

TCDD is also a potent fetotoxic agent in various animal species. In mice, it has been shown to induce kidney anomalies and cleft palate (Weber et al., 1985).

The International Agency for Research on Cancer (IARC), the U.S. National Toxicology Program (NTP) and the U.S. EPA have concluded in recent reviews that TCDD as well as related analogs are human carcinogens (NTP, 1998; IARC, 1997; U.S. EPA, 2000). U.S. EPA also concluded in its draft Dioxin Reassessment document that TCDD and its analogs can cause immune system alterations, reproductive, developmental and nervous system effects, endocrine disruption, altered lipid metabolism, liver damage and skin lesions in humans (U.S. EPA, 2000).

## References

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## **MOLINATE (ORDRAM)**

Molinate is a selective herbicide used to control the germination of grasses and broadleaf weeds in rice fields. Its registered trade name is Ordran, and its chemical name is *S*-ethyl hexahydro-1H-azepine-1-carbothioate. The Chemical Abstract Service (CAS) Registry Number is 2212-67-1. Molinate is a clear to amber-colored liquid with an aromatic or spicy odor. Its water solubility is 970 mg/L at 25°C and its vapor pressure is  $5.6 \times 10^{-3}$  mm Hg at 25°C, making it a volatile pesticide (HSDB, 2001).

During the years 1991 to 1997, an average of 1.35 million pounds of molinate was used yearly in California, the majority of which was used on rice (DPR, 1999a, 2000). The molinate products registered for use in California are Ordran 8-E (emulsifiable concentrate), which contains 8 pounds of active ingredient per gallon, and Ordran 15-GM (granules), which contains 15 pounds of active ingredient per 100 pounds (Zeneca Ag Products, 1999).

Molinate applied to rice paddies may volatilize into the air from both water and soil surfaces (HSDB, 2001). High temperatures and windy conditions increase the rate of volatilization. Molinate concentrations up to 23  $\mu\text{g}/\text{m}^3$  have been measured in air sampled near rice fields in Colusa County (Baker et al., 1996). Molinate was not detected in California groundwater wells sampled between July 1, 1997, and June 30, 1999 (DPR, 1999b, 2000). Molinate was detected in surface waters in the Sacramento Valley in a 1995 survey (Bennett et al., 1998), including sites at the Colusa Basin Drain (2.8 to 25  $\mu\text{g}/\text{L}$ ), Butte Slough (2.1 to 8.5  $\mu\text{g}/\text{L}$ ), and the Sacramento Raw Water Intake (0.12 and 0.16  $\mu\text{g}/\text{L}$ ).

Human exposure may occur through inhalation in the vicinity of a molinate-treated rice field, by dermal contact during occupational use, or possibly through ingestion of contaminated water or food (HSDB, 2001). A federal tolerance level for molinate in or on raw rice grain and straw is 0.1 ppm (HSDB, 2001).

Molinate has been shown to cause adverse reproductive and neurological effects in laboratory species (DPR, 1996). The U.S. EPA Carcinogenicity Peer Review Committee recommended in 1992 that molinate should be classified under Group C (possible human carcinogen) (U.S. EPA, 1992a). This was based on an increased incidence of combined kidney tumors in male rats exposed to 300 ppm molinate in the diet over their lifetime. U.S. EPA estimated a unit risk,  $Q_1^*$  (in human equivalents), for molinate of  $0.11 \text{ (mg/kg-d)}^{-1}$ , based on the kidney tumors, using a body weight<sup>2/3</sup> extrapolation (U.S. EPA, 1992b).

A California MCL of 20 µg/L (20 ppb) was established for molinate in 1988 (DHS, 1988). A federal MCL has not been developed; however, molinate has been placed on the drinking water contaminant candidate list published by the U.S EPA (1998).

