# **Dichloromethane**

### Guideline

The maximum acceptable concentration (MAC) for dichloromethane in drinking water is 0.05 mg/L (50 µg/L).

# Identity, Use and Sources in the Environment

Dichloromethane (methylene chloride) is a highly volatile, colourless liquid that is completely miscible with a variety of lipophilic solvents and is appreciably soluble in water (0.02 g/mL at 20°C). It is used extensively as an industrial solvent, for paint stripping, as a degreasing agent and as an aerosol propellant. Dichloromethane is not manufactured in Canada, but approximately 11 kilotonnes were imported annually between 1980 and 1984, principally from the United States. 3

About 85% of the dichloromethane produced in the United States is estimated to be lost to the environment (and hence to the drinking water supply) via sewage treatment, whereas only a small fraction is lost as fugitive emissions to the atmosphere.<sup>2</sup>

# **Exposure**

Dichloromethane was detected in 30 to 53% of potable water samples taken from 30 treatment facilities across Canada. Mean concentrations ranged from 6 to 10  $\mu$ g/L, with a maximum of 50  $\mu$ g/L recorded in several instances. The total amount that would be ingested daily by drinking 1.5 L of water containing 8  $\mu$ g/L dichloromethane is 12.0  $\mu$ g. Because dichloromethane is a volatile compound, there is a potential for its release from tap water to indoor air.

Available information on the presence of dichloromethane in foods is limited to decaffeinated tea (0.5 to 16  $\mu$ g/g), decaffeinated coffee (0.5 to 4  $\mu$ g/g) and spice oleoresins (10 to 83  $\mu$ g/g).<sup>5–7</sup> Dichloromethane is used as an extraction solvent in the preparation of these foods, and the estimated intake by humans from these sources is considered to be very small. The usual background concentration of dichloromethane in ambient air

is no more than 50 ppt (180 ng/m<sup>3</sup>). Near industrial sources, concentrations range from 7.1 to 14.3 ppb (26 to 51  $\mu$ g/m<sup>3</sup>), averaged over one year.<sup>2</sup>

# **Analytical Methods and Treatment Technology**

Dichloromethane is detected by a purge and trap gas chromatographic procedure.<sup>8</sup> The practical quantitation limit (PQL) (based on the ability of laboratories to measure dichloromethane within reasonable limits of precision and accuracy) is 5 µg/L.<sup>9,10</sup>

Removal of volatile chlorinated aliphatic hydrocarbons similar to dichloromethane by packed tower aeration and granular activated carbon adsorption is estimated to be 90 to 99% effective. It would appear that, using advanced technology, a reduction to concentrations of dichloromethane below 1 µg/L is feasible.

### **Health Effects**

Pharmacokinetic studies with dichloromethane have demonstrated efficient uptake via the lung, some 55% being retained after inhalation of air containing between 250 and 750 ppm (900 and 2700 mg/m<sup>3</sup>).<sup>11,12</sup> Dichloromethane is also efficiently absorbed from the gastrointestinal tract from oil or aqueous solution,13 although dermal absorption is slow and relatively inefficient in humans. 14 Dichloromethane is rapidly and efficiently distributed to various organs and tissues. It crosses the blood-brain barrier, affecting neurological functions, 15 crosses the placental barrier 16 and is sequestered by body fat.<sup>12</sup> Metabolism proceeds via two major metabolic pathways. The predominant pathway at low doses involves a saturable P-450 microsomal oxidation producing carbon monoxide. The other is a cytosolic glutathione-dependent pathway, leading to the formation of carbon dioxide. 17,18 The mixed-function oxidase pathway is saturable when concentrations of about 500 ppm (1800 mg/m<sup>3</sup>) in air are inhaled, whereas the cytosolic pathway shows no signs of saturation at concentrations up to 10 000 ppm (36 000 mg/m<sup>3</sup>) in air.19 After administration by various routes, the

elimination of dichloromethane from the blood is dose-dependent and follows a two- or three-compartment mathematical model. 13,19–21

