Chlorite and Chlorate in Drinking Water

Document for public comment

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

Comment period ends
October 14, 2005

May 2005

Chlorite and Chlorate in Drinking Water

Document for public comment

Table of Contents

May 2005

Chlorite and Chlorate in Drinking Water

Purpose of Consultation

For the past several years, the Federal-Provincial-Territorial Committee on Drinking Water (CDW) has been assessing the available information on chlorine dioxide, which is used as a drinking water disinfectant, and its by-products, chlorite and chlorate, with the intent of developing drinking water guidelines. The purpose of this consultation is to solicit comments on the proposed guidelines, on the approach used for their development and on the potential economic costs of implementing them, as well as to determine the availability of additional exposure data.

The CDW has requested that this document be made available to the public and open for comment. Comments are appreciated, with accompanying justification, if required. Comments can be sent to the CDW Secretariat via E-mail at water_eau@hc-sc.gc.ca. If this is not feasible, comments may be sent by mail to the CDW Secretariat, Water Quality and Health Bureau, 4th Floor, Sir Charles Tupper Bldg., A.L. 6604B, Ottawa, Ontario K1A 0K9. **All comments must be received before October 14, 2005.**

It should be noted that this supporting document on chlorite and chlorate in drinking water will be revised following evaluation of comments received, and drinking water guidelines will be established, if required. This document should be considered a draft for comment only.

May 2005

Chlorite and Chlorate in Drinking Water

1.0 Proposed Guidelines

The proposed maximum acceptable concentration (MAC) for chlorite in drinking water is 1 mg/L. The proposed MAC for chlorate in drinking water is 1 mg/L. A guideline for chlorine dioxide is not proposed because of chlorine dioxide's rapid hydrolysis to chlorite.

2.0 Executive Summary

The use of disinfectants in the treatment of drinking water has virtually eliminated waterborne diseases. The majority of drinking water treatment plants in Canada use some form of chlorine to disinfect drinking water: to treat the water directly in the treatment plant and/or to maintain a residual in the distribution system to prevent bacterial regrowth. Chlorine dioxide is a chlorinated disinfectant that can be used as an alternative to chlorine.

Chlorite and chlorate are disinfection by-products that are found in drinking water when chlorine dioxide is used as a disinfectant. Chlorine dioxide is an effective drinking water disinfectant, but it is very reactive and must be produced on site. Chlorite and chlorate ions are formed during the generation of chlorine dioxide and the generation technology and the generator "tuning" will affect the levels of chlorite and chlorate fed into the drinking water. Subsequently, the majority of chlorine dioxide added to drinking water will eventually form chlorite. Chlorate can also be formed when hypochlorite solutions do not meet quality specifications and are not stored and/or used appropriately.

Health Canada recently completed its review of the health risks associated with chlorite, chlorate and chlorine dioxide in drinking water. Its review, which is summarized in this supporting document, assessed all identified health risks, taking into account new studies and approaches and incorporating appropriate safety factors. Based on this review, the proposed guideline for chlorite in drinking water is 1 mg/L; the proposed guideline for chlorate in drinking water is 1 mg/L; and no guideline is proposed for chlorine dioxide.

The Federal-Provincial-Territorial Committee on Drinking Water has reviewed the proposed guidelines for chlorite and chlorate and has given approval for these guidelines and the corresponding supporting document to undergo public consultation.

2.1 Health Effects

Studies on chlorite, chlorate and chlorine dioxide do not provide sufficient information to assess their potential as carcinogens. The proposed guideline for chlorite was based on a two-generation study in rats in which the effects of concern were lower startle amplitude (reaction to sudden noise), decreased brain weight and altered liver weights in two generations. As sodium chlorate is used as a weed killer, several cases of chlorate poisoning in humans have been reported. Animal studies on chlorate suggest an increase in the utilization or metabolism of thyroid hormones.

Chlorine dioxide can affect the neurobehavioural and neurological development of rats exposed before birth at levels that are significantly higher than those that could exist in drinking water.

2.2 Exposure

Chlorine dioxide hydrolyses quickly to chlorite and chlorate. Because of this rapid reaction, the concentrations of chlorine dioxide in drinking water are expected to be much lower than levels of concern, and no guideline is proposed for chlorine dioxide.