## References

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## **POLYCHLORINATED BIPHENYL COMPOUNDS (PCBS)**

Polychlorinated biphenyls (PCBs, CAS Registry number 1336-36-3 for all PCBs) are complex mixtures of chlorinated biphenyl congeners, with the empirical formula of  $C_{12}H_{10-n}Cl_n$  where  $n$  (the number of chlorine atoms) is in the range 1-10. Theoretically, 209 congeners with different numbers and/or positions of chlorine atoms on the two phenyl rings are possible. PCBs may also contain impurities of polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzodioxins (PCDDs). The concentrations of individual congeners and impurities in commercial PCB mixtures would depend on the manufacturing conditions. Only about 130 of the possible 209 congeners are expected in the commercial technical mixtures (Safe, 1990).

In general PCBs are chemically inert, resistant to heat, non-flammable, and have a low vapor pressure and a high dielectric constant (i.e., low electrical conductivity). These properties made them valuable for industrial use (WHO, 1993). Several investigators have published physical properties such as solubility, vapor pressure, log  $K_{ow}$  values, and Henry's law constant for individual congeners (Dunnivant and Elzerman, 1988; Dunnivant et al., 1992; Falconer and Bidleman, 1994; Murphy et al., 1987; Sabljic and Guesten, 1989; Sabljic et al, 1993).

Commercial production of PCBs in the United States began in 1929 and ended in 1977 (IARC, 1978). The most frequent uses for these chemicals were as dielectrics in transformers and large capacitors and as heat resistant (cooling) liquids in heat transfer and hydraulic systems

(WHO, 1993). They were also used in formulations of lubricating and cutting oils and wax extenders, and as plasticizers in paints, flame-retardants, plastics and other compounds. PCBs are no longer produced in the United States, except under exemption for use as a mounting medium in microscopy, immersion oil in microscopy, optical liquid, and research and development (U.S. EPA, 2001a).

PCBs enter the environment through accidental spills and leakage, volatilization and surface runoff. Once released in the environment PCBs are stable, very persistent and accumulate in biological organisms. PCB residues are found chiefly in soil, sediment, and fatty biological tissues. Non-occupational exposure to PCBs is primarily through ingestion of animal protein (meat, fish, poultry, dairy products and oils and fats) contaminated with PCBs. Inhalation of contaminated air and ingestion of contaminated water are also additional sources of human exposure to PCBs.

General health effects described from the exposure to PCBs include systemic changes (respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, endocrine, dermal, and ocular), immunological/lymphoreticular, neurological, reproductive, developmental, genotoxic, and carcinogenic effects (ASTDR, 1998).

The U.S. EPA MCL for PCBs is 0.0005 mg/L (0.5 ppb) and the MCLG is zero (U.S. EPA, 2001b). The MCL is set at the practical quantitation limit for PCBs. This MCL was considered to be associated with a theoretical maximum lifetime excess individual cancer risk of  $10^{-4}$  which was calculated using an oral  $q_1^*$  of  $7.7 \text{ (mg/kg-d)}^{-1}$ . The current California MCL is 0.0005 mg/l (0.5 ppb) [DHS, 2001]. Oklahoma, Tennessee, Utah, Wisconsin, and Florida have also adopted an MCL of 0.0005 mg/L. New Hampshire has an MCL of 0.005  $\mu\text{g/L}$  and Kentucky has an MCL of 0.000079  $\mu\text{g/L}$ .

U.S. EPA has placed PCBs in Group B2 as a “probable human carcinogen” (IRIS, 1996). A cancer potency estimate using animal data for Aroclor 1260 was previously adopted by U.S. EPA for discussions of the MCL and MCLG. The California Environmental Protection Agency adopted cancer potency estimate for PCBs of  $2.2 \text{ (mg/kg-d)}^{-1}$  [OEHHA, 1999]. The differences were due to several factors such as not using a time-weighted average dose, a new cross-species slope factor, and a reevaluation of the tumor data. Under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65), PCBs are listed as a chemical known to the State of California to cause cancer and reproductive toxicity (OEHHA, 2001).

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## RADIONUCLIDES

This category in the water regulations includes:

Gross alpha	Radium 226 and 228	Tritium
Gross beta	Strontium	Uranium

OEHHA has a separate PHG for uranium, so the present efforts do not include this substance. Many naturally occurring substances and a few man-made ones have the potential to emit ionizing radiation, and are therefore referred to as radioactive. For the sake of simplicity, radioactive materials can be grouped into alpha, beta and photon emitters, depending on the particles or energy that they emit. The gross alpha and beta measures allow for the screening of nearly all known radioactive materials found in drinking water, according to their radioactive emissions, without chemical speciation. Radium 226/228 monitoring reflects alpha radiation. Strontium and tritium monitoring reflects beta radiation (U.S. EPA, 2000a,b).

