



# *Benzene in Drinking Water*

Document for Public Comment

Prepared by the Federal-Provincial-Territorial  
Committee on Drinking Water

Consultation period ends  
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Document for Public Consultation

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## **Benzene in Drinking Water**

### **Purpose of consultation**

The Federal-Provincial-Territorial Committee on Drinking Water (CDW) has assessed the available information on benzene with the intent of revising the current drinking water guideline. The purpose of this consultation is to solicit comments on the proposed guideline, on the approach used for its development, and on the potential economic costs of implementing it, as well as to determine the availability of additional exposure data.

This document was developed to update the science on the existing drinking water guideline for benzene. The previous drinking water guideline for benzene, originally developed in 1987, was based on a 2-year cancer study in rats and mice and used a standard drinking water consumption rate of 1.5 L/day. It was developed using a robust linear extrapolation model, incorporating a surface area correction from rodents to humans. The current risk assessment is based on the same animal study, but using a modified consumption rate to account for absorption by inhalation and through the skin. It estimates the unit lifetime cancers risks by using a linearized multistage model with a scaling factor to correct for differences in metabolism between animals and humans.

The CDW has requested that this document be made available to the public and open for comment. Comments are appreciated, with accompanying rationale, where required. Comments can be sent to the CDW Secretariat via email at [water\\_eau@hc-sc.gc.ca](mailto:water_eau@hc-sc.gc.ca). If this is not feasible, comments may be sent by mail to the CDW Secretariat, Water, Air and Climate Change Bureau, Health Canada, 3rd Floor, 269 Laurier Avenue West, A.L. 4903D, Ottawa, Ontario K1A 0K9. All comments must be received before September 14, 2007.

It should be noted that this Guideline Technical Document on benzene in drinking water will be revised following evaluation of comments received, and a drinking water guideline will be established, if required. This document should be considered as a draft for comment only.

July 2007

## Benzene

### **Part I. Overview and Application**

#### **1.0 Proposed guideline**

*The proposed maximum acceptable concentration (MAC) for benzene in drinking water is 0.001 mg/L (1 µg/L).*

#### **2.0 Executive summary**

Although benzene is naturally occurring at low concentrations, its presence in the environment is mostly related to human activities. Gasoline contains low concentrations of benzene (below 1%), and emissions from vehicles are the main source of benzene in the environment. Benzene can be introduced into water by industrial effluents and atmospheric pollution.

Health Canada recently completed its review of the health risks associated with benzene in drinking water. This Guideline Technical Document reviews and assesses all identified health risks associated with benzene in drinking water, incorporating multiple routes of exposure to benzene from drinking water, including ingestion and both inhalation and skin absorption from showering and bathing. It assesses new studies and approaches, and takes into consideration the availability of appropriate treatment technology. From this review, a guideline for benzene in drinking water is proposed as a maximum acceptable concentration (MAC) of 0.001 mg/L (1 µg/L).

During its fall 2006 meeting, the Federal-Provincial-Territorial Committee on Drinking Water reviewed the proposed guideline for benzene and approved that this guideline and the corresponding Guideline Technical Document undergo public consultations.

#### **2.1 Health effects**

Benzene is classified as a human carcinogen. Both animal and human studies report similar toxic effects from exposure to benzene. The most sensitive effects are found in the blood-forming organs, including the bone marrow.

The MAC for benzene in drinking water is established based on the incidence of bone marrow effects and oral cancer in rats and mice, through the calculation of a lifetime unit risk. The MAC for benzene has been set at a level that is considered to be associated with an “essentially negligible” risk.

## 2.2 Exposure

Benzene can be found in both surface water and groundwater sources, although it is not generally a concern in surface water, because benzene tends to evaporate into the atmosphere. Some provinces and territories across Canada have detected benzene in drinking water supplies; however, data collected indicate that the levels are generally below the proposed MAC of 0.001 mg/L.

For most Canadians, the major source of exposure to benzene is air; this accounts for an estimated 98 to 99% of total benzene intake for Canadian non-smokers. Like food, drinking water is considered to be only a minor source of exposure to benzene.

## 2.3 Analysis and treatment

The establishment of a drinking water guideline must take into consideration the ability to both measure the contaminant and remove it from drinking water supplies. Benzene can be reliably measured to concentrations as low as 0.4 µg/L, which is below the proposed MAC.

Several municipal-scale treatment processes can remove benzene from drinking water to levels of 0.001 mg/L. At the residential scale, drinking water treatment devices are available that have been certified to reduce the concentrations of volatile organic compounds, including benzene, to 0.001 mg/L, although lower levels may be achieved with the use of these devices.

## 3.0 Application of the guideline

*Note: Specific guidance related to the implementation of drinking water guidelines should be obtained from the appropriate drinking water authority in the affected jurisdiction.*

Benzene is a human carcinogen, which means that exposure to any level in drinking water may increase the risk of cancer. Every effort should be made to maintain benzene levels in drinking water as low as reasonably achievable.

Benzene is not a concern for the majority of Canadians who rely on surface water as their source of drinking water, because it volatilizes easily. Benzene is not a widespread problem in Canada, affecting only some groundwater supplies; however, anthropogenic releases of benzene may occur at any stage of the production, storage, use, and transport of isolated benzene and crude oil and gasoline, including emissions resulting from fuel combustion.

The drinking water guideline is based on lifetime exposure (70 years) to benzene from drinking water. For drinking water supplies that occasionally experience short-term exceedances above the guideline value, it is suggested that a plan be developed and implemented to address these situations. For more significant, long-term exceedances that cannot be addressed through treatment, it is suggested that alternative sources of water for drinking and bathing be considered.

The guideline for a carcinogen is normally established at a level at which the increased cancer risk is “essentially negligible” when a person is exposed at that level in drinking water over a lifetime. In the context of drinking water guidelines, Health Canada has defined this term as a range from one new cancer above background levels per 100 000 people to one new cancer above background levels per 1 million people (i.e.,  $10^{-5}$  to  $10^{-6}$ ). In the case of benzene, the proposed MAC falls within this range and is therefore considered to be protective of human health. It is also achievable and measurable with current treatment technology.

The overall risk associated with exposure to benzene in drinking water is reported as a range, since lifetime exposure to benzene has been linked to several types of cancers in animals.

**Table 1:** Estimated lifetime range of risk of excess of cancers associated with various concentrations of benzene in drinking water.

Benzene Levels in Drinking Water	Estimated Lifetime Range of Risk of Excess Cancers <sup>a</sup> (x10 <sup>-6</sup> )
1 µg/L	1.2 - 4.9
5 µg/L	6.0 - 24.5

<sup>a</sup>The estimated lifetime risk of excess cancer is calculated from the risk range associated with ingesting 1µg/L of benzene in drinking water. This estimated unit risk range is  $1.14 \times 10^{-6}$  to  $4.85 \times 10^{-6}$ , with the lower bound representing oral cancer and the upper bound representing bone marrow tumours in male rats; malignant lymphoma in mice also falls within this range (Health Canada, 2005a).

## **Part II. Science and Technical Considerations**

### **4.0 Identity, use, and sources in the environment**

Benzene, the simplest homologue of the aromatic hydrocarbons, is a planar, cyclic molecule with six carbon atoms arranged in a regular hexagon. The molecular formula for benzene is  $C_6H_6$ . It is a volatile, colourless liquid with a characteristic odour; the odour threshold for benzene is 4.68 ppm.\* Benzene has a relatively high vapour pressure (10.1–13.2 kPa at 25°C), a high water solubility (820–2167 mg/L at 25°C), and a low log octanol/water partition coefficient (1.56–2.69) (Mackay et al., 1992).

Benzene is produced commercially from petroleum, natural gas, or coal. From 1988 to 2002, benzene production in Canada rose from 827 to 1142 kt per year; imports dropped from 29 to 2 kt per year, and exports rose from 92 to 210 kt per year (CPI, 2003). In Canada, benzene is produced in Ontario, Alberta, and Quebec. Benzene is used in industry as a volatile solvent and as an intermediate in the production of many chemicals, including ethylbenzene/styrene (used in plastics), cumene, linear alkyl benzene, and maleic anhydride (Jaques, 1990; CPI, 2003). The majority of benzene produced or imported into Canada is used in the production of ethylbenzene/styrene, with benzene usage for this purpose increasing from 582 kt in 1988 to 737 kt in 2002 (CPI, 2003). Benzene is also present in gasoline as an octane enhancer and anti-knock agent; since July 1999, however, levels of benzene in gasoline have been reduced to below 1% by volume.

Benzene is found naturally in the environment in very low concentrations; concentrations in the Atlantic and Pacific oceans have been reported to range between 100 and 200 parts per trillion (Singh and Zimmerman, 1992). Natural sources of benzene include volcanoes, crude oil, forest fires and plant volatiles (Graedel, 1978; IARC, 1982). Benzene may enter water and soil through petroleum seepage and weathering of exposed coal-containing rock. It can enter groundwater from petroliferous rocks and can enter air from volcanoes, forest fires, and releases of volatile chemicals from plants (Graedel, 1978; Westberg et al., 1981; Whelan et al., 1982; Fishbein, 1984; Slaine and Barker, 1990). Natural sources are believed to be generally low in comparison with anthropogenic sources (Rasmussen and Khalif, 1983; Rudolph et al., 1984). Anthropogenic releases of benzene may occur at any stage of the production, storage, use, and transport of isolated benzene and crude oil and gasoline, including emissions resulting from fuel combustion. Vehicular emissions constitute the main source of benzene in the environment.

The atmosphere and surface waters are the major environmental sinks for benzene due to its relatively high vapour pressure, moderate water solubility, and low octanol/water partition coefficient. Virtually all (99.9%) of the benzene released into the environment eventually distributes itself into the air (Wallace, 1989a). Volatilization and biodegradation are the major processes involved in the removal of benzene from water. The half-life of benzene in water 1 m deep is estimated to be 4.8 hours as a result of volatilization (ATSDR, 2005); ice cover will impair benzene volatilization from surface waters. Reported half-lives of benzene have ranged

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\* Conversion factor in air: 1 ppm = 3.19 mg/m<sup>3</sup> at 20°C and 101.3 kPa.



from 33 to 384 hours for aerobic biodegradation in surface waters; for anaerobic biodegradation in deeper waters or in groundwater, half-lives ranged from 28 days to 720 days (Vaishnav and Babeu, 1987; Howard et al., 1991).

It is estimated that every year in Canada, 34 kt of benzene are released into the atmosphere (Jaques, 1990); major sources include combustion of gasoline and diesel fuels, emissions during benzene production, primary iron and steel production, solvent uses, residential fuel combustion, and gasoline marketing. Benzene is generally introduced into water from industrial effluents and atmospheric pollution.

## 5.0 Exposure

### 5.1 Water

Monitoring results are available for benzene in surface water and groundwater; if benzene is present, its levels are generally less than 1 µg/L.