Canadians can be exposed to chlorite and chlorate from drinking water that has been treated with chlorine dioxide either as a disinfectant or to help control taste and odour. As few drinking water treatment plants in Canada currently use chlorine dioxide, this is not expected to be a significant source of exposure for the average Canadian. Exposure to chlorate may also be linked to the use of hypochlorite solutions as a source of chlorine in municipal treatment plants. This exposure can be reduced through appropriate storage/use of hypochlorite solutions at the treatment plant.

2.3 Treatment

If chlorine dioxide and chlorite ion are not removed prior to post-chlorine disinfection, they will react with free chlorine to form chlorate ion. Once chlorate ion is present in water, it is very persistent and very difficult to remove. It is therefore recommended that municipal treatment plants control the production of chlorate ion. In the case of treatment plants using hypochlorite solutions, operators must ensure that the solution they use meets quality specifications and is stored and used appropriately. In the case of treatment plants using chlorine dioxide generators, the formation of chlorate can be reduced by tuning the chlorine dioxide generator, ensuring maximum efficiency of chlorine dioxide production and removing any chlorite ion with activated carbon, iron-reducing agents or sulphur-reducing agents before adding a chlorine residual.

It is not generally recommended that drinking water treatment devices be used to provide additional treatment to municipally treated water. Nevertheless, some residential-scale treatment devices using a granular activated carbon filter may remove chlorite, although none is currently certified for this use.

3.0 Identity, Use and Sources in the Environment

Sodium chlorite is a white crystal or crystalline powder with a density of 2.468 g/cm^3. It has a melting point of 180–200°C (analytical grade) and a solubility of 390 g/L at 17°C (Noack and Doerr, 1976; U.S. NRC, 1987; Lewis, 1993). Sodium chlorite is a very strong oxidizer (Simpson et al., 1995). It is used in on-site production of chlorine dioxide at water treatment plants.

Chlorine dioxide is a greenish to reddish-yellow gas at ambient temperature and pressure (Gates, 1989; Lewis, 1993). It has a water solubility of 3.01 g/L at 25°C and 4.6 kPa (Budavari, 1976). It is also soluble in alkaline and sulphuric acid solutions (Haller and Northgraves, 1955; Budavari, 1996). Chlorine dioxide has a melting point of –59.5°C, a boiling point of 11°C and a density of 1.642 at 0°C (U.S. NRC, 1987; Budavari, 1996). The taste and odour threshold for chlorine dioxide is 0.4 mg/L (U.S. NRC, 1987). Chlorine dioxide has an oxidation potential of 1.275 (relative to hydrogen electrodes) and an oxidation power relative to chlorine (1.00) of 0.94.

As chlorine dioxide is a strong oxidizing agent, it is used to help control tastes and odours in drinking water and serves as an alternative disinfectant to chlorine. Due to its volatile and reactive nature, chlorine dioxide must be generated on site and has a very limited shelf life. Chlorine dioxide disinfection requires less contact time and lower dose levels than chlorine for comparable coliform reductions (Aieta et al., 1980).

Chlorine dioxide is typically used as a primary disinfectant, but it is also quite effective in neutralizing nitrifying bacteria in distribution areas when post-chloramination is practised. Some utilities have carried a chlorine dioxide residual into the distribution system to maintain water quality (Volk et al., 2002). Studies have shown that approximately 70% of the applied chlorine dioxide will eventually form chlorite, while about 10% will form chlorate (Volk et al., 2002). Chlorine dioxide is also used as a bleaching agent for cellulose, paper pulp, flour and oils and for cleaning and detanning leather (U.S. NRC, 1987; Budavari et al., 1989; Meister, 1989).

Chlorine dioxide hydrolyses to chlorous and chloric acids (Budavari, 1996). Aqueous solutions of chlorine dioxide are subject to partial photodecomposition (White, 1992). In alkaline solution, a mixture of chlorite (ClO_2^-) and chlorate(ClO_3^-) ions is formed rapidly. Approximately 50% conversion of chlorine dioxide to chlorite is reported (Cotton and Wilkinson, 1980; U.S. NRC, 1980). Chlorine dioxide does not react with water or ammonia but oxidizes the bromide ion to hypobromide and bromate in the presence of intense sunlight and at high concentrations. Generally, chlorine dioxide does not react with primary amines but will react slowly with secondary and tertiary amines (e.g., formaldehyde and acetaldehyde), producing secondary aliphatic amines without the formation of N-oxides. Chlorine dioxide does not produce any trihalomethanes as by-products in the presence of humic and fulvic substances. Instead, both quinones and hydroxyquinones are formed. From pure chlorine dioxide, four classes of oxidation products were obtained at pH 3 and pH 7.8: benzylenepolycarboxylic acids, aliphatic dibasic acids, carboxyphenylglyoxylic acids and aliphatic monobasic acids (Rice and Gomez-Taylor, 1986). Other degradation products include aldehydes and carboxylic acids (Trevors and Basaraba, 1980; Rav-Acha, 1984).