Most prominent uses of radioactive compounds are in energy generation and medical procedures, both for treatment and diagnosis. Most of the radioactivity found in the environment comes from natural weathering of rocks bearing radioactive ores and natural radioactive decay. Some of the natural radioactivity occurs as a result of cosmic radiation, such as conversion of carbon 12 to carbon 14 and hydrogen to tritium, which occurs largely in the atmosphere. Some radioactivity is derived from various human activities, such as medical wastes, emissions from reactors (e.g., iodine and cesium isotopes) and fallout from nuclear explosions (e.g. strontium).

All individuals are exposed to radioactivity whether natural or man-made. The major sources of radiation exposure for the general population are cosmic rays and medical X-rays. Persons involved in occupations such as mining, flying, and medical or dental diagnostics have a higher degree of exposure to radioactivity. Drinking water is not considered to be a major source of exposure to radioactivity. Ionizing radiation in drinking water is usually due to naturally occurring radiation found in groundwater. When radioactive materials from human activities contaminate water, it is usually the result of leaks, improper waste storage, or transportation accidents.

The major health effect of concern with exposure to ionizing radiation is cancer. Ionizing radiation involves the application of energy or particles that have the ability to displace electrons from atoms. For the more penetrating forms of ionizing radiation, this may occur inside cells. This is particularly harmful when the radiation affects the deoxyribonucleic acid (DNA) of the cell, which can alter the genetic code, and result in altered cell function. This altered cell function is associated with the development of cancer. Based on health information obtained on atomic bomb blast survivors, it is established that persons exposed to higher amounts of radiation than background have an increased risk of getting cancer, and this risk increases with the amount of exposure. Other data on sensitivity to cancer-inducing effects of radiation comes from studies of uranium miners, who have an increased risk of lung cancer (U.S. EPA 1999).

Although not every radionuclide has been proven to be carcinogenic, based on the overall capacity to generate potentially harmful radiation, it is assumed that they are all potentially

carcinogenic. Therefore, it is desirable to minimize exposure to ionizing radiation whenever possible.

The standards for radioactivity are somewhat confusing because they may be based on absorbed radiation dose (in millirems, or mrem), radioactivity (in picoCuries per liter, or pCi/L), or on isotope concentration (in  $\mu\text{g/L}$ ), and may be based on different chemical groupings. The federal MCL for beta/photon emitters is 4 mrem/year, for gross alpha emissions is 15 pCi/L (not including radon or uranium), and for combined radium-226/228 is 5 pCi/L. The average annual isotope concentrations assumed to produce a total body or organ dose of 4 mrem/year are 8 pCi/L for strontium 90 and 20,000 pCi/L for tritium. These may be combined to meet the standard (U.S. EPA 2000a,b). The California MCL for gross alpha particle activity (including radium 226, but excluding radon and uranium) is 15 pCi/L, for gross beta particle activity is 50 pCi/L, and for combined radium 226 and 228 is 5 pCi/ liter. There are also separate standards for strontium at 8 pCi/L and tritium at 20,000 pCi/L (DHS, 2001).

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## SELENIUM

Selenium (Se) is a semi-metallic element and it exists in various chemical forms. The primary oxidation states of selenium are -2 (e.g.  $\text{H}_2\text{Se}$ , hydrogen selenide), 0 (e.g.  $\text{Se}^0$ ), +4 (e.g.  $\text{Na}_2\text{SeO}_3$ , sodium selenite) and +6 (e.g.  $\text{Na}_2\text{SeO}_4$ , sodium selenate). Selenium is known to exist in the atmosphere from sea spray, windblown mineral dust, biogenic materials, volcanic effluvia, or coal combustion emissions. The use of selenium in photocopiers may create elevated airborne levels in the workplace. Anthropogenic activities such as mining, smelting, the burning of coal and oil and application of fertilizers may contribute to local selenium deposition on soil.