In Alberta, benzene levels in municipal treated surface water ranged from 0.01 to 4.92 µg/L (mean 0.28 µg/L, 30 samples) for 26 locations from 1998 to mid-2005; levels in more than 96% of samples were less than 1 µg/L. Levels in municipal treated groundwater ranged from 0.01 to 0.23 µg/L (mean 0.097 µg/L, 15 samples) for 11 locations for the same period. These ranges represent 45 detects out of a total of 1500 samples. Approximately 60 samples of raw “feed” water were analysed for benzene, and all samples had levels below the method detection limit (MDL); the reported MDLs ranged from 1.0 µg/L in 1988 to 0.1 µg/L from 1999 to 2005. Ambient benzene levels from six different river/stream sampling sites as part of an ambient monitoring program from 2000 to 2004 ranged from 0.02 to 0.42 µg/L; this range represented six detects out of a total of 860 samples (Alberta Department of Environment, 2005).

In Saskatchewan, levels of benzene in municipal treated surface water ranged from <0.2 µg/L to <1 µg/L (mean 0.25 µg/L, 30 samples) in nine locations from 1995 to 2005; levels in all samples were less than 1 µg/L. Municipal treated groundwater levels ranged from 0.1 to 1700 µg/L\*\* (mean 0.71 µg/L, 34 samples) for 13 locations from 1995 to 2005; levels in more than 91% of samples were less than 1 µg/L. The level of benzene in raw (pretreated) water from two locations using surface water and one location using groundwater was 0.2 µg/L (three samples). Municipal treated water from a mixed surface water and groundwater source for three locations over the same period had benzene levels ranging from 0.1 to 1 µg/L (mean 0.46 µg/L, 12 samples); levels in all of the samples were less than 1 µg/L (Saskatchewan Department of Environment and Resource Management, 2005). The reported MDLs ranged from 0.0005 to 1 µg/L, depending on the analytical method used.

Benzene was not detected in raw or municipal treated surface water or groundwater in Newfoundland sampled between 1995 and 2005 (detection limit 1 µg/L) (Newfoundland Department of Environment and Labour, 2005).

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\*\* This value represents a one-time sample taken near a leaky underground storage tank. Although it is included in the range, it has not been included in the calculation of the mean.

In Quebec, levels of benzene in municipal treated drinking water ranged from 0.03 to 3.6 µg/L (mean 0.35 µg/L, 26 samples) in 21 locations from 2001 to 2005; only one sample out of a total of 26 samples had a concentration greater than 1 µg/L. The above range represents 26 total detects out of 2388 samples from 191 locations that use either groundwater or surface water sources for drinking water. The remaining 2362 samples were reported as being below the limits of detection; the detection limits ranged from 0.03 to 2 µg/L, depending on the accredited laboratory used (Ministère de l'Environnement du Québec, 2005).

In Nova Scotia, levels of benzene in 104 municipally treated surface water or groundwater samples from 95 locations from 2001 to 2005 were all below the MDLs, which ranged from 0.5 to 1 µg/L (five samples out of the 104 total samples were reported as non-detects); levels of benzene in 27 raw (pretreated) surface water and groundwater samples were also reported as being below the MDL of 1 µg/L (six samples were reported as non-detects) (Nova Scotia Department of the Environment, 2005).

## 5.2 Food

Benzene has been detected in a variety of foods. The U.S. Food and Drug Administration (FDA) sponsored a 5-year study to determine the amount of volatile organics in food from 1996 to 2000. Benzene was found in a variety of foods, including dairy products — cheddar cheese, cream cheese, margarine, butter, sour cream; meats and fish — ground beef, bologna, hamburger, cheeseburger, pork, beef frankfurters, tuna canned in oil, chicken nuggets; desserts and baked goods — chocolate cake icing, sandwich cookie, chocolate chip cookies, graham crackers, sugar cookies, cake doughnuts with icing, apple pie, sweet roll danish, blueberry muffins; nuts and nut products — mixed nuts, peanut butter; fruits and vegetables — bananas, avocados, oranges, strawberries; and eggs. Concentrations of benzene in foods generally ranged from 1 to 190 µg/kg; some examples include: ground beef (9-190 µg/kg), bananas (11-132 µg/kg), carbonated cola (1-138 µg/kg), and coleslaw with dressing (11-102 µg/kg) (Fleming-Jones and Smith, 2003). Benzene detections in the above food types represented only a few detects per sample, indicating that food does not represent a significant source of benzene exposure. Further support is provided by a Canadian review of benzene exposures (Environment Canada and Health and Welfare Canada, 1993).

In another study by the U.S. FDA (2006), the Center for Food Safety and Applied Nutrition conducted an initial limited survey on benzene levels in beverages, with a focus on soft drinks that contain both benzoate salts and ascorbic or erythorbic acid. Over 100 soft drinks and other beverage samples were collected from retail stores in Maryland, Virginia, and Michigan. Two beverage products containing added benzoates and 27 beverage products containing both added benzoates and ascorbic acid had benzene levels above 1 µg/L. Four cranberry beverage products and one orange beverage product with added ascorbic acid and natural levels of benzoic acid (i.e., no added benzoates) also contained benzene above 1 µg/L. In general, however, most of the beverages sampled contained either no detectable benzene or levels below 1 µg/L. Exposure to heat and light can stimulate the formation of benzene in some beverages that contain benzoate salts and ascorbic acid (vitamin C). Benzoate salts are naturally present in some fruits and their juices, or sodium or potassium benzoate may be added to beverages to prevent the growth of bacteria, yeast, and moulds.

### 5.3 Air

In general, mean benzene concentrations in ambient air were found to be highest at sites influenced by industrial sources and urban sites and lowest at rural and suburban sites (Environment Canada, 2001). Mean benzene concentrations in Canadian ambient air between 1989 and 1998 ranged from 1.8 to 3.6  $\mu\text{g}/\text{m}^3$  for typical urban sites with no industrial source influences; mean benzene levels were found to range from as high as 10.3  $\mu\text{g}/\text{m}^3$  at an urban site in Sault Ste. Marie influenced by emissions from a coke oven/iron and steel mill facility to as low as 0.3  $\mu\text{g}/\text{m}^3$  at a rural remote site in Kejimikujik National Park, Nova Scotia (Environment Canada, 2001). Survey data from the period 1995–1997 showed mean concentrations at the urban/suburban sites ranging from 1.0 to 3.5  $\mu\text{g}/\text{m}^3$ , with approximately 78% (31 out of 40) of sites recording mean concentrations of less than 2.5  $\mu\text{g}/\text{m}^3$  (Environment Canada, 2001). Mean concentrations for rural sites reportedly ranged from 0.3 and 0.8  $\mu\text{g}/\text{m}^3$ . Sites near roadways or industrial sources had mean benzene concentrations ranging from 4.1 to 13.1  $\mu\text{g}/\text{m}^3$  (Environment Canada, 2001).

Benzene levels in indoor air are generally higher than those in outdoor air. Sources of benzene in indoor air include glues, paints, furniture wax, and some detergents. Zhu et al. (2005) measured indoor and outdoor air levels of benzene for 75 residences in Ottawa, Ontario, during the winter of 2002–2003. Indoor temperatures remained relatively constant ( $19 \pm 2^\circ\text{C}$ ), and the majority of participating homes were single family homes located in residential areas using natural gas as the heating source. The average age of the houses was 37 years, with a range from newly constructed to over 100 years old. Roughly 13% (10 homes) of the homes in the study were homes with smokers. Mean indoor air levels of benzene were reported as 2.85  $\mu\text{g}/\text{m}^3$  (range 0.025–20.99  $\mu\text{g}/\text{m}^3$ ),<sup>\*\*\*</sup> with a detection frequency of 97%; outdoor air sampling revealed a mean benzene level of 1.19  $\mu\text{g}/\text{m}^3$  (0.025–16.88  $\mu\text{g}/\text{m}^3$ ), with a detection frequency of 62%.

### 5.4 Consumer products

The general population may also be exposed to benzene through automobile-related activities and cigarette smoking. An average smoker (smoking 32 cigarettes per day with an average tar content) inhales approximately 1.8 mg of benzene per day, which is about 10 times the daily intake of a non-smoker; environmental tobacco smoke can also result in measurable increases in benzene intake (Wallace, 1989b, 1996; Thomas et al., 1993). Duarte-Davidson et al. (2001) compared the daily doses of rural non-smokers, urban non-smokers, urban passive smokers (non-smokers exposed to secondhand smoke), and urban smokers and found very little difference between the rural non-smokers' estimated absorbed dose of 70–75  $\mu\text{g}/\text{day}$  and the urban non-smokers' estimated absorbed dose of 89–95  $\mu\text{g}/\text{day}$ ; the absorbed dose for passive urban smokers was estimated to be 116–122  $\mu\text{g}/\text{day}$ , whereas smokers were estimated to be exposed to 516–522  $\mu\text{g}/\text{day}$ . On average, non-smokers in urban and rural environments have estimated benzene intakes of 1.15 and 1.5  $\mu\text{g}/\text{kg bw per day}$ . Daily doses were determined using time–activity patterns and inhalation and absorption rates, in conjunction with measured benzene air concentrations.

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<sup>\*\*\*</sup> Levels below the detection limit were reported as one-half of the MDL of 0.05  $\mu\text{g}/\text{m}^3$ .

Automobile-related activities can contribute to increased benzene intake through inhalation of gasoline fumes and from tailpipe emissions. Increased benzene exposure has been attributed to driving times, filling gas tanks, and indoor air of homes with attached garages (Wallace, 1989b). A 1990 German study analysed factors predicting human exposures to volatile organic compounds (VOCs) and found that cigarette smoking was the most significant determinant of benzene exposure; automobile-related activities, such as refuelling and driving, were found to be the second highest source of benzene exposure (Hoffmann et al., 2000).

## 5.5 Soil

Benzene contamination of soil generally results from the spilling or leaking of gasoline or other benzene-containing petroleum products from containment vessels, such as underground storage tanks. The primary pathways responsible for benzene loss from soil are volatilization to the atmosphere, runoff to surface water and groundwater, and, to a much lesser extent, biodegradation (Environment Canada and Health and Welfare Canada, 1993). Hydrocarbon-degrading microorganisms are ubiquitous in soil, and both sorbed and vapour-phase benzene are likely biodegraded under aerobic conditions (Rosenberg and Gutnick, 1981; English and Loehr, 1991); biodegradation practically ceases when conditions become anaerobic (Smith, 1990; Aelion and Bradley, 1991; Barbaro et al., 1991). Soil contamination does not lead directly to significant levels of human exposure to benzene, since benzene volatilizes rapidly from soil (IPCS, 1993). Benzene levels in the soil surrounding industrial facilities that produce or use benzene have been reported to range between <2 and 191 µg/kg (U.S. EPA, 1979; IARC, 1982).