4.0 Exposure

The major route of environmental exposure to chlorine dioxide, chlorite and chlorate is through drinking water. Chlorite and chlorate ions are disinfection by-products that are often found in drinking water where chlorine dioxide is used in the treatment process. They are formed in the generation of chlorine dioxide, and it is the generation technology and, to a lesser degree, the generator "tuning" that will determine the types and quantities of impurities, such as chlorite, chlorate and perchlorate (ClO_4^-) ions, that may be found in the final chlorine dioxide feed (Gordon, 2001). In addition, chlorine dioxide precursors will influence what by-products may be formed in the distribution system. Additional formation of chlorate ion in water may occur through the photolytic decomposition of pre-existing chlorine dioxide and chlorite by sunlight and fluorescent lighting (Griese et al., 1992).

The levels of chlorite ion in water reported in one study ranged from 3.2 to 7.0 mg/L, and chlorate ion concentration ranged from 0.17 to 1.79 mg/L (Michael et al., 1981). Chlorine dioxide, chlorite and chlorate ions were measured in 8 systems in Quebec between February and March 2003 (winter) as well as in July 2003 (summer) at different locations along the distribution system: after treatment but before the distribution system (T) and at three points along the distribution system (D1, D2 and D3). A range and average of concentrations for all locations are found in the following Table 1.

Table 1. Concentration of chlorine dioxide, chlorite and chlorate in Québec in 2003

Chemical	Season	T	D1	D2	D3
Chlorine Dioxide (mg/L)	Winter	0.01-0.53 (0.22)	<0.01-0.21 (0.09)	<0.01-0.22 (0.09)	<0.01-0.06 (0.03)
	Summer	<0.01 - 0.63 (0.32)	not analyzed	not analyzed	not analyzed
Chlorite Ion (mg/L)	Winter	<0.026-0.872 (0.36)	<0.026-0.846 (0.36)	<0.026-0.769 (0.34)	<0.026-0.686 (0.29)
	Summer	<0.033-1.617 (0.48)	<0.033-1.557 (0.45)	<0.033-1.58 (0.44)	<0.033-1.253 (0.39)
Chlorate Ion (mg/L)	Winter	<0.032-0.308 (0.13)	<0.032-0.321 (0.13)	<0.032-0.289 (0.12)	<0.032-0.308 (0.13)
	Summer	0.081-0.586 (0.21)	0.115-0.611 (0.22)	0.112-0.592 (0.22)	0.151-0.576 (0.22)

Chlorine dioxide, chlorite and chlorate may occur in foodstuffs as a result of their use in flour processing, as a decolorizing agent for carotenoids and other natural pigments (chlorine dioxide), as a bleaching agent in the preparation of modified food starch (sodium chlorite), as an indirect additive in paper and paperboard products used for food packaging (sodium chlorite) and as a defoliant, desiccant and fungicide in agriculture (sodium chlorate) (U.S. EPA, 1983; CMA, 1989; U.S. FDA, 1990).

Although the formation of chlorate is most often associated with the use of chlorine dioxide, the treatment of drinking water with either sodium hypochlorite (NaOCl) or calcium hypochlorite ($Ca(OCl)_2$) can also increase the concentration of chlorate in finished water. The decomposition of hypochlorite solution results in the reduction of its strength and the formation of chlorate and, to a lesser extent, oxygen. Solid forms of hypochlorite are not affected by this decomposition (Gordon et al., 1995).