Elemental selenium ( $\text{Se}^0$ ) is virtually insoluble in water. Selenium in water exists primarily as  $\text{Se}^{+4}$  or  $\text{Se}^{+6}$  in the form of biselenite, selenite and selenate ion. Selenium dioxide and selenium trioxide dissolve in water to form selenious acid and selenic acid, respectively, and the

corresponding salts are selenites and selenates. For  $\text{Se}^{+4}$ , biselenite is more abundant at the lower drinking water pH range of 6.5 to 8.5. At pH 8, biselenite and selenite are at about equal concentrations. For  $\text{Se}^{+6}$ , selenate would be the only species present. Sodium selenate in neutral or alkaline conditions is water soluble and stable, and is the usual form of selenium in water (ATSDR, 1996).

Selenium is used in photoelectric devices to conduct electricity. Selenium supplements for human and livestock diets are the largest pharmaceutical and agricultural uses of selenium (ATSDR, 1996). The primary source of selenium intake in humans originates from selenium in plants taken up from the soil and used as food, mainly in the form of selenomethionine incorporated into proteins. Brewer's yeast is another source for human and animal diets.

Selenium is an essential trace element in animals and humans. It has been used as a dietary supplement to optimize nutrition especially in poultry and livestock. Selenium deficiency diseases include exudative diathesis in poultry and white muscle disease in lambs, calves, horses, goats, poultry, rabbits, deer and rats. In humans, the observations of the Chinese Keshan disease and Kashin-Beck disease suggest strongly that poor selenium status is closely linked with susceptibility to the diseases. This view is accepted by the World Health Organization and the Food and Nutrition Board of the United States National Institute of Medicine (IOM, 2000). Recently, selenium has been reported to enhance immune functions (Kiremidjian-Schumacher et al., 1998) as well as to reduce cancer incidence (Clark et al., 1996.). Selenium compounds have been reported to inhibit or retard tumorigenesis in a variety of experimental animal models (Combs and Gray, 1998).

Selenium exerts its biological functions as selenocysteine residues specifically integrated in distinct proteins, for example, as an essential part of the enzyme glutathione peroxidase. Humans cannot synthesize selenomethionine but obtain it from diets. Exogenous selenium in drinking water occurs as selenite and selenate ions which are distinct from selenomethionine or selenocysteine-proteins.

The most characteristic sign of selenium exposure in humans and animals, under conditions of excess exposure to selenium diets and to the inorganic selenium salts is "garlic breath." Poisoning of farm animals had led to "blind staggers" (neurological condition in cattle characterized by motor incoordination, impaired vision, aimless wandering behavior, lassitude and ultimately paralysis and death) and "alkali disease" (general dullness, lack of vitality, emaciation, stiffness and lameness). In experimental animals, a more recent study (Abdo, 1994) reported that sodium selenate and sodium selenite were more toxic to rats than mice based on mortality, bodyweight depression and renal lesions. In humans, the principal manifestation of selenium toxicity are brittleness and loss of hair and nails, and a skin rash. More detailed information on chronic toxicity has been described by Yang et al. (1983) based on endemic selenosis in Enshi County, China, which resulted from dietary intake (of crops grown in soil affected by selenium-rich coal), and effects were observed on hair nail, skin, the nervous system and teeth. Yang et al. (1989a,b, 1994, 1995) analyzed the Enshi County data, used blood levels of selenium to provide an index of selenium intake and included brittle fingernails as a toxic endpoint. The manifestations of selenium intoxication in the skin and integument have been ascribed to the replacement of sulfur in keratin or keratin-associated proteins by selenium

(Abdo, 1994; Yang et al., 1983, 1994; IOM, 2000). A study in the United States in the seleniferous region of eastern Wyoming and western South Dakota did not find physical or clinical changes or symptoms of selenium toxicity (Longnecker et al., 1991).

The U.S. EPA MCL and MCLG for selenium is 0.05 mg/L. The California MCL for selenium is also 0.05 mg/L [California Code of Regulations (CCR) Title 22 for inorganic chemicals Section 64468.1]. The FDA has established an acceptable concentration for selenium in bottled water at 0.01 mg/L.