## 5.6 Multi-route exposure through drinking water

Exposure to benzene in drinking water was previously assessed (Health Canada, 1986) using ingestion as the only route of exposure. Owing to benzene's high volatility, exposure by inhalation and dermal absorption during bathing and showering may also serve as important routes of exposure. Lindstrom et al. (1994) carried out a study looking at the exposure to benzene while showering with gasoline-contaminated groundwater in a home in North Carolina. The groundwater had a measured benzene concentration of 292 µg/L. Three 20-minute showers on consecutive days were reported to have resulted in peak shower-stall concentrations of 800–1670 µg/m<sup>3</sup>, with bathroom concentrations reaching 370–500 µg/m<sup>3</sup> and concentrations in the remainder of the house peaking 0.5–1 hours later at 40–140 µg/m<sup>3</sup>. The dose of benzene inhaled during the 20-minute shower ranged from 80 to 100 µg. A dermal dose of 160 µg was also determined using measured breath concentrations. The combined dose of about 250 µg from the 20-minute shower was found to be within the same magnitude of the mean total daily inhalation dose of about 200 µg for all non-smokers in the total exposure assessment methodology (TEAM) study (assuming 15 µg/m<sup>3</sup> × 14 m<sup>3</sup>/day alveolar inspiration) (Wallace, 1987).

To assess the overall exposure to benzene in drinking water, the relative contribution of each exposure route is assessed through a multi-route exposure assessment approach (Krishnan, 2004). Contributions developed through this approach are expressed in litre-equivalents (L-eq) per day. Both the dermal and inhalation routes of exposure for a volatile organic chemical are considered significant if they contribute to at least 10% of the drinking water consumption level

(Krishnan, 2004). Therefore, to determine whether dermal exposure represents a significant route of exposure for benzene, tier 1 of the multi-route exposure assessment determines whether or not this route of exposure contributes a minimum of 10% of the drinking water consumption level (i.e., 10% of 1.5 L = 0.15 L). The tier 1 goal of 0.15 L-eq is associated with a skin permeability coefficient ( $K_p$ ) for volatile organic chemicals of 0.024 cm/h. Since the  $K_p$  for benzene of 0.14 cm/h (Nakai et al., 1997) is greater than 0.024 cm/h, dermal absorption is considered to be significant during showering and bathing. Tier 2 of the assessment calculates what the L-eq value should be as a function of  $K_p$  using the following formula:

$$\text{L-eq, dermal exposure} = 6.30 \text{ (L}\cdot\text{h/cm)} \times K_p \text{ (cm/h)} \quad [1]$$

where 6.30 is obtained by multiplying the following constants: the area of skin exposed (18 000 cm<sup>2</sup> for adults), the duration of exposure (0.50 h), a conversion factor of 0.001 (to convert cm<sup>3</sup> to L), and the fraction of the dose absorbed (0.70, based on Krishnan, 2003a, 2003b).

For benzene,

$$\begin{aligned} \text{L-eq, dermal exposure} &= 6.30 \text{ L}\cdot\text{h/cm} \times 0.14 \text{ cm/h} \\ &= 0.88 \text{ L} \end{aligned}$$

A two-tier assessment was also used to evaluate the inhalation route of exposure. Similar to the approach used for dermal exposure, tier 1 of the assessment determines whether the inhalation of benzene during bathing or showering is likely to contribute at least 10% of the drinking water consumption level. In this case, the tier 1 goal of 0.15 L-eq is associated with an air to water benzene concentration ( $F_{\text{air-water}}$ ) value of 0.00063 (which is determined using an exposure time of 0.5 hours, a ventilation rate of 675 L/h for adults, and an absorption fraction of 0.7). Using the estimated Henry's law constant ( $K_{\text{aw}}$ ) obtained from the U.S. EPA's EPI Suite program (U.S. EPA, 2000), the  $F_{\text{air-water}}$  value for benzene was determined to be 0.0072, indicating that exposure to benzene through inhalation during showering and bathing contributes significantly to the daily dose. In tier 2, the L-eq for the inhalation route is calculated as a function of  $F_{\text{air-water}}$  using the following formula:

$$\text{L-eq, inhalation exposure} = 236.25 \times F_{\text{air-water}} \quad [2]$$

where 236.25 is determined by multiplying the following constants: alveolar ventilation rate (675 L/h), duration of exposure (0.50 h), and the fraction absorbed (0.70, based on Krishnan, 2003a, 2003b).

For benzene,

$$\begin{aligned} \text{L-eq, inhalation exposure} &= 236.25 \text{ L} \times 0.0072 \\ &= 1.70 \text{ L} \end{aligned}$$

It should be noted that this multi-route exposure assessment is a conservative approach used to estimate the contribution that both the dermal and inhalation routes of exposure make towards total exposure. Using physiologically based pharmacokinetic (PBPK) modelling to estimate the L-eq contributions to the total daily dose from the dermal and inhalation pathways does not take into account exposure to benzene metabolites. The approach, therefore, does not place any “toxicological” weight on a particular route of exposure due to metabolite production.

Using the above approach, the L-eq exposure was calculated as 0.88 L for the dermal route and 1.70 L for the inhalation route. Adding these values to the standard Canadian drinking water consumption rate of 1.5 L/day results in a total litre-equivalent daily exposure of 4.0 L-eq (rounded down from 4.08 L-eq). To derive its public health goal for benzene in drinking water, the California Environmental Protection Agency (CalEPA) (OEHHA, 2001) used a daily water consumption of 4.7 L-eq based on a best estimate by Lindstrom et al. (1994) to incorporate exposure to benzene through dermal contact and inhalation during showering and bathing. OEHHA (2001) also reported that this 4.7 L-eq/day was supported by an estimate obtained from the multimedia total exposure model CalTOX (DTSC, 1999) of 4.6 L-eq/day.

In a Canadian review of benzene exposures (Environment Canada and Health and Welfare Canada, 1993), it was concluded that food and drinking water each contributed a total daily benzene intake of only 0.02 µg/kg bw; the total daily intake of benzene from airborne exposures was reported to be 2.4 µg/kg bw per day (3.3 µg/kg bw per day if exposed to cigarette smoke). It can, therefore, be concluded that airborne exposure accounts for an estimated 98–99% of total benzene intake for Canadian non-smokers.

## 6.0 Analytical methods

The United States Environmental Protection Agency (U.S. EPA) has approved two analytical methods, based on purge and trap gas chromatography, for the analysis of benzene in drinking water (U.S. EPA, 2002a). EPA Method 502.2 Revision 2.1, which employs purge and trap capillary gas chromatography with photoionization detectors and electrolytic conductivity detectors in series, has an MDL of 0.01 µg/L. EPA Method 524.2 Revision 4.1, which uses purge and trap capillary gas chromatography with mass spectrometry detection, has an MDL range of 0.03–0.04 µg/L. A detection limit range is cited, as multiple detection limits are possible due to variability in reagents, instrumentation, and/or laboratory analyst performance (U.S. EPA, 1995).

The current U.S. EPA practical quantitation limit (PQL) for benzene is set at 5 µg/L. This limit was previously considered the lowest level that could be reliably achieved within specified limits of accuracy and precision (U.S. EPA, 1985a). More recently, however, the U.S. EPA has identified benzene as a possible candidate for a PQL revision. Analysis of laboratory survey data indicated that a high percentage of laboratories were capable of measuring benzene concentrations in water at lower levels using common analytical methods (EPA Method 524.2) (U.S. EPA, 2003a). As a result, the U.S. EPA (2002b) has estimated a lower possible PQL of 0.4 µg/L.

Two equivalent standard methods, SM 6200B and SM 6200C, are based on purge and trap capillary gas chromatography followed by mass spectrometry detectors or photoionization detectors and electrolytic conductivity detectors in series, respectively. SM 6200B has an MDL

of 0.036  $\mu\text{g/L}$ , and SM 6200C has an MDL of 0.017  $\mu\text{g/L}$ . The minimum quantitation levels, defined as the lowest level that can be quantified accurately, are 0.144  $\mu\text{g/L}$  and 0.068  $\mu\text{g/L}$  for methods SM 6200B and SM 6200C, respectively (APHA et al., 2005).

## 7.0 Treatment technology

### 7.1 Municipal scale

Municipal water filtration plants that rely on conventional treatment techniques (coagulation, sedimentation, filtration, and chlorination) have generally been found to be ineffective in reducing concentrations of VOCs in drinking water (Love et al., 1983; Robeck and Love, 1983). Coagulation and filtration treatment techniques were reported to achieve benzene reductions ranging from 0 to 29%; however, the observed reductions may be partially attributed to incidental volatilization during the treatment process (Clark et al., 1988; Najm et al., 1991; U.S. EPA, 1991a; Lykins and Clark, 1994).

Two common treatment technologies reported to be effective for the reduction of benzene in drinking water are granular activated carbon (GAC) adsorption and air stripping (Love et al., 1983; U.S. EPA, 1985a, 1991a,b; AWWA, 1991; Lykins and Clark, 1994). These treatment methods are capable of achieving effluent concentrations of benzene below 1  $\mu\text{g/L}$ . To a lesser degree, oxidation and reverse osmosis membrane filtration may also be effective for the removal of benzene from drinking water (Whittaker and Szaplanczay, 1985; Fronk, 1987; Lykins and Clark, 1994).

The selection of an appropriate treatment process for a specific water supply will depend on many factors, including the characteristics of the raw water supply and the operational conditions of the specific treatment method. These factors should be taken into consideration to ensure that the treatment process selected is effective for the reduction of benzene in drinking water.

#### 7.1.1 Activated carbon adsorption

GAC adsorption is widely used to reduce the concentration of VOCs in drinking water, and a removal efficiency of 99% (U.S. EPA, 1985a, 2003b; Lykins and Clark, 1994) to achieve effluent concentrations below 1  $\mu\text{g/L}$  is considered feasible for benzene under reasonable operating conditions (Koffskey and Brodtmann, 1983; Lykins et al., 1984; AWWA, 1991; Dyksen et al., 1995).

The adsorption capacity of activated carbon to remove VOCs is affected by a variety of factors, such as concentration, pH, competition from other contaminants, preloading with natural organic matter (NOM), contact time, and the physical/chemical properties of the VOC and carbon (Speth, 1990). In addition, GAC filtration effectiveness is also a function of the empty bed contact time (EBCT), flow rate, and filter run time.

Full-scale studies of fixed-bed GAC adsorbers and GAC sand replacement filters have demonstrated that both methods are capable of reducing influent benzene concentrations of 10  $\mu\text{g/L}$  to below 0.1  $\mu\text{g/L}$  in the finished water. Operating conditions of the GAC filter adsorber included a bed volume of 23.8  $\text{m}^3$ , a flow rate of 1.5 ML/day, and an EBCT of 23.7 minutes. No breakthrough of benzene was observed during the 180-day study period (Koffskey and

Brodthmann, 1983). Other full-scale data demonstrated that three GAC adsorbers operating in parallel with a flow rate of 5 ML/day, an EBCT of 21 minutes, and a bed life of 12 months were capable of reducing benzene concentrations of 20  $\mu\text{g/L}$  to 0.2  $\mu\text{g/L}$  (AWWA, 1991).