5.0 Analytical Methods

The U.S. Environmental Protection Agency (EPA) recognizes and approves the following three methods for the determination of chlorite in drinking water: (1) Standard Method 4500-ClO2 E (APHA et al., 1998), (2) EPA Method 300.0 (U.S. EPA, 1999b) and (3) EPA Method 300.1 (U.S. EPA, 1998). The U.S. EPA recognizes and approves the following two methods for the determination of chlorate in drinking water: (1) EPA Method 300.0 (U.S. EPA, 1999b) and (2) EPA Method 300.1 (U.S. EPA, 1998). In addition, the U.S. EPA has proposed the following three methods for the determination of chlorite and chlorate in drinking water: (1) EPA Method 317.0, Revision 2.0 (U.S. EPA, 2001a), (2) EPA Method 326.0, Revision 1.0 (U.S. EPA, 2002) and (3) EPA Method 327.0, Revision 1.0 (U.S. EPA, 2003b); however, these methods have not yet been approved. As well, flow injection analysis can be used for the detection of both chlorite and chlorate. The analytical methods for the determination of chlorite and chlorate in drinking water are summarized in Appendix 1.

Standard Method 4500-ClO2 E (APHA et al., 1998) is an amperometric determination of chlorine dioxide, chlorine, chlorite and chlorate in water, done by performing successive titrations at varying pH ranges using either phenyl arsine oxide or sodium thiosulphate as the titrant. The application of potassium bromide as a reducing agent at one stage of the titration will minimize the oxidation of iodide to iodine by oxygen at a low pH, while the addition of potassium iodide crystals will prevent the reduction of iodate to iodine. At the low pH ranges necessary for chlorite and chlorate determination, this method is susceptible to interferences from manganese, copper and nitrite. The chlorite determination has a method detection limit (MDL) of 100 μg/L and a practical quantitation limit (PQL) of 500 μg/L (U.S. EPA, 1999a). The amperometric method is useful when knowledge of the various chlorine fractions in a water sample is desired, and it is suitable for utility use in daily testing; however, a great deal of analytical skill is required.

In EPA Method 300.0, Revision 2.2 (U.S. EPA, 1999b), a small volume of sample is introduced into an ion chromatograph. The anions of interest are separated and measured using a system composed of a guard column, analytical column, suppressor device and conductivity detector. The chlorite determination has an MDL of 10 μg/L and a PQL of 50 μg/L, while the chlorate determination has an MDL of 3 μg/L and a PQL of 15 μg/L.

In EPA Method 300.1, Revision 1.0 (U.S. EPA, 1998), the same procedure is followed as for EPA Method 300.0. However, EPA Method 300.1 uses a superior analytical column to attain improved sensitivity for analysis. The chlorite determination has an MDL of 0.45 μg/L and a PQL of 2.2 μg/L, while the chlorate determination has an MDL of 0.78 μg/L and a PQL of 3.9 μg/L.

EPA Method 317.0, Revision 2.0 (U.S. EPA, 2001a), is nearly identical to EPA Method 300.1 but includes a post-column reactor with o-dianisidine dihydrochloride and an ultraviolet/visible detector that targets bromate. The chlorite determination has an MDL of 1.6 µg/L and a PQL of 8.0 µg/L.

EPA Method 326.0, Revision 1.0 (U.S. EPA, 2002), again is nearly identical to EPA Method 300.1 but includes a post-addition of potassium iodide and molybdenum(VI) and an ultraviolet/visible detector that specifically targets bromate. The chlorite determination has an MDL of 1.6 µg/L and a PQL of 8.0 µg/L

EPA Method 327.0, Revision 1.0 (U.S. EPA, 2003b), is a spectrophotometric method using the colour indicator Lissamine Green B and is another simple method that is suitable for determining chlorite at levels typically found at water treatment plants. The reagent Lissamine Green B/horseradish peroxidase is added to the water sample, where the horseradish peroxidase helps catalyse the conversion of chlorite to chlorine dioxide. The chlorine dioxide then oxidizes the Lissamine Green B and reduces its absorbance, which is proportional to the original chlorite concentration and is measured by a spectrophotometer at 633 nm. The detection limit for this method has a range of 78–110 µg/L for chlorite.

Flow injection analysis can also be used for the detection of both chlorite and chlorate. This method, however, is prone to interference from chloramines and other oxidants present in drinking water. The detection limits for chlorite and chlorate are 0.01 and 0.02 mg/L, respectively, using the flow injection analysis method (Novatek, 1991).

6.0 Treatment Technology

Chlorine dioxide and chlorite ion will react with free chlorine to form chlorate ion. Once chlorate ion is present in water, it is very persistent and very difficult to remove (Gallagher et al., 1994; U.S. EPA, 1999a). Given that 70% of the applied chlorine dioxide can eventually form chlorite (Volk et al., 2002), two strategies are recommended to minimize initial chlorite formation,: (1) the control of treatment processes to reduce disinfectant demand; and (2) the control of disinfection processes to ensure maximum efficiency of chlorine dioxide production.