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## **STYRENE**

Styrene is a flammable, volatile liquid with a penetrating odor. Low levels of styrene occur in some foods, probably as a result of microbial action, and small amounts are permitted for flavoring purposes. The major source of styrene is industrial synthesis. Styrene is used in the production of polystyrene plastics and resins from which are manufactured many industrial and consumer products (e.g., luggage, construction and packaging materials, tub/shower units and boats (ATSDR, 1992; U.S. EPA, 1994; Steele, 1995, FDA, 1999).

Human exposure to styrene occurs under occupational and environmental conditions. OSHA (2001) estimates about 90,000 workers are exposed to styrene. Environmental exposure occurs during the release of styrene during transportation, manufacture and storage activities, during human activities such as smoking cigarettes or breathing automobile exhaust, and during the use of consumer products (ATSDR, 1992; U.S. EPA, 1994). Exposure to styrene in consumer products may arise through the breakdown of styrene polymers (ATSDR, 1992; U.S. EPA, 1994).

Because styrene does not bind well to soil, it is able to move through the ground and into groundwater (U.S. EPA, 1994), where it has been detected at hazardous waste sites (ATSDR, 1992). Exposure to styrene by inhalation is also possible during its evaporation from water (ATSDR, 1992; U.S. EPA, 1994). In California, no styrene was detected in surface water discharges in 1998 from facilities that report under the Toxics Release Inventory (TRI) program, although nationwide, surface water discharges of about 13,000 pounds of styrene were reported (U.S. EPA, 2000).

In high-level, acute exposures, styrene is a sedative. At lower levels in humans, nausea, impaired reaction times and impaired vestibular function have been reported (Arlien-Soborg, 1992; OEHHA, 1999). Eye and throat irritation have also been observed among acutely exposed humans (OEHHA, 1999).

Decrements in central and peripheral nervous function resulting from chronic exposure to styrene have been documented in several occupational studies (Arlie-Soborg, 1992; OEHHA, 2001). Among styrene exposed workers in the reinforced plastics industry, excess deaths were observed for pancreatitis, degenerative disorders of the myocardium and all central nervous system diseases (in particular epilepsy) (OEHHA, 2001; Welp et al., 1996). Endpoints associated with altered catecholamine metabolism have been observed in occupational studies (OEHHA, 2001).

Genotoxic effects (e.g., DNA adducts and chromosomal aberrations) have been observed in many but not all studies of styrene exposed workers. In isolated human whole blood or lymphocyte cultures, styrene induced DNA strand breaks, sister chromatid exchange, micronuclei or chromosomal aberrations have been observed (IARC, 1994).

Acute exposures of laboratory animals to styrene can cause irritation and central nervous system decrements. Exposure of mice to styrene by inhalation resulted in liver damage. Multiple administrations of styrene to mice resulted in suppressed antibody and enhanced hypersensitivity responses (OEHHA, 1999).

Subchronic inhalation exposures of mice resulted in lesions in the lung olfactory epithelium, forestomach and adrenal gland. Mice exposed for two years by inhalation to styrene exhibited liver necrosis, respiratory tract lesions and reduced body weight gain (OEHHA, 2001; Cruzan et al., 2001). Rats subchronically exposed to styrene exhibited alterations in the astroglial filaments and lesions of the respiratory tract (OEHHA, 2001).

Many developmental toxicity studies have been carried out on styrene (e.g. Murray et al., 1978; Kishi et al., 1995) and these will be analyzed during the development of the PHG. The weight of evidence suggests that high doses of styrene may damage the developing nervous system (Brown et al., 2000).

Styrene has been classified as possibly carcinogenic to humans (Group 2B) by the International Agency for Research on Cancer (IARC, 1994). Mice exposed for two years by inhalation to styrene developed bronchiolar-alveolar adenoma and carcinoma (Cruzan et al., 2001). In one strain of mice that received styrene by gavage for the first 16 weeks of life, there was an increased incidence of lung tumors, whereas in a different strain of mice that received styrene by gavage for 120 weeks from birth, no tumors were observed (IARC, 1994). Mixed tumorigenicity results have been reported for rats (IARC, 1994). Rats exposed for one year to styrene vapors exhibited an increased mammary tumor incidence which was statistically significant at the high dose (IARC, 1994). In a drinking water study (Beliles et al., 1985) in which rats were exposed to styrene for two years, the authors reported no increased incidences of tumors.