Model predictions using equilibrium data (Weber and Pirbazari, 1982; Speth and Miltner, 1990) have been used to predict full-scale GAC performance for the reduction of benzene in drinking water (Clark et al., 1990; Lykins and Clark, 1994). The estimated carbon-use rate to reduce an influent benzene concentration of 100  $\mu\text{g/L}$  to an effluent concentration of 5  $\mu\text{g/L}$  is 0.013  $\text{kg/m}^3$  using an EBCT of 15 minutes and a bed life of 389 days (Lykins and Clark, 1994). As demonstrated with the full-scale data reported above, effluent benzene concentrations of 1  $\mu\text{g/L}$  or lower should be achievable within reasonable operating conditions and costs.

The use of powdered activated carbon (PAC) adsorption has shown limited success as a treatment for the removal of benzene in drinking water. Pilot-scale studies demonstrated that a combined jet flocculation/PAC system was capable of reducing benzene concentrations from 100 to 5  $\mu\text{g/L}$  using 60 mg/L of PAC, 100 mg/L of silica clay, and a contact time ranging between 2 and 8 minutes (Sobrinho et al., 1997).

### 7.1.2 Air stripping

Air stripping is commonly used to reduce the concentration of VOCs in drinking water (Cummins and Westrick, 1990; U.S. EPA, 1991a; WHO, 2004; Dyksen, 2005). Although various air stripping equipment configurations exist, packed tower aeration (PTA) is recognized as the most effective method for the reduction of benzene in drinking water. Removal efficiencies of 99% (U.S. EPA, 1985a, 2003b) to obtain effluent concentrations of 1  $\mu\text{g/L}$  are considered to be achievable using PTA (Crittenden et al., 1988; U.S. EPA, 1990; Adams and Clark, 1991).

Design considerations for PTA include the temperature of the air and water, physical and chemical characteristics of the contaminant, air-to-water ratio, contact time, and available area for mass transfer (Adams and Clark, 1991; U.S. EPA, 1991a; Crittenden et al., 2005; Dyksen, 2005). PTA provides an optimum system for the removal of VOCs from water, as it allows for greater air-to-water ratios than with traditional diffused aeration systems. As PTA transfers VOCs from water to air, treatment of the stripping tower off-gas to reduce the contaminant concentrations prior to discharge may be necessary (Crittenden et al., 1988; Adams and Clark, 1991).

Data from a full-scale drinking water treatment plant demonstrated that countercurrent-flow PTA can reduce average influent levels of benzene of 30  $\mu\text{g/L}$  to 1.5  $\mu\text{g/L}$  in finished water using an air-to-water ratio of 75, an air stripper length of 5.50 m, and a packed column diameter of 1.52 m (Allan, 1988). Other full-scale data demonstrated that PTA using an air-to-water ratio of 100, an air stripper length of 10.05 m, and a packed column diameter of 3.05 m was capable of reducing influent benzene concentrations of 200  $\mu\text{g/L}$  to less than 2  $\mu\text{g/L}$  (AWWA, 1991). Pilot testing data have demonstrated that modification of the air-to-water ratio, air stripper length, or packing material can increase the removal efficiencies to achieve effluent concentrations below 1  $\mu\text{g/L}$  (U.S. EPA, 1990).

Typical and model-generated PTA designs for the removal of commonly occurring VOCs have been reported by several authors (Crittenden et al., 1988; Adams and Clark, 1991; Clark and Adams, 1991). Typical full-scale plant design (> 8 ML/day) parameters for the



reduction of benzene from drinking water include an air-to-water ratio of 32.7, an air stripper length of 11.05 m, and a packed column diameter of 2.55 m. Under these conditions, a 99% reduction of benzene in drinking water from an influent concentration of 100 µg/L to an effluent concentration of 1 µg/L may be achievable (Crittenden et al., 1988). Modelling conducted by Adams and Clark (1991) to determine the cost-effective design criteria for PTA contactors estimated that an air-to-water ratio of 40 and a packing depth of 12.95 m may also be capable of achieving a 99% reduction of benzene to effluent concentrations of 1 µg/L.

Pilot plant studies examining the most effective operating conditions of PTA for the reduction of VOCs in groundwater demonstrated removal efficiencies for benzene ranging from 77% to over 99% and in some cases achieved effluent concentrations below 1 µg/L (Stallings et al., 1985; U.S. EPA, 1985b, 1990; Ball and Edwards, 1992).

Alternative air stripping treatment technologies that have been identified as potential methods for the reduction of benzene in drinking water include diffused aeration, multistage bubble aerators, tray aeration, and shallow tray aeration. These technologies may be particularly useful for small systems where the installation of GAC or PTA treatment is not feasible (U.S. EPA, 1998a).

Cost evaluations conducted by Adams and Clark (1991) indicate that in most cases the use of PTA for the reduction of benzene in drinking water is more cost-effective than GAC, even when vapour-phase GAC treatment of the stripping tower off-gas is required (Adams and Clark, 1991). The analysis included evaluation of system sizes ranging from 1 to 100 ML/day. Combining PTA and GAC into a two-step treatment train has been suggested as the most effective method for achieving low effluent levels of VOCs. In a municipal-scale treatment plant combining these processes, air stripping is used for the bulk reduction of VOCs in the water, and activated carbon is used in the second step to further reduce the residual VOC concentrations (McKinnon and Dyksen, 1984; Stenzel and Gupta, 1985; U.S. EPA, 1991a). In addition, the use of air stripping preceding GAC can significantly extend carbon bed life. However, no performance data were available for demonstrating benzene removal efficiencies using this combined treatment method.

### 7.1.3 Oxidation

Oxidation and advanced oxidation processes (AOPs) have been reported to be effective for the reduction of benzene in drinking water, although full-scale data were not obtained for these treatment methods.

Pilot-scale treatment tests demonstrated that ozone doses of 6 mg/L achieved an 81% degradation of benzene in distilled water from approximately 50 µg/L to effluent concentrations of 10 µg/L. Ozone doses of 12 mg/L achieved a 94% reduction of benzene in both distilled water and groundwater matrices over a wide range of pH (Fronk, 1987). Additional pilot studies observed greater than 75% degradation of benzene with an ozone dose between 0.8 and 1.5 mg/L (Kang et al., 1997).

The rate of degradation of benzene in natural water is also dependent on the reaction of ozone with NOM, which produces hydroxyl radicals. The reaction rate between hydroxyl radicals and benzene is higher than the reaction rate between benzene and ozone; therefore, the ratio of the concentration of hydroxyl radical to the concentration of ozone is considered to be an important factor in the effectiveness of ozonation for the reduction of benzene in drinking water

(Crittenden et al., 2005). Lower effluent concentrations may be achievable depending on the influent concentrations of benzene and NOM in the source water and by varying the ozone dose, contact time, and pH of the water.

A pilot-scale photocatalytic oxidation system was successful at reducing influent benzene concentrations from 123 µg/L to below 0.5 µg/L in the finished water. The oxidation system utilized ultraviolet (UV) light with a titanium dioxide semiconductor combined with the addition of 70 mg/L of hydrogen peroxide and 0.4 mg/L of ozone. To prevent fouling of the photocatalytic reactor, an ion-exchange pretreatment system was used to remove iron and manganese from the groundwater (Topudurti et al., 1998). Similar pilot studies found that greater than 99% removal of benzene could be achieved using a UV/titanium dioxide oxidation process (Al-Bastaki, 2003).

The formation of by-products during the application of ozonation or AOPs for the treatment of benzene in drinking water should be considered in the process selection, optimization, and post-treatment monitoring. By-product formation will depend on several factors, including the source water quality, the type and dose of the oxidant, and the reaction contact time. Smaller, oxygenated compounds such as phenolics, aldehydes, ketones, and carboxylic acids have been suggested as potential by-products of the ozonation of benzene (Fronk, 1987). In addition, by-products such as bromate and nitrite may form as a result of the oxidation of inorganic material present in the source water.

#### 7.1.4 Membrane filtration

Reverse osmosis has shown some promise for its potential to remove VOCs from drinking water (Clark et al., 1988). Pilot plant investigations demonstrated that selected reverse osmosis membranes were capable of reducing 94% of benzene in water; however, the influent concentrations were 1000 µg/L, and the applicability of this treatment to achieve lower effluent concentrations was not investigated (Whittaker and Szaplanczay, 1985). Other studies, however, have found less than 20% removal of benzene using cellulose, polyamide, and thin film composite membranes (Lykins et al., 1988). The ability of reverse osmosis to remove other synthetic organic chemicals has been found to be dependent on a variety of system components, including type of membrane, flux, recovery, chemical solubility, charge, and molecular weight (Taylor et al., 2000).

#### 7.1.5 Emerging treatment technologies

New drinking water treatment technologies for benzene are being developed but are still primarily in the experimental stage and/or do not have published information on the effectiveness of pilot- or large-scale application. Some of the emerging technologies include the following:

- *Other AOPs:* Laboratory studies examining the effectiveness of various AOP methods demonstrated the complete degradation of benzene using a UV-assisted photo-Fenton process and titanium dioxide-mediated photocatalysis (Ollis et al., 1991; Tiburtius et al., 2005).
- *Alternative adsorbents:* Synthetic carbonaceous resins and fibreglass-supported activated carbon filters have been shown to have a higher adsorbent capacity for benzene, toluene,

ethylbenzene, and xylenes (BTEX) in water relative to activated carbon (Yue et al., 2001; Shih et al., 2005). In addition, the use of an adsorbent impregnated with a platinum and titanium dioxide catalyst demonstrated high removal efficiencies over a prolonged adsorbent bed life (Crittenden et al., 1997). The use of organoclays to enhance carbon filtration has also been shown to be successful (Alther, 2002).

- *Bioreactors*: Bioreactors using various materials to support microbial growth have been effective for the biodegradation of benzene in water (De Nardi et al., 2002; Sedran et al., 2003).
- *Electron beam radiation*: The use of a low-energy electron beam to generate electrons and hydroxyl radicals that oxidize benzene in water has demonstrated moderate effectiveness for the reduction of benzene in water (Lubicki et al., 1997).
- *Membrane pervaporation*: Although the use of membranes for the pervaporation extraction of benzene has been applied primarily in wastewater treatment, this technique has more recently been studied for the removal of benzene from groundwater (Jian and Pintauro, 1997; Uragami et al., 2001; Peng et al., 2003).

## 7.2 Residential scale

Municipal treatment of drinking water is designed to reduce contaminants to levels at or below their guideline values. As a result, the use of residential-scale treatment devices on municipally treated water is generally not necessary, but is primarily based on individual choice. In cases where an individual household obtains its drinking water from a private well, a private residential drinking water treatment device may be an option for reducing benzene concentrations in drinking water.