6.1 Municipal

6.1.1 Chlorite

There are four available treatment options control chlorite ion concentrations in drinking water at the municipal scale: (1) tuning of the chlorine dioxide generator; (2) activated carbon; (3) iron reducing agents; and (4) sulphur reducing agents. These are described briefly below:

(1) *Chlorine dioxide generator tuning*: Chlorine dioxide generator design and performance have a large impact on the amount of chlorite ion formed during chlorine dioxide production. Precise operation ("tuning"), proper maintenance and the generation technology employed with the chlorine dioxide generator have a large bearing on the chlorine dioxide production efficiency and the rate at which chlorite and other undesirable by-products, such as

chlorate, hydrogen peroxide and perchlorate, are formed and fed into the water with the chlorine dioxide dose. A properly tuned generator will have high purity thus limiting the presence of chlorine dioxide precursors such as chlorite in the feed. These chlorine dioxide precursors can carry through into the distribution system and increase the total concentration of chlorate and chlorite (Gordon, 2001). Current commercial chlorine dioxide generators may be broadly classified as chlorite based, chlorate based or electrochemical systems.

Chlorite ion-based systems rely on the oxidation of chlorite ion to chlorite through the use of an acid (sulphuric acid), which may attain a maximum conversion efficiency of 80% by stoichiometry; or through the use of chlorine gas, which can result in chlorite carry-through if the chlorine gas feed is too low and chlorate formation if the chlorine gas feed is too high.

Recently developed chlorate ion-based systems typically depend on the reduction of chlorate ion through the reaction of sodium chlorate with an acid and hydrogen peroxide. The product may be quite acidic, and the risk of high hydrogen peroxide and perchlorate levels in the water may detract from the viability of this method.

Electrochemical systems can either directly or indirectly generate chlorine dioxide. The direct method involves the electrolysis of chlorite ion to chlorine dioxide at the anode, and the indirect method is the production of an acid or chlorine gas as a precursor chemical, resulting in the formation of chlorine dioxide, again at the anode. When the chlorine dioxide is formed at the anode, it must be extracted as a gas from the solution by gas-stripping columns, eductors/venturis, low-pressure air flow over a packed bed or perstraction, which involves the use of a gas-permeable hydrophobic membrane. Proper balance and control are required with these systems to prevent the formation and carry-through of impurities such as acid, chlorate ion, perchlorate ion and chlorine (Gordon, 2001).

(2) *Activated carbon*: Activated carbon will remove chlorite ion through adsorption and chemical reduction. Early break-through has been reported in granular activated carbon (GAC) filters when the adsorptive sites have been exhausted, perhaps by competing organic compounds, and only the reduction mechanism remains. The performance of GAC filters for chlorite removal is further complicated by the oxidation of chlorite to chlorate, which may occur if free chlorine is present in the feed water. Short bed life, high operating costs and the potential for chlorate formation make GAC an impractical choice for chlorite removal at the municipal scale (Dixon and Lee, 1991).

(3) *Iron reducing agents*: Ferrous iron (Fe^{2+}) will chemically reduce chlorite ion, thereby lowering its concentration in water. Chlorate ion will form only if the pH drops below 5, which can occur at localized application points where acidic reducing agents such as ferrous chloride are added to the water. Good application and rapid mix and/or pH adjustment to neutral pH 7 may prevent the occurrence of micro-regions of low pH and the subsequent formation of chlorate (Griese et al., 1992). When the pH exceeds 7, the subsequent reaction of chlorite and ferrous iron forms insoluble ferric hydroxide, which may be beneficial by aiding clarification when used in conjunction with filtration to capture the solids (Iatrou and Knocke, 1992). However, if the pH exceeds 9, elevated dissolved oxygen and dissolved organic carbon levels impede the effectiveness of ferrous iron and require increased ferrous dosages to attain

adequate chlorite removal. Ferrous iron dosing of 3.5–4.0 mg/mg chlorite provides efficient removal of chlorite ion over the targeted pH range (Hurst and Knocke, 1997). Any residual chlorite will react with chlorine to form chlorate and should be removed before post-chlorine disinfectant is applied. Ferrous iron or thiosulphate, when used as treatment options for chlorite removal and fed in excess of the demand, can complicate post-disinfection (U.S. EPA, 2001b).