*In vivo* genotoxicity has been documented in many but not all studies in mice and rats (IARC, 1994). DNA strand breaks, mutation at the *hprt* locus and sister chromatid exchange were observed *in vitro* in mammalian cell cultures, and metabolic activation was often required (IARC, 1994). Gene conversion but not forward mutation occurred in yeast, and sex-linked lethal mutations but not aneuploidy were observed in flies (IARC, 1994). Bacterial mutagenicity results are inconsistent and positive responses require metabolic activation (IARC, 1994).

The federal MCL and MCLG for styrene in drinking water is 100 ppb, based on liver, kidney and blood effects in a chronic study (IRIS, 2001). The California MCL is the same, based on the same endpoints (DHS, 2001).

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## **1,1,1-TRICHLOROETHANE**

1,1,1-trichloroethane (1,1,1-TCA), or methyl chloroform (CAS RN 71-55-6) is a clear liquid chlorinated hydrocarbon with a sweet, chloroform-like odor. It is moderately volatile with a vapor pressure of 127 Torr at 25°C. The chemical is slightly soluble in water with a solubility of 4.4 g/L at 20°C (U.S. EPA, 2001).

1,1,1-TCA has been used as a chemical intermediate in the production of organic chemicals, as a coolant and lubricant in metal cutting oils, and as a component of inks and drain cleaners. The solvent uses have included vapor degreasing, precision instrument cleaning, textile processing and dyeing (U.S. EPA, 2001).

1,1,1-TCA enters the atmosphere as a vapor from degreasing, cleaning, and other industrial processes. It can also enter water supplies via wastewater from the above-mentioned processes and also from leaching from landfills. Earlier estimates of the discharge of 1,1,1-TCA waste to the United States environment were as high as 800,000 pounds annually (U.S. EPA, 2001). These emissions have now been curtailed because of concern over the contribution of this chemical as a greenhouse gas. Production of 1,1,1-TCA was stopped as of January 1, 1996 under the Montreal Protocol (U.S. EPA, 1996).

1,1,1-TCA can evaporate from water surfaces, with evaporation half-lives ranges of a few hours (laboratory), 3-29 hours (rivers), and about 4-12 days for ponds and lakes. Little of the chemical will be lost by adsorption to soil, with a biodegradation half-life in aquifers of 321 days. Atmospheric degradation proceeds slowly in the troposphere and more rapidly in the stratosphere, where photolysis occurs. Human exposure to 1,1,1-TCA is primarily from

occupational exposure, from ambient air near industrial sources and contaminated drinking water (U.S. EPA, 2001).

Like other chlorinated solvents, 1,1,1-TCA causes acute sedation (Bruckner et al., 2001). Although it appears to have less potential for acute hepatotoxicity than many similar solvents, it can induce hepatic cytochrome P450 enzymes. In animal tests, chronic exposure resulted in damage to liver, nervous system, and circulatory system, and a decreased number of offspring in reproductive tests. In oral and inhalation cancer bioassays, no evidence of carcinogenicity was found (NCI, 1977; Maltoni et al., 1986, Quast et al., 1988). U.S. EPA has classified 1,1,1-TCA into group D, not classifiable as to human carcinogenicity (IRIS, 2001).

The federal MCL and MCLG for 1,1,1-TCA are the same, 0.2 mg/L. The California MCL is also 0.2 mg/L (DHS, 2001).

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## **1,1,2-TRICHLOROETHANE**

1,1,2-trichloroethane (1,1,2-TCA) (CASRN 79-00-5) is a clear liquid chlorinated hydrocarbon chemical with a pleasant, chloroform-like odor. It is moderately volatile with a vapor pressure of 23 Torr at 25°C. The chemical is slightly soluble in water with a solubility of 4.4 g/L at 20°C (U.S. EPA, 2001).