A number of residential treatment devices from various manufacturers are available that can remove benzene from drinking water to concentrations below 1 µg/L. Filtration systems may be installed at the faucet (point-of-use) or at the location where water enters the home (point-of-entry). Point-of-entry systems are preferred for VOCs such as benzene because they provide treated water for bathing and laundry as well as for cooking and drinking. Certified point-of-use treatment devices as well as a limited selection of point-of-entry devices are currently available for the reduction of VOCs, including benzene. In the case where certified point-of-entry treatment devices are not available for purchase, systems can be designed and constructed from certified materials. Periodic testing by an accredited laboratory should be conducted on both the water entering the treatment device and the water it produces to verify that the treatment device is effective. Devices can lose removal capacity through usage and time and need to be maintained and/or replaced. Consumers should verify the expected longevity of the components in their treatment device as per the manufacturer's recommendations.

Health Canada does not recommend specific brands of drinking water treatment devices, but it strongly recommends that consumers use devices that have been certified by an accredited certification body as meeting the appropriate NSF International (NSF)/American National Standards Institute (ANSI) drinking water treatment unit standards. These standards have been designed to safeguard drinking water by helping to ensure the material safety and performance of products that come into contact with drinking water. Certification organizations provide assurance that a product conforms to applicable standards and must be accredited by the

Standards Council of Canada (SCC). In Canada, the following organizations have been accredited by the SCC to certify drinking water devices and materials as meeting NSF/ANSI standards (SCC, 2003):

- Canadian Standards Association International ([www.csa-international.org](http://www.csa-international.org));
- NSF International ([www.nsf.org](http://www.nsf.org));
- Water Quality Association ([www.wqa.org](http://www.wqa.org));
- Underwriters Laboratories Inc. ([www.ul.com](http://www.ul.com));
- Quality Auditing Institute ([www.qai.org](http://www.qai.org));
- International Association of Plumbing & Mechanical Officials ([www.iapmo.org](http://www.iapmo.org)).

An up-to-date list of accredited certification organizations can be obtained from the SCC ([www.scc.ca](http://www.scc.ca)).

Treatment devices to remove benzene from untreated water (such as a private well) can be certified either specifically for benzene removal or for the removal of VOCs as a group. However, only treatment devices certified for the removal of VOCs as a group can verify that a final benzene concentration of less than 0.001 mg/L is achieved. For a drinking water treatment device to be certified to NSF/ANSI Standard 53 (Drinking Water Treatment Units — Health Effects) for the removal of VOCs, the device must be capable of reducing the concentration of benzene by greater than 99% from an influent (challenge) concentration of 0.081 mg/L to a maximum final (effluent) concentration of less than 0.001 mg/L (NSF/ANSI, 2006). Treatment devices that are certified to remove VOCs under NSF/ANSI Standard 53 are generally based on activated carbon adsorption technology. Reverse osmosis systems certified to NSF/ANSI Standard 58 (Reverse Osmosis Drinking Water Treatment Systems) may also be certified for the reduction of VOCs to achieve a final concentration of less than 0.001 mg/L (NSF/ANSI, 2005). This standard is applicable only for point-of-use reverse osmosis systems.

## 8.0 Kinetics and metabolism

Oral exposure to benzene at low concentrations in animals has been shown to result in complete absorption. Sabourin et al. (1987) administered radiolabelled (<sup>14</sup>C) benzene orally (through corn oil gavage and intraperitoneally) to Sprague-Dawley and F344/N rats and B6C3F1 mice and analysed urine and faeces at 4, 8, 16, 24, 32, and 48 hours after dosing for radiolabelled benzene (and/or benzene metabolites). The percentages of the dose excreted by each route were similar following gavage or intraperitoneal injection. The absorption of benzene in F344/N rats, Sprague-Dawley rats, and B6C3F1 mice was determined by comparing excretion routes following administration (by gavage or intraperitoneal injection) of benzene at 0.5 or 150 mg/kg bw; it was found that the absorption of benzene was essentially 100% for all three test species.

Results from the Sabourin et al. (1987) study are supported by a study on rats, mice, and hamsters by Mathews et al. (1998). Animals treated by oral gavage (in corn oil) with a range of benzene doses that overlapped those in the Sabourin et al. (1987) study displayed complete absorption from the gastrointestinal tract (in all three species); however, excretion routes were influenced by dose. For example, at a high dose of 100 mg/kg bw, a significant portion of benzene was eliminated by exhalation (from 22% in mice to 50% in rats). Both studies reported a greater proportion of metabolites excreted in urine at the low doses, with a shift to greater amounts of unmetabolized benzene excreted in exhaled air at the high doses. These

results suggest that saturation of metabolism occurs at doses greater than approximately 100 mg/kg bw. At oral doses that could be found in drinking water, however, animal results suggest a linear increase in total metabolite production with exposure level.

No relevant animal studies are available that allow a comparison of absorption between gavage and drinking water administration. In theory, ingesting drinking water or food containing benzene may result in some loss from the stomach through volatilization, whereas administration by gavage using an oil vehicle may limit benzene volatilization. It is also possible that a greater proportion of benzene from large bolus doses would escape absorption and pass through into the faeces, while smaller doses would be better absorbed. Since essentially complete absorption has been observed even at high gavage doses in animals, in the absence of human data it is postulated that complete absorption of benzene by ingestion can be expected in humans as well.

Absorption of benzene through inhalation, like absorption following ingestion, depends on the dose. As seen in oral exposure studies, a larger proportion of benzene is retained at lower exposures versus higher exposures. Humans experimentally exposed to low to moderate levels of benzene (1.7–32 ppm) absorbed on average 50% of the benzene inhaled. Pekari et al. (1992) exposed three males to both 1.7 and 10 ppm benzene for 4 hours, during which six samples of exhaled air and blood were taken from each subject. After exposure, phenol was measured in exhaled air, blood, and urine. The average absorption was found to be  $52\% \pm 7.3\%$  at 1.7 ppm and  $48\% \pm 4.3\%$  at 10 ppm.

Nomiyama and Nomiyama (1974) exposed three females and three males to benzene levels ranging from 52 to 62 ppm for 4-hour periods. At 1-hour intervals during exposure, exhaled air was sampled. The average absorption at the 1-hour exposure period was found to be approximately 60% for women and 45% for men. After 2 hours of exposure, absorption was approximately 43% for women and 35% for men. The average absorption over the 3- to 4-hour time periods was reported at 30.2%. In general, absorption was higher for both sexes during early exposure, approaching a steady state only after 3 hours.

Studies measuring exhaled air from occupational and environmental exposures further support a 50% absorption of benzene following inhalation exposure. In an occupational study by Perbellini et al. (1988), exhaled air from subjects who had low background exposure to benzene (median 19 ng/L in air, or 0.019 ng/m<sup>3</sup>) showed an average absorption of 55%. Another study by Wallace et al. (1993) found 70% absorption of benzene from measurements of exhaled air for non-smokers. In most studies of this sort, exhaled air samples are collected in the post-exposure period, with the concentration of benzene in exhaled air falling rapidly following removal from exposure; therefore, post-exposure samples would be expected to predict a lower absorption. In general, however, experimental, occupational, and environmental exposure studies suggest that an absorption fraction of 50% is a good estimate.

Human and animal studies have shown that benzene is readily absorbed through the skin from both the liquid and vapour phases (Franz, 1975; Maibach and Anjo, 1981; Franz, 1984; Susten et al., 1985). Absorption of benzene through the skin, however, depends on several factors, including skin permeability, which increases with increasing temperature (Nakai et al., 1997). Susten et al. (1985) estimated the amount of benzene absorbed through the skin of tire industry workers by conducting a series of *in vivo* studies in hairless mice. Percutaneous absorption, following single dermal applications of [<sup>14</sup>C]benzene contained in rubber solvent at a

concentration of 0.5% (v/v) benzene, was calculated directly from the sums of radioactivity found in excreta, expired breath, and the carcass. Data from the study suggested that benzene absorption via the skin could contribute from 20% to 40% of the total benzene dose of these workers.

Although animal studies show that exposure to oral doses to which humans are likely exposed suggest a linear increase in total metabolite production with exposure level, the dose-related production of benzene metabolites in humans is not well understood, particularly at low levels of exposure. Kim et al. (2006) investigated unmetabolized benzene in urine and all major urinary metabolites (phenol, E,E-muconic acid, hydroquinone, and catechol), as well as the minor metabolite, S-phenylmercapturic acid, in 250 benzene-exposed workers and 139 control workers in Tianjin, China. Metabolite concentrations in urine were found to be consistently elevated when the median air benzene levels were at or above the following: 0.2 ppm for E,E-muconic acid and S-phenylmercapturic acid, 0.5 ppm for phenol and hydroquinone, and 2 ppm for catechol. The dose-related production of E,E-muconic acid, phenol, hydroquinone, catechol, and total metabolites reportedly declined by 2.5- to 26-fold as the median air benzene levels increased from 0.027 to 15.4 ppm. Reductions in metabolite production were found to be most pronounced for catechol and phenol at levels below 1 ppm, indicating that metabolism favoured the production of the toxic metabolites, hydroquinone and E,E-muconic acid, at low exposures. Another study by Rappaport et al. (2005) investigated the production of benzene oxide and 1,4-benzoquinone in 160 Chinese workers exposed to benzene at levels ranging from 0.074 to 328 ppm. Both benzene oxide and 1,4-benzoquinone levels plateaued at approximately 500 ppm benzene, suggesting that cytochrome P4502E1 (CYP2E1) (which is responsible for oxidizing benzene to benzene oxide, the first step in benzene metabolism) became saturated at this point. These results indicate that benzene metabolism may be much more effective at low levels of benzene and that perhaps exposure to levels of benzene above 50 ppm may have a diminished impact on the human health risk of leukemia, since benzene metabolism becomes substantially saturated at this level. On the other hand, these results suggest that exposure to levels of benzene below 50 ppm may produce the maximum amount of metabolites per unit of benzene exposure.

Scientific evidence suggests that metabolism plays an important role in benzene toxicity (Snyder and Hedli, 1996). As an example, competitive inhibition of metabolism by toluene (at levels much higher than found in drinking water) decreases benzene toxicity. Valentine et al. (1996) reported that transgenic mice lacking CYP2E1 expression had lower benzene metabolism, cytotoxicity, or genotoxicity compared with wild-type mice; there is no indication, however, that the route of exposure has an effect on the metabolites formed (IPCS, 1993). Two major pathways are proposed as being responsible for benzene toxicity. The first involves the metabolites phenol, catechol, and hydroquinone, and the second pathway involves open ring forms of benzene. Benzene is primarily metabolized in the liver by CYP2E1 (Johansson and Ingleman-Sundberg, 1988) to form benzene oxide, which spontaneously rearranges to phenol. Catechol is formed by the oxidation of phenol, or it can be formed by the conversion of benzene oxide to benzene-1,2-dihydrodiol in the liver by epoxide hydrolase, with subsequent conversion to catechol by dehydrogenases. It is believed that catechol formation from phenol oxidation may be significant only during high-dose exposures. Hydroquinone is formed from the oxidation of phenol by mixed-function oxidases.