Health effects induced by dichloromethane have been studied in humans exposed to concentrations up to about 800 ppm (2880 mg/m<sup>3</sup>) in air. Exposure to 868 ppm (3125 mg/m<sup>3</sup>) induced signs of neurotoxicity, including feelings of "light-headedness," difficulties with speech articulation and hand-eve co-ordination impediments. Carboxyhaemoglobin levels also increased. 15 Chronic exposures to dichloromethane do not produce any demonstrable irreversible effects at concentrations up to about 500 ppm (1800 mg/m<sup>3</sup>).<sup>22</sup> In one case of excessive chronic exposure (300 to 1000 ppm, or  $1080 \text{ to } 3600 \text{ mg/m}^3$ , over three years), bilateral temporal lobe degeneration was ascribed either to the neurotoxic effects of dichloromethane or to increased carboxyhaemoglobin levels.<sup>23</sup> The results of epidemiological studies, designed (in part) to examine the carcinogenic potential of dichloromethane, have been negative because of the limitations of these studies (e.g., insufficient exposure to provide the statistical power to detect a significant carcinogenic effect,<sup>24</sup> or the lack of a latency period sufficient for the development of site-specific cancer). Precise conclusions cannot, therefore, be drawn.<sup>22</sup>

Acute inhalation exposures of animals to concentrations of 500 to 1000 ppm (1800 to 3600 mg/m³) indicate that the central nervous system is the primary target for dichloromethane.²5 Cardiovascular effects are seen after a five-minute exposure to 5000 ppm (18 000 mg/m³), and concentrations of 15 000 ppm (54 000 mg/m³) for six hours are lethal to rats and mice.²6-28 Chronic exposures to high concentrations (>5000 ppm or 18 000 mg/m³) result in hepatic and renal effects. Deaths are usually caused by pulmonary congestion.¹8,29 Dogs exposed to 10 000 ppm (36 000 mg/m³) for four hours per day, five days per week for eight weeks, showed centrilobular congestion and fatty degeneration of the liver, as well as effects on the central nervous system.²9

The results of a number of carcinogenicity bioassays of dichloromethane are equivocal and do not permit a clear conclusion regarding the carcinogenic potential of this compound. These studies, conducted by Dow Chemical U.S.A., the National Coffee Association, the National Toxicology Program (NTP) (gavage, in mice) and Theiss and his co-workers (intraperitoneal, in mice), have been extensively reviewed in the United States.<sup>2</sup>

The best-designed and most definitive study is the recent NTP inhalation study in rats and mice.<sup>30</sup> In this study, groups of 50 F344/N male or female rats were exposed, by inhalation, to concentrations of 0, 1000, 2000 or 4000 ppm (0, 3600, 7200 or 14 400 mg/m³) of

dichloromethane for six hours per day, five days per week for 102 weeks. The incidence of fibroadenomas or fibroadenomas and adenomas combined was significant for the high-dose males and showed a significant positive trend with increasing dose for the females. Mesotheliomas of the tunica vaginalis and other organs occurred in male rats with a significant dose-related trend. Mononuclear cell leukaemia in male and female rats also occurred with significant dose-related trends.

In a parallel (NTP) study, groups of  $50~B6C3F_1$  male and female mice were exposed to 0,2000 and 4000~ppm (0,7200~and  $14~400~mg/m^3$ ) of dichloromethane for six hours per day, five days per week for two years. Alveolar or bronchiolar adenomas, alveolar or bronchiolar carcinomas of the lung or the two combined occurred with significant positive trends in both males and females. Hepatocellular adenomas or carcinomas, as well as the two combined, occurred with significant positive trends in both male and female mice.