1,1,2-TCA is used as a chemical intermediate in the production of 1,1-dichloroethylene, in the production of adhesives, Teflon tubing, in lacquers and paints, and as a solvent for fats, waxes, and oils (U.S. EPA, 2001).

1,1,2-TCA enters the atmosphere from chemical and manufacturing industrial processes. It can enter water supplies via wastewater from the above mentioned processes and also from leaching from landfills. The U.S. EPA estimated the gross annual discharge of 1,1,2-TCA waste to the United States environment to be about four million pounds (U.S. EPA, 2001).

1,1,2-TCA readily evaporates from water surfaces. Little of the chemical will be lost by adsorption to sediment or biodegradation. The atmospheric half-life is 24-50 days in unpolluted atmospheres to a few days in polluted atmospheres; and hydroxyl radical photodegradation is the principal atmospheric removal process. Human exposure to 1,1,2-TCA is primarily from occupational exposure, ambient air near industrial sources and contaminated drinking water (U.S. EPA, 2001).

Potentially, 1,1,2-TCA may cause irritation of the gastrointestinal tract, hemorrhages of the lungs, and pale liver on an acute exposure basis. Chronic exposure has the potential to cause damage to liver and kidneys at exposures above the MCL. There is limited evidence of potential carcinogenicity in animals (IARC, 1999; U.S. EPA, 2001).

The federal MCL value for 1,1,2-trichloroethane is 0.005 mg/L. The California MCL is also 0.005 mg/L (DHS, 2001). The U.S. EPA RfD is 0.004 mg/kg-d based on changes in serum chemistry indicative of adverse effects on the liver (Sanders et. al., 1985; White et al., 1985; IRIS, 2001).

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## **TRIHALOMETHANES**

The trihalomethanes (THMs) represent an important group of drinking water disinfection byproducts. Among the THMs the most commonly occurring in terms of water concentration is chloroform (CHCl<sub>3</sub>), followed by bromodichloromethane (CHBrCl<sub>2</sub>), dibromochloromethane (CHBr<sub>2</sub>Cl), and bromoform (CHBr<sub>3</sub>) (U.S. EPA, 1998c). These halogenated organic chemicals have relatively low solubility in water (0.1 to 0.5 percent). Their boiling points increase with increasing bromination, i.e., 61°C, 88°C, 122°C, and 150°C, respectively, for the above series.

In the United States, over 200 million people are served by public water systems that apply a disinfectant such as chlorine to water in order to provide protection against microbial contaminants. While these disinfectants are effective in controlling many microorganisms, they react with natural organic and inorganic matter in the water to form disinfection byproducts including THMs. Most of the human exposure to these chemicals occurs through consumption of drinking water treated with chlorine for disinfection. Volatilization of the disinfection byproducts in normal household uses of water will also result in some inhalation exposure.

Federal regulations controlling THMs in drinking water were established in 1979 with a MCL for total trihalomethanes (TTHMs) of 0.1 mg/L. In 1994 U.S. EPA (U.S. EPA, 1994) proposed that this level be reduced to 0.08 mg/L. In the same proposed rule, MCLGs were also listed for: chloroform, zero; bromodichloromethane, zero; dibromochloromethane, 0.06 mg/L; and bromoform, zero. The TTHM MCL of 0.08 mg/L became effective in 1998 (U.S. EPA, 1998b). Also in 1998 U.S. EPA proposed a much higher MCLG for chloroform of 0.3 mg/L, later adjusted to 0.07 mg/L based on the assumption of a nonlinear dose-response and a margin of exposure approach (U.S. EPA, 1998a,b). Other assessments of the health effects of chloroform include DHS, 1990 and an updated health risk assessment of chloroform in California groundwater produced by the Lawrence Livermore National Laboratory under contract to OEHHA (Bogen et al., 1992).