It is suggested that benzene-induced haematotoxicity, such as aplastic anaemia, pancytopenia, thrombocytopenia, granulocytopenia, lymphocytopenia, and carcinogenesis, involves the metabolism of phenolic metabolites of benzene, in particular the metabolism of hydroquinone to benzoquinone, semiquinones, and free radicals (Smith, 1996; Snyder and Hedli, 1996; Smith and Fanning, 1997). Blood transports phenolic metabolites (phenol, hydroquinone, catechol, and 1,2,4-trihydroxybenzene) to bone marrow, where they can be converted to reactive species by peroxidases and other enzymes. The redox reactions that accompany these reactions generate oxygen free radicals, lipid peroxidation products, and other free radicals (Subrahmanyam et al., 1991). Bone marrow contains approximately 3% dry weight of myeloperoxidase in addition to other peroxidases, such as eosinophil peroxidase and prostaglandin synthetase (Smith, 1996). The primary biological function of a peroxidase enzyme is to oxidize hydrogen donors at the expense of peroxide or molecular oxygen. Snyder and Kalf (1994) found that NADPH-dependent quinone oxidoreductase, an enzyme that efficiently reduces (detoxifies) quinones, is found in low concentrations (relative to other tissues) in bone marrow, which may explain in part why the bone marrow is a target tissue for benzene toxicity. Glutathione conjugates of hydroquinone and 1,2,4-benzenetriol readily auto-oxidize to quinone species, which may react with cellular macromolecules directly or generate free radical species (Snyder and Hedli, 1996). In a review by Witz et al. (1996), it was reported that some researchers have hypothesized that metabolites of benzene where the aromatic ring has been broken may also significantly contribute to benzene haematotoxicity. *Trans,trans*-muconaldehyde co-administration with hydroquinone, for example, is very potent in damaging bone marrow cells.

## 9.0 Health effects

### 9.1 Effects in humans

#### 9.1.1 Acute toxicity

Acute exposure to high levels of benzene affects the central nervous system, causing dizziness, nausea, vomiting, headache, and drowsiness. Exposure to levels between 50 and 150 ppm by inhalation over 5 hours can reportedly result in headaches, lethargy, and weakness, although exposure to 25 ppm for 8 hours produced no acute clinical effects (IPCS, 1993; Paustenbach et al., 1993). Inhaling benzene at 20 000 ppm for 5–10 minutes, at 7500 ppm for 30 minutes, or at 1500 ppm for 60 minutes may cause death or severe toxicity in humans (Holliday and Englehardt, 1984; IPCS, 1993). Individuals who have died from sniffing glue containing benzene reportedly had blood concentrations from 1 to 65 mg/L, with death resulting from pulmonary haemorrhaging and inflammation, renal congestion, cerebral oedema, or a combination of these (IPCS, 1993). ATSDR (2005) estimates a lethal oral dose of benzene in humans to be about 125 ppm.

#### 9.1.2 Subchronic and chronic toxicity

Subchronic and chronic exposure to benzene leads to numerous adverse effects, including damage to bone marrow, changes in circulating blood cells, immunological effects, and cancer

(see Section 9.1.5). The most commonly reported non-cancer effects from chronic exposure to inhaled benzene include blood disorders, such as aplastic anaemia, pancytopenia, thrombocytopenia, granulocytopenia, lymphocytopenia, and leukaemia. The effects of benzene exposure on several blood cell lineages suggest that benzene and/or its metabolites target the bone marrow or early progenitor cells (IPCS, 1993; ATSDR, 2005). A study by Lan et al. (2004) of 250 shoe workers in China exposed to benzene found a highly significant dose-dependent decrease in colony formation of progenitor cells with increasing benzene exposure. With a greater proportional decrease in progenitor cell colony formation than the proportional decrease in the levels of differentiated white blood cells and granulocytes, Lan et al. (2004) suggested that early progenitor cells are more sensitive to the haematotoxic effects of benzene than mature blood cells. This is in agreement with other earlier findings in both humans and animals (Smith et al., 2000; Abernathy et al., 2004).

### 9.1.3 Genetic toxicity

Benzene is reported to be clastogenic in humans, with effects including aneuploidy, ploidy, micronuclei, chromosomal deletions, translocations, and rearrangements (IARC, 1982; ATSDR, 2005). Most cytogenetic studies have looked at the blood lymphocytes of exposed workers and report increased structural (chromatid and/or chromosome breaks) and/or numerical chromosomal aberrations in mitogen-stimulated peripheral lymphocytes (ATSDR, 2005). Benzene exposure in humans has also been shown to result in the types of chromosomal aberrations that are common with certain leukaemias, such as acute myelogenous leukaemia and myelodysplastic syndromes (Smith and Zhang, 1998). Aberrations include specific gains or losses in chromosomes, translocations, deletions, and inversions, most commonly associated with chromosome 5, 7, 8, 9, 21, or 22.

Lymphocytes in Chinese workers occupationally exposed to benzene have been shown to contain higher frequencies of specific chromosomal alterations such as chromosome 9 hyperdiploidy, translocations between chromosomes 8 and 21, and aneusomies of chromosomes 8 and 21 (Zhang et al., 1996; Smith and Zhang, 1998). Significant increases in the rates of monosomy for chromosomes 5 and 7 ( $p < 0.001$  and  $p < 0.0001$ , respectively) and increases in the frequencies of trisomy and tetrasomy of chromosomes 1, 5, and 7 have also been reported (Zhang et al., 1998). Many of these chromosomal alterations have also been observed *in vitro* in human cells treated with benzene metabolites. Zhang et al. (1994) and Stillman et al. (1997) found dose-related increases of aneuploidy of chromosomes 5 and 7 in human haematopoietic cells treated with hydroquinone or 1,2,4-trihydroxybenzene. Zhang et al. (1994) reported trisomy and tetrasomy of chromosomes 7 and 9 in a human cell line treated with hydroquinone or 1,2,4-benzenetriol. Human lymphocytes exposed to hydroquinone resulted in hyperdiploidy in chromosome 9 (Eastmond et al., 1994).

### 9.1.4 Developmental and reproductive toxicity

Studies are limited regarding the effects of maternal exposure to benzene. Abnormal menstruation and excessive blood loss during childbirth have been reported in women occupationally exposed to benzene (OEHHA, 1997). These reports, however, are limited, since the comparison groups were exposed to different environments that were not described, the



methods were poorly described, and co-exposure to other solvents associated with employment in rubber and/or leather factories likely occurred. More definitive studies with accurate assessment of benzene-specific exposure are needed.

#### 9.1.5 Carcinogenicity

There are numerous studies that report increased cancer rates from occupational exposure to benzene (Bond et al., 1986; Wong, 1987; Hayes et al., 1996; Schnatter et al., 1996; Rushton and Romaniuk, 1997). Reviews of benzene carcinogenicity due to occupational exposure have been published by IARC (1982), IPCS (1993), and ATSDR (2005).

The Ohio Pliofilm (rubber hydrochloride) cohort represents a good published set of data for assessing human cancer risks from exposure to benzene, since it has the fewest reported co-exposures to other possible carcinogenic substances in the workplace that could impact a risk analysis for benzene, and the Pliofilm workers were exposed to a wider range of estimated benzene concentrations than were workers in other cohort studies (U.S. EPA, 1998b). Rinsky et al. (1981) was the first to extensively study the Pliofilm cohort, which included 748 male workers in three facilities in Ohio who were exposed to benzene during employment between 1940 and 1949 and were followed until the end of 1981. Benzene exposure levels were estimated to range from 100 ppm in 1941 to 10 ppm (8-hour time-weighted average) in 1949. A statistically significant increase in mortality due to malignancies of the lymphatic and haematopoietic tissue (standardized mortality ratio [SMR] = 330;  $p < 0.01$ ) was reported, with seven of the deaths due to leukaemia (SMR = 560;  $p < 0.001$ ). Workers exposed for longer than 5 years had an SMR due to leukaemia of 2100. Rinsky et al. (1987) subsequently updated and expanded the Ohio cohort study to include individuals who worked at least 1 day between 1940 and 1965, with person-years at risk starting in 1950. The updated cohort was composed of 1165 white males followed through 1981, which included an additional 6.5 years of follow-up from the earlier study, as well as individual estimates of personal exposure. Duration of employment and personal exposure estimates during that time of employment were used to generate risk estimates based on grouped data. Once again, a strong positive trend in leukaemia mortality was seen with increasing exposure to benzene; a statistically significant increase was observed for all lymphatic and haematopoietic cancers (15 deaths) compared with that expected in the general population (SMR = 227, 95% confidence interval [CI] = 127–376). For total leukaemia deaths (nine deaths), the SMR was 337 (95% CI = 159–641). An increased risk of multiple myeloma (four deaths) was also reported (SMR = 398, 95% CI = 110–1047). Analyses by other authors (Paustenbach et al., 1993; Paxton et al., 1994) with expanded periods of follow-up and altered exposure estimates have yielded slightly different results; however, the differences fall within the same range of uncertainty.

A large retrospective cohort study of benzene-exposed workers in China by Yin et al. (1987) examined 28 460 exposed workers from 233 factories and 28 257 control workers from different industries. Thirty leukaemia cases were identified (23 acute, 7 chronic) in the exposed workers compared with four cases in the unexposed controls (SMR = 574,  $p < 0.01$ ). Exposure estimates at the time of the survey ranged from 3 to 313 ppm, with the majority of exposures in the range of 16–157 ppm. In 1994, the cohort was expanded by Yin et al. (1994) to include 74 828 benzene-exposed workers (since 1949) and 35 805 controls from 712 factories located in

12 Chinese cities. Dosemeci et al. (1994) described the exposure assessment, which included job title and assignment to individual work units reflecting exposures of individual workers. Yin et al. (1996) reported the overall cancer findings among the expanded benzene-exposed and control worker cohorts. An increased incidence in the benzene-exposed group compared with controls was observed for leukaemia (relative risk [RR] = 2.6, 95% CI = 1.3–5.0), malignant lymphoma (RR = 3.5, 95% CI = 1.2–14.9), and lung cancer deaths (RR = 1.4, 95% CI = 1.0–2.0). Among leukaemia cases, incidence of acute myelogenous leukaemia was increased in the benzene-exposed group (RR = 3.1, 95% CI = 1.2–10.7). Significant increases were also reported for aplastic anaemia and myelodysplastic syndromes.

### 9.1.6 Mode of action for carcinogenesis

Benzene biotransformation results in the generation of several metabolites (see Section 8.0) that can induce cytotoxicity through different metabolic mechanisms (Smith, 1996; Ross, 2000; Snyder, 2000). These reactive metabolites include quinones that can bind to cellular macromolecules (including DNA), tubulin, histones, and topoisomerase II. Benzoquinones and other benzene metabolites can cause oxidative DNA damage, lipid peroxidation *in vivo*, formation of hydroxylated deoxyguanosine residues, and strand breaks in the DNA of bone marrow cells, implicating a role for reactive oxygen species and covalent binding in benzene-induced toxicity. The formation of DNA double-strand breaks by reactive oxygen species and other mechanisms can lead to increased mitotic recombination, chromosomal translocations, and aneuploidy (Smith, 1996). Genetic events such as these can result in protooncogene activation, tumour suppressor gene inactivation, gene fusions, and other changes in stem cells that can ultimately result in leukaemia.