(4) *Sulphur reducing agents*: Sulphur agents such as sulphite, metabisulphite and thiosulphate will reduce chlorine dioxide and chlorite ion, thereby lowering their concentrations in water. In the presence of dissolved oxygen, sulphite and metabisulphite will reduce chlorite to form chloride ion and the undesirable chlorate ion and, as such, are not recommended for the removal of chlorite in drinking water. Thiosulphate is effective at reducing chlorine dioxide and chlorite and does not form chlorate as a by-product, but it requires a long contact time and is pH dependent, which may limit its effectiveness (Griese et al., 1991).

6.1.2 Chlorate

Currently, there is no known practical and economical treatment available to remove chlorate ion once it has been formed in drinking water. As much as 35% of the chlorate found in a distribution system can be attributed to the type and performance (tuning) of the chlorine dioxide generator. If chlorite ion is present in water and is not removed, it will react with any applied free chlorine to produce chlorate and chloride ions. In order to control persistent disinfection by-product formation, it is important to minimize production of chlorate ion in the chlorine dioxide generation process and to remove the chlorite ion before adding post-chlorine (Gallagher et al., 1994).

The formation of chlorate ion in a hypochlorite solution is influenced by storage conditions such as pH, temperature, length of time in storage, presence of ultraviolet light, concentration of solution and presence of transition metals (Gordon et al., 1995). Hypochlorite solutions should:

- contain less than 1500 mg chlorate/L;
- have a pH greater than 12;
- be used within a relatively short time frame after delivery (within 3 months);
- be stored in a cool dry location where the temperature does not exceed 30°C, away from sunlight; and
- contain less than 0.08 mg/L of transition metals (AWWA, 2004).

Manufacturers are able to produce bleach that has a lower initial concentration of chlorate; utilities should specify hypochlorite solutions with a chlorate concentration as low as possible to ensure that they will meet the proposed guideline for chlorate in finished water .

6.2 Residential

Generally, it is not recommended that drinking water treatment devices be used to provide additional treatment to municipally treated water. Since chlorine dioxide would not be used to disinfect individual water systems, it is not likely that chlorite or chlorate would be present in individual surface water or groundwater sources. Some residential-scale treatment devices may remove chlorite, but none is currently certified for this use.

Health Canada does not recommend specific brands of drinking water treatment devices, but it strongly recommends that consumers look for a mark or label indicating that the device has been certified by an accredited certification body as meeting the appropriate NSF International (NSF)/American National Standards Institute (ANSI) standard. 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 or service conforms to applicable standards and must be accredited by the Standards Council of Canada (SCC). The following organizations have been accredited by the SCC to certify drinking water devices and materials as meeting NSF/ANSI standards:

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

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

6.2.1 Chlorite

Where point-of-entry or point-of-use treatment technology is being considered at the residential scale, chlorite removal options are limited solely to adsorption through a GAC filter. However, there are currently no certified drinking water treatment devices that specifically remove chlorite ion. NSF has developed several standards for residential water treatment devices designed to reduce the concentrations of various types of contaminants in drinking water. However, chlorite is currently not included in any NSF standard.

Research is ongoing in the private and public sectors to test and adopt efficient methods for the reduction of chlorite in drinking water. Products that use adsorption technology such as activated carbon lose removal capacity through usage and time and need to be replaced. Consumers should verify the expected longevity of the adsorption media in their treatment device as per the manufacturer’s recommendations and service it when required, understanding that research shows break-through occurs earlier for chlorites than for other chlorine compounds.

6.2.2 Chlorate

There is no known residential-scale treatment technology available at the present time to remove chlorate ion from residential tap water once it has been formed (Gallagher et al., 1994).

7.0 Kinetics and Metabolism

7.1 Absorption and Metabolism

Chlorite ion, chlorate ion and chlorine dioxide are rapidly absorbed from the gastrointestinal tract in rats. No particular organ appears to selectively concentrate the dose following exposure to chlorite ion, chlorate ion and chlorine dioxide (Abdel-Rahman, 1985). Following oral ingestion, chlorine dioxide was rapidly converted into chloride ion and, to a lesser extent, chlorite and chlorate by monkeys (Abdel-Rahman et al., 1982a; Bercz et al., 1982). It was transformed mainly into chloride in rats, smaller amounts appearing as unchanged chlorite.