Dichloromethane is a weak mutagen in three strains of *Salmonella*<sup>31</sup> and causes gene conversions, mitotic recombination and reverse mutations in the yeast *Saccharomyces cerevisiae*.<sup>32</sup> Embryotoxicity and minor increases in skeletal abnormalities were apparent in rats and mice exposed to concentrations above 1000 ppm (3600 mg/m³), seven hours per day, on days 6 to 15 of gestation.<sup>33</sup>

# **Classification and Assessment**

The evidence for the carcinogenicity of dichloromethane is inadequate in humans, but evidence from animal studies (both sexes of two species) is sufficient to classify it in Group II — probably carcinogenic to man.

Using a physiologically based model, Andersen and his colleagues calculated the delivered "internal" dose to specific organs and tissues after administration by any route, not only of dichloromethane per se but also of its two major metabolites.<sup>34,35</sup> They pointed out that dichloromethane is not genotoxic and that the mixedfunction oxidase pathway, which proceeds via a putative formyl chloride intermediate, probably does not induce tumours and may be regarded as a detoxification pathway. There is good supporting evidence that the glutathione-S-transferase pathway, yielding S-chloromethyl glutathione, does result in tumour formation. Because the physiological blood flow, organ mass and volume parameters in rodents and man are known with reasonable certainty and the glutathione-S-transferase activities in man and several animal species are also known for specific organs, the empirical methods for species extrapolation used by the U.S. Environmental Protection Agency are not necessary. Further, the kinetics for both the mixedfunction oxidase and cytosolic metabolism are known.

The Andersen methodology allows the calculation of the actual dose of active metabolite delivered to the tumour-susceptible organs (the lung and the liver) in the rodent species used in the NTP carcinogenicity bioassay<sup>30</sup> for any exposure scenario.

Using the physiologically based pharmacokinetic model methodology to calculate the surrogate delivered dose to the liver\* and selecting the liver adenoma and carcinoma response in female mice in the robust linear extrapolation model, one can calculate that the unit lifetime risk associated with the ingestion of 1  $\mu$ g/L dichloromethane in drinking water is  $1.7 \times 10^{-9}$ . The estimated concentrations in drinking water corresponding to lifetime risks of  $10^{-5}$ ,  $10^{-6}$  and  $10^{-7}$ , based on the model described above,\*\* are 5900, 590 and 59  $\mu$ g/L, respectively.

### **Rationale**

Because dichloromethane has been classified in Group II (probably carcinogenic to man), the maximum acceptable concentration (MAC) is derived based on consideration of available practicable treatment technology and estimated lifetime cancer risks. Because the MAC must also be measurable by available analytical methods, the PQL is also taken into consideration in its derivation.

A MAC of 0.05 mg/L ( $50 \mu g/L$ ) for dichloromethane was established, therefore, on the basis of the following considerations:

- (1) The estimated unit lifetime risk associated with the ingestion of 1  $\mu$ g/L dichloromethane in drinking water is  $1.7 \times 10^{-9}$  (based on hepatocellular adenomas or carcinomas in female mice). Therefore, the estimated lifetime risk associated with the ingestion of drinking water containing 50  $\mu$ g/L dichloromethane (i.e.,  $8.5 \times 10^{-8}$ ) is within a range that is considered to be "essentially negligible."
- (2) Although it is unlikely that dichloromethane concentrations are reduced significantly during conventional drinking water treatment processes, concentrations in Canadian drinking water supplies are generally considerably less than 50  $\mu$ g/L. It is likely that concentrations of dichloromethane below 1  $\mu$ g/L can be achieved by packed tower aeration and granular activated carbon adsorption.
- (3) The PQL (based on the ability of laboratories to measure dichloromethane within reasonable limits of precision and accuracy) is  $5 \mu g/L$ .

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<sup>\*</sup> The sum of the adenomas and carcinomas of the liver (counting each mouse no more than once) is selected because female mice gave the higher risk estimate (i.e., are more sensitive) and there were "suggestively positive findings" of liver tumours in the mice of the National Coffee Association drinking water study.

<sup>\*\*</sup> Average adult body weight = 70 kg; average daily intake of drinking water = 1.5 L.

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