## 9.2 Effects in experimental animals

### 9.2.1 Acute toxicity

Animals exposed to a one-time high dose of benzene have displayed narcotic effects and death. Oral LD<sub>50</sub> values for rats fall in the 300–8100 mg/kg bw range. An LC<sub>50</sub> of 10 000 ppm for short-term exposure to benzene in air was reported for rats, mice, rabbits, and guinea pigs (IPCS, 1993; Paustenbach et al., 1993).

### 9.2.2 Subchronic and chronic toxicity

Subchronic and chronic exposure of experimental animals to benzene has resulted in haematological effects similar to those observed in humans following occupational exposure. Lymphocytopenia, anaemia, leukopenia, and changes in bone marrow morphology and cellularity have been consistently reported by many authors (Snyder et al., 1978, 1984; Cronkite et al., 1985; Ward et al., 1985; Aoyama, 1986; Li et al., 1986; NTP, 1986; ATSDR, 2005). A 2-year study by the U.S. National Toxicology Program (NTP, 1986) reported haematological effects in rats and mice (both sexes), which included lymphoid depletion of the splenic follicles (rats) and thymus (male rats), bone marrow haematopoietic hyperplasia (mice), lymphocytopenia, and associated leucocytopenia (rats and mice). Several of these effects occurred at the lowest exposure level (25 mg/kg bw per day). In animals, lymphocyte levels

generally appear to fall the most in the shortest time, whereas granulocytes appear to be the most resistant of the circulating cells; anaemia does not appear to occur as frequently as lymphocytopenia (ATSDR, 2005).

### 9.2.3 Genetic toxicity

Benzene has also been shown to be genotoxic in animals. *In vitro* studies have shown benzene to exhibit mixed results, with positive findings reported for gene mutations in bacteria and inhibition of DNA or RNA synthesis in mammalian cells (ATSDR, 2005). Benzene metabolites such as phenolic, quinone, epoxide, and aldehyde species cause mutations in bacteria, as well as sister chromatid exchanges, micronuclei formation, DNA strand breaks, DNA adducts, and oxidative DNA damage in mammalian cells (ATSDR, 2005). *In vivo*, benzene induces chromosomal aberrations in lymphocytes (mice) and in bone marrow cells (rats and hamsters) and increases the incidence of micronuclei in bone marrow (mice and hamsters), peripheral erythrocytes (mice), and lymphocytes (rats). Other genotoxic effects include gene mutations and polyploidy in mouse lymphocytes, as well as sister chromatid exchanges in the mouse fetus, liver, bone marrow, and rat and mouse lymphocytes. Sperm head abnormalities have also been observed in benzene-exposed male mice (ATSDR, 2005).

### 9.2.4 Developmental and reproductive toxicity

Benzene has not been found to be teratogenic in animals, although embryotoxic and fetotoxic effects have been reported at airborne concentrations as low as 47 ppm in rats (a level found not to be toxic to the dams) (Tatrai et al., 1980). Haematological effects are also reported in mice exposed to levels as low as 5 ppm *in utero* (Keller and Snyder, 1986).

### 9.2.5 Carcinogenicity

A 2-year study by the U.S. National Toxicology Program (NTP, 1986) exposed F344 rats and B6C3F1 mice (50 animals per sex per group) orally (by gavage) to benzene in corn oil 5 days per week for 103 weeks. Female rats and mice were exposed to 0, 25, 50, or 100 mg/kg bw, and males were exposed to 0, 5, 100, or 200 mg/kg bw. Female rats in the mid- and high-dose groups had significantly higher incidences of cancer of the oral cavity, Zymbal gland (an auditory sebaceous gland that opens into each external ear canal; not found in humans), and uterus; in males, an increased incidence of cancers of the oral cavity, Zymbal gland, and skin was observed. Female mice were reported to have significant dose-related increases in the rate of cancer of the Zymbal gland, ovary, mammary gland, Harderian gland, and lung. In male mice, a dose-related increase in the rate of cancer of the Zymbal, preputial, and Harderian glands and lungs was also observed.

Numerous other studies have shown benzene to be carcinogenic in rats and mice. Maltoni et al. (1982, 1983, 1985, 1989) reported that benzene administered (by stomach tube) to 13-week-old Sprague-Dawley rats at 0, 50, or 250 mg/kg bw in olive oil, 4–5 times per week for 52 weeks, resulted in dose-related increases in the incidence of Zymbal gland carcinomas in female rats only. In another study by Maltoni et al. (1989), 7-week-old male and female Sprague-Dawley rats orally exposed (by stomach tube) to 0 or 500 mg of benzene per kg bw in olive oil 4–5 times per week for 105 weeks displayed significantly higher incidence (related to controls)

of Zymbal gland and oral cavity carcinomas (males and females), nasal cavity and skin carcinomas (males), and cancer of the forestomach (females). Wistar rats, Swiss mice, and RF/J mice (50 animals per sex per group) orally exposed to 0 or 50 mg/kg benzene in olive oil 4–5 times per week for 104, 78, and 52 weeks, respectively, showed an increased incidence in cancer compared with controls (Maltoni et al., 1989). Wistar rats displayed an increased incidence of cancers of the Zymbal gland (males) and oral cavity (females); Swiss mice had an increased incidence in cancers of the Zymbal gland (males), mammary gland (females), and lung tissue (males and females); and RF/J mice were found to have a higher incidence of pulmonary tumours (males and females) and mammary gland carcinomas (females). Maltoni et al. (1982, 1983, 1985, 1989) also assessed the carcinogenic potential of benzene through inhalation studies using pregnant Sprague-Dawley rats and their offspring. Exposure to 0, 200, or 300 ppm of benzene for 15 or 104 weeks also showed increased incidences (compared with controls) of Zymbal gland cancers and mammary gland tumours in adults, with significantly higher incidences in Zymbal gland cancers and non-significant increases in cancers of the oral and nasal cavity, mammary gland, and liver also reported in the offspring. In another experiment by Maltoni et al. (1989), Sprague-Dawley rats were exposed to benzene *in utero* (via dams exposed to 0, 200, or 300 ppm) from day 12 of gestation and during lactation. Slight increases in the incidences of Zymbal gland carcinoma, oral cavity carcinoma, hepatoma, and leukaemia were reported (Maltoni et al., 1989).

Leukaemia and lymphoma have been reported in several other studies investigating benzene-mediated effects following inhalation and oral exposure. In a series of studies by Cronkite et al. (1984, 1985, 1989) and Cronkite (1986), C57BL/6 and CBA/Ca mice were exposed to 300 ppm benzene in air 6 hours daily, 5 days per week, for 16 weeks at variable intervals mimicking patterns of human occupational exposure to benzene. A significant increase in both leukaemia and lymphoma was reported in both strains of mice, as well as solid tumours (mammary and hepatoma) for CBA/Ca mice. Cronkite et al. (1989) reported a higher incidence of leukaemia in male and female CBA/CA mice exposed to 300 and 3000 ppm for 16 weeks; exposure to 3000 ppm, however, did not shorten the latency or increase the incidence compared with the 300 ppm treatment group. In a study by Farris et al. (1993), 125 male CBA/Ca mice were exposed to 300 ppm benzene for 6 hours daily, 5 days per week, for 16 weeks and sacrificed after 18 months; controls (sham-exposed, n = 125) were treated with filtered air. Significant increases in incidences of malignant lymphoma was observed in addition to preputial gland squamous cell carcinoma, lung adenoma, carcinoma of the Zymbal gland and forestomach squamous cells, as well as increased granulocytic hyperplasia of the bone marrow and spleen.

#### 9.2.6 Immunotoxicity

Concentrations of benzene as low as 10 ppm in air have been reported to cause immunological effects (depression of the response of B cells and T cells) in rats (Rozen et al., 1984). Mice exposed to 300 ppm benzene for 6 hours per day, 5 days per week, for 115 days showed reduced numbers of B cells in the spleen and bone marrow and T cells in the thymus and spleen (Rozen and Snyder, 1985).

## 10.0 Classification and assessment

Benzene is a documented human carcinogen; it has been classified as a Group 1 carcinogen (carcinogenic to humans) by Health Canada (Environment Canada and Health and Welfare Canada, 1993) and by the International Agency for Research on Cancer (IARC, 1987). Although non-cancer effects have been observed in animals exposed to benzene either orally or through inhalation, as well as in humans exposed to benzene occupationally by inhalation, carcinogenicity is considered to be the critical health effect upon which a drinking water guideline should be based. It is important to note that both animals and humans display similar toxic effects following exposure to benzene regardless of exposure pathway (i.e., via inhalation or ingestion). The most sensitive effects from benzene exposure in both animals and humans are the effects related to the blood-forming organs.

Epidemiological studies were deemed insufficient by Health Canada to serve as the basis for the quantitative estimation of cancer risks from exposure to benzene in the previous drinking water guideline (Health Canada, 1986). The guideline had been developed based on a 2-year cancer study in rats and mice (NTP, 1986), incorporating a surface area correction from rodents to humans and using a robust linear extrapolation model and a standard drinking water consumption rate of 1.5 L/day. Based on this approach, the unit lifetime risk associated with the ingestion of 1 µg/L benzene in drinking water was estimated to range from  $6.1 \times 10^{-7}$  (based on leukemia and lymphomas in female mice) to  $6.7 \times 10^{-6}$  (based on oral cavity squamous cell carcinomas in male rats).

In 2006, data on the carcinogenic risk to humans following the ingestion of benzene are still not available. The risk to humans can be estimated by extrapolation from human occupational inhalation exposure data. However, because only summary data are available to Health Canada for estimating the unit risk of cancer from benzene exposure, and since animals and humans display similar blood-related effects following benzene exposure, the U.S. NTP (1986) study is still deemed to be the best study with which to derive a MAC in drinking water.

Using a linearized multistage model and an allometric scaling factor (to correct for differences in metabolism between animals and humans), the estimated unit lifetime risks associated with ingestion of drinking water containing 1 µg benzene/L are estimated to range from  $1.14 \times 10^{-6}$  to  $4.85 \times 10^{-6}$  (Health Canada, 2005a), which fall within the range considered to be “essentially negligible.” In the context of drinking water guidelines, Health Canada has defined the term “essentially negligible” as a range from one new cancer above background per 100 000 people to one new cancer above background per 1 000 000 people (i.e.,  $10^{-5}$  to  $10^{-6}$ ) over a lifetime. The overall unit risk associated with the ingestion of benzene in drinking water is reported as a range, given that lifetime exposure to benzene has been shown to result in more than one cancer endpoint in animals. The above unit risk range has oral cavity squamous cell papilloma or carcinoma (oral cancer) in male rats ( $1.14 \times 10^{-6}$ ) as its lower bound (least sensitive) and bone marrow haematopoietic hyperplasia ( $4.85 \times 10^{-6}$ ) as its upper bound (most sensitive); malignant lymphoma in mice is included in this range (Health Canada, 2005a). These unit risks assume 4.0 L-eq/day as the human drinking water consumption rate in order to account for additional uptake of benzene through dermal and inhalation exposure, estimated using Krishnan (2004).