## **Chloroform**

IARC (1991) has determined that chloroform is possibly carcinogenic to humans, Group 2B. U.S. EPA has determined that chloroform is a probable human carcinogen, Group B2, and derived an oral slope factor of  $0.0061 \text{ (mg/kg-d)}^{-1}$  based on kidney tumors in male rats administered chloroform in drinking water (IRIS, 1999a; Jorgenson et al., 1985). Liver toxicity is the primary health effect following chloroform exposure. U.S. EPA has derived a drinking water unit risk of  $1.7 \times 10^{-7} \text{ (}\mu\text{g/L)}^{-1}$  and a negligible drinking water concentration of  $6 \text{ }\mu\text{g/L}$  for chloroform (IRIS, 1999a).

Chloroform is listed as a chemical known to the state to cause cancer under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65). A unit risk of  $5.3 \times 10^{-6} \text{ (}\mu\text{g/m}^3\text{)}^{-1}$  has been developed for chloroform (DHS, 1990). An oral cancer potency of  $0.031 \text{ (mg/kg-d)}^{-1}$  was also developed based on the linearized multistage model.

## **Bromodichloromethane (BDCM)**

IARC (1991) concluded that there was inadequate evidence for the carcinogenicity of BDCM in humans and sufficient evidence for the carcinogenicity of DBCM in experimental animals. U.S. EPA has classified BDCM as a probable human carcinogen, Group B2, and derived an oral slope factor of  $0.062 \text{ (mg/kg-d)}^{-1}$  based on kidney tubular cell adenoma and adenocarcinomas in B6C3F1 mice (NTP, 1987; IRIS 1999b). Genotoxicity and reproductive toxicity of BDCM has also been reported. U.S. EPA has derived a drinking water unit risk value of  $1.8 \times 10^{-6} \text{ (}\mu\text{g/L)}^{-1}$  and a negligible risk water concentration of  $0.6 \text{ }\mu\text{g/L}$  for BDCM (IRIS, 1999b). U.S. EPA has derived an oral RfD of  $0.02 \text{ mg/kg-d}$  for BDCM based on renal cytomegaly in a chronic mouse gavage bioassay (NTP, 1987; IRIS. 1999b). U.S. EPA (1998b) has also promulgated an MCLG of zero for BDCM in drinking water.

## **Dibromochloromethane (DBCM)**

IARC (1991) concluded that there was inadequate evidence for the carcinogenicity of DBCM in humans and limited evidence for the carcinogenicity of DBCM in experimental animals. The overall classification was Group 3, not classifiable as to its carcinogenicity to humans. Liver toxicity is the primary health effect following DBCM exposure. U.S. EPA has classified DBCM as a possible human carcinogen, Group C, and has derived an oral slope factor of  $0.084 \text{ (mg/kg-d)}^{-1}$  based on hepatocellular adenoma or carcinoma observed in female B6C3F1 mice (IRIS, 1999c) and a drinking water unit risk of  $2.4 \times 10^{-6} \text{ (}\mu\text{g/L)}^{-1}$ . U.S. EPA has also derived a negligible risk drinking water concentration of  $0.4 \text{ }\mu\text{g/L}$  for DBCM, and an oral RfD of  $0.02 \text{ mg/kg-d}$  based on hepatic lesions in a rat subchronic corn oil gavage study (IRIS, 1999c). U.S. EPA (1998b) has promulgated an MCLG of  $0.06 \text{ mg/L}$  for DBCM in drinking water.

## **Bromoform**

IARC (1991) concluded that there was inadequate evidence for the carcinogenicity of bromoform in humans and limited evidence for its carcinogenicity in experimental animals. They gave bromoform an overall classification of Group 3, not classifiable as to its carcinogenicity to humans. U.S. EPA has classified bromoform as a probable human carcinogen, Group B2, and derived an oral slope factor of  $0.0079 \text{ (mg/kg-d)}^{-1}$  for bromoform based on neoplastic lesion of the large intestine in female rats (IRIS, 1999d). Genotoxicity of bromoform has been reported. U.S. EPA has also derived a drinking water unit risk of  $2.3 \times 10^{-7} \text{ (}\mu\text{g/L)}^{-1}$  and a negligible risk drinking water concentration of  $4 \text{ }\mu\text{g/L}$  for bromoform (IRIS, 1999d), and has promulgated an MCLG of zero (U.S. EPA, 1998b).

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