Since the 1986 guideline, evidence for benzene's leukaemogenic potential in humans has been reported by many authors for workers occupationally exposed to benzene by inhalation. The Ohio Pliofilm cohort (Rinsky et al., 1981, 1987; Crump and Allen, 1984; Paustenbach et al., 1993; Paxton et al., 1994) and Chinese worker cohort studies (Yin et al., 1987, 1994, 1996; Dosemeci et al., 1994, 1996) have emerged as good studies for assessing the carcinogenic potential of benzene in humans following inhalation exposure in the workplace. Recently, in developing its public health goal for benzene in drinking water, CalEPA reanalysed the Ohio Pliofilm and Chinese worker cohort data (OEHHA, 2001). For the Pliofilm cohort, original data were obtained, allowing for a thorough sensitivity analysis of several outstanding issues identified in the literature, including choice of exposure matrix, start date for determining person-years at risk, worker subset, choice of model, and choice of background incidence rates for calculating lifetime risks. CalEPA was unable to obtain a full set of data for the Chinese worker cohort. As a result, grouped summary data published by the original study author (Hayes et al., 1997) were used, which did not allow for a complete analysis.

In a detailed assessment of the CalEPA analysis, Health Canada agreed with its balanced approach and thorough consideration of the outstanding issues identified above. With only summary data available to Health Canada for reassessment of the two cohort studies, no new follow-up data since the CalEPA assessment, and thorough analysis of these two cohorts by many other international authors, it was concluded that another new analysis using virtually the same approach would be redundant. The only change necessary to the CalEPA analysis would be to use Canadian standard death rates to calculate the lifetime risk of cancer instead of using U.S. or Californian death rates. Given the expected similarity of Canadian leukaemia death or incidence rates and those in the United States and California, this change would have a minimal impact on the lifetime risk estimates (Health Canada, 2005b).

In using CalEPA's estimated unit risks of leukaemia for ingestion of benzene, which were extrapolated from the Pliofilm and Chinese cohort inhalation data, Health Canada estimated the lifetime risks associated with ingestion of 1 µg/L of benzene in drinking water as  $5.6 \times 10^{-6}$  (95% CI) from the Pliofilm cohort and  $7.2 \times 10^{-6}$  (95% CI) from the Chinese worker cohort. Once again, these estimated lifetime risks fall within the range considered to be "essentially negligible" and are comparable to the unit lifetime risks estimated from the animal data. These unit lifetime risks assume 4.0 L-eq/day as the human drinking water consumption rate (in order to account for inhalation and dermal exposure). Inhalation unit risks were converted to unit risks for ingestion using a standard bw of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, an inhalation absorption rate of 50%, and a conversion factor of 1 ppm = 3190 µg/m<sup>3</sup> of air (OEHHA, 2001).

## 11.0 Rationale

Since benzene is classified as a Group 1 carcinogen (carcinogenic to humans), the proposed Maximum Acceptable Concentration (MAC) is based on estimated lifetime cancer risks and consideration of available practicable treatment technology. Both animal and human epidemiological studies report similar toxic effects following exposure to benzene regardless of exposure pathway (inhalation or ingestion). The most sensitive endpoints resulting from exposure to benzene in both animals and humans are those related to the blood-forming organs.

Benzene can be found in both surface water and groundwater, although in surface water, benzene tends to volatilize into the atmosphere. Benzene may enter water through petroleum seepage, weathering of exposed coal-containing strata, air from volcanoes, forest fires, releases from plants, and anthropogenic sources. In Canada, levels of benzene in raw water sources have been reported as ranging between 0.02 and 0.42 µg/L, and levels in treated drinking water are generally less than 1 µg/L.

Several municipal-scale treatment processes can remove benzene from drinking water to levels of 0.001 mg/L. At the residential scale, drinking water treatment devices are available that have been certified as reducing VOC concentrations to 0.001 mg/L, although lower levels may be achieved with the use of these devices.

Since benzene is classified in Group 1 (carcinogenic to humans), the proposed MAC is derived based on the estimated lifetime cancer risk and takes into consideration the availability of practical treatment technology and the PQL.

A MAC of 0.001 mg/L (1 µg/L) is proposed for benzene, established on the basis of the following considerations:

- The concentration of benzene in drinking water representing an “essentially negligible” risk is 1 µg/L. Levels of benzene in drinking water should be below this level.
- The MAC must be measurable. The estimated PQL, based on the ability of laboratories to measure benzene within reasonable limits of precision and accuracy, is 0.4 µg/L.
- The MAC must be achievable at reasonable cost. Both municipal-scale and residential-scale treatment options can remove benzene from drinking water to below the guideline value.

The estimated lifetime cancer risk associated with the ingestion of drinking water containing benzene at 1 µg/L is within the range considered generally to be “essentially negligible” (i.e., between  $10^{-5}$  and  $10^{-6}$ ). Based on the incidence of oral cancer and bone marrow effects in animals following exposure to benzene by ingestion, the estimated lifetime risk associated with ingestion of water containing benzene at 1 µg/L is  $1.14 \times 10^{-6}$  to  $4.85 \times 10^{-6}$  (derived by multiplying the unit risk by the proposed MAC). The estimated unit risks from the human epidemiological data overlap those estimated from the animal data, providing additional support for a proposed MAC of 0.001 mg/L (1 µg/L) for benzene in drinking water.

In considering the health risks associated with concentrations of benzene in drinking water above the guideline value, the Federal-Provincial-Territorial Committee on Drinking Water has proposed a MAC of 0.001 mg/L for benzene in drinking water.

As part of its ongoing guideline review process, Health Canada will continue to monitor new research in this area and recommend any change(s) to the guideline that it deems necessary.

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**Appendix A: List of acronyms**

ANSI	American National Standards Institute
AOP	advanced oxidation process
BTEX	benzene, toluene, ethylbenzene, xylenes
CalEPA	California Environmental Protection Agency (U.S.A.)
CI	confidence interval
CYP2E1	cytochrome P4502E1
DNA	deoxyribonucleic acid
EBCT	empty bed contact time
GAC	granular activated carbon
$K_p$	skin permeability coefficient
LC <sub>50</sub>	median lethal concentration
LD <sub>50</sub>	median lethal dose
L-eq/day	litre equivalents per day
MAC	maximum acceptable concentration
MDL	method detection limit
NADPH	reduced nicotinamide adenine dinucleotide phosphate
NOM	natural organic matter
PAC	powdered activated carbon
PBPK	physiologically based pharmacokinetic
ppb	parts per billion
ppm	parts per million
PQL	practical quantitation limit
PTA	packed tower aeration
RNA	ribonucleic acid
RR	relative risk
SCC	Standards Council of Canada
SMR	standardized mortality ratio
U.S. EPA	United States Environmental Protection Agency
UV	ultraviolet
VOC	volatile organic compound

## **Appendix B: Provincial/territorial cost estimates**

### **Prince Edward Island**

The principal impact of a lower benzene guideline is likely to be the effect on clean-up criteria for contaminated sites, which is very difficult to quantify in economic terms. From a pure drinking water perspective, benzene contamination is most likely to effect a low percentage of private wells in immediate proximity to hydrocarbon spills. Public acceptance of any level of benzene in these cases is unlikely, and the detection of any level of benzene will likely result in treatment/replacement of supply regardless of concentration - thus a small change in the guideline is unlikely to have major impacts from this perspective.

### **Newfoundland and Labrador**

Benzene is not considered to be an issue in Newfoundland and Labrador and the province does not maintain a benzene contaminant database. Ad hoc benzene testing of drinking water sources is generally in response to a complaint. It is difficult to provide cost data due to lack of information.

### **Nova Scotia**

Based on a review of available drinking water quality data, levels of benzene in municipally treated drinking water were below detection limits. Detection limits ranged from 0.5 to 1 µg/L. As such, benzene is not expected to be an issue in Nova Scotia. A review of water quality data from semi-public drinking water supplies or private wells was not conducted. Based on a review of the supporting documentation, the following concerns are noted:

- drinking water appears to be minor source of benzene - 98 to 99% of exposure for Canadian non-smokers is from air;
- the detection limit in Nova Scotia is at or very close to the proposed maximum acceptable concentration.

### **New Brunswick**

No impact paragraph submitted.

### **Quebec**

Au Québec, entre juillet 2001 et juin 2005, plus de 2400 analyses de benzène ont été réalisées dans environ 220 réseaux de distribution d'eau potable, majoritairement approvisionnés en eau de surface. Près de 99% des analyses ont présenté un résultat inférieur à la limite de détection, représentant 0,3 µg/L ou moins. Parmi les analyses ayant présenté un résultat supérieur à la limite de détection, un seul se trouvait entre 1 et 5 µg/L et aucun n'a dépassé la norme du Règlement sur la qualité de l'eau potable établie à 5 µg/L; la médiane des résultats détectés était de 0,2 µg/L. Considérant les résultats d'analyse disponibles, les impacts attendus d'une éventuelle réduction de la norme de benzène du Règlement sur la qualité de l'eau potable en fonction de la révision de la recommandation publiée par Santé Canada seraient donc faibles.

**Ontario**

Review of the available data for the years 2001-2006 inclusive suggests that the adoption of the Canadian Drinking Water Quality Guideline of 1.0 microgram per litre may have an economic impact on some smaller drinking water systems in Ontario. Although the economic impact is minimal, there are a few small systems that may have to address the presence of benzene above the proposed MAC using appropriate treatment options. The province will provide technical guidance to these systems.

**Manitoba**

No impact paragraph submitted.

**Saskatchewan**

The presence of Benzene in surface or groundwater in Saskatchewan is most likely due to human activities such as fuel or chemical use or storage. In Saskatchewan, the mean concentrations of benzene analyzed from 30 treated surface water samples (collected from 9 locations) and 34 groundwater samples (collected from 13 locations) from 1995 to 2005 are 0.25 and 0.71 microgram/L, respectively, and these concentrations are lower than the proposed MAC level. Additionally given the ability of treatment technologies such as GAC filtration/adsorption and air stripping (packed tower aeration) to achieve effluent concentrations of benzene well below 1 microgram/L, Saskatchewan Environment does not see significant concerns associated with the proposed MAC of 1 microgram/L for benzene at this time.

**Alberta**

Benzene levels in drinking water in Alberta's public waterworks systems are very low. There will be little economical impact on Alberta's public waterworks systems as a result of the new benzene guideline.

**British Columbia**

No impact paragraph submitted.

**Yukon**

No impact paragraph submitted.

**Northwest Territories**

The Northwest Territories does not anticipate any impact due to implementation of the proposed new guideline for Benzene.

**Nunavut**

No impact paragraph submitted.