Following oral administration of chlorine dioxide to rats, the plasma levels of chlorine dioxide peaked after 1 hour. The plasma half-life was 44 hours (U.S. NRC, 1982).

7.2 Distribution

The distribution of ^{36}Cl-labelled chlorite ion (10 mg/L solution) and chlorate ion (5 mg/L solution) was studied in rats following oral administration. The amounts found in various fluids and tissues (as a percentage of the initial dose) after 72 hours for chlorite ion were as follows: 0.55% in plasma, 0.63% in packed cells, 0.64% in whole blood and a total of about 3% in kidneys, lungs, stomach, duodenum, ileum, liver, spleen, bone marrow, testes, skin and carcass, with the highest concentrations found in the testis, skin, stomach and lungs (0.4% each). Chlorate was distributed in the tissues as follows: 0.68% in plasma, 0.23% in packed cells and 0.57% in whole blood, with a total of 3.6% in kidneys, lungs, stomach, duodenum, ileum, liver, spleen, bone marrow, testes, skin and carcass and with the highest concentrations (0.4% each) in kidney, lung, stomach, testis and skin (Abdel-Rahman et al., 1982a).

7.3 Excretion

Rats excreted 30% of an oral dose of ^{36}Cl-labelled chlorine dioxide in the urine after 72 hours. About 27% of the chlorine label was in the form of chloride and 3% in the form of chlorite ion. An additional 9% was excreted in the faeces. Of the labelled chlorite ion administered orally to rats, 40% was excreted in the urine as chloride after 72 hours. No chlorate ion was found after ingestion of chlorine dioxide or chlorite. When labelled chlorate ion was administered orally to rats, approximately 38% of the labelled material was excreted in the urine; 20% was in the form of chloride, 4% was in the form of chlorite ion and 13% was in the form of chlorate ion. The authors concluded that once these compounds are ingested, they are rapidly degraded in the body to chloride and consequently are not considered to be of toxicological concern following chronic exposure in drinking water (Abdel-Rahman et al., 1980b, 1984a, 1984b). Excretion of chlorite, chlorate and chlorine dioxide is mainly via the urine, smaller amounts being excreted in faeces (Abdel-Rahman et al., 1982a, 1985).

8.0 Health Effects

8.1 Effects in Humans

8.1.1 Acute Toxicity

Because of its use as a weed killer, a large number of cases of chlorate poisoning have been reported (U.S. NRC, 1987). Symptoms include methaemoglobinaemia, anuria, abdominal pain and renal failure. For an adult human, the oral lethal dose is estimated to be as low as 20 g of sodium chlorate (230 mg chlorate/kg bw) (U.S. NRC, 1982).

Six different doses of chlorine dioxide (0.1, 1, 5, 10, 18 and 24 mg/L), chlorite ion (0.01, 0.1, 0.5, 1.0, 1.8 and 2.4 mg/L) and chlorate ion (0.01, 0.1, 0.5, 1.0, 1.8 and 2.4 mg/L) in drinking water were administered to each of 10 male volunteers. Each volunteer ingested 1000 mL of the water in two portions. The study involved a series of six sequences of 3 days each. Serum chemistry, blood count and urinalysis parameters were monitored. A treatment-related change in group mean values for serum uric acid was observed with chlorine dioxide exposure, which the authors concluded was not physiologically detrimental. The highest dose tested, 24 mg/L (about 0.34 mg/kg bw per day), can be identified as a single-dose no-observed-adverse-effect level (NOAEL) for chlorine dioxide. Changes in group mean values for serum urea nitrogen, creatinine and urea nitrogen/creatinine ratio were observed in the chlorite exposure groups, which the authors concluded were not adverse physiological effects. Very slight changes in group mean serum bilirubin, iron and methaemoglobin were observed in the chlorate exposure groups, but the authors concluded that they were not adverse physiological effects. A NOAEL of 2.4 mg/L (0.034 mg/kg bw per day) was identified for both chlorite ion and chlorate ion (Lubbers et al., 1981).

The same male volunteers drank 0.5 L of water containing 5 mg chlorine dioxide/L each day for approximately 12 weeks and were then kept under observation for 8 weeks. Serum chemistry, blood counts and urinalysis revealed no abnormalities, except for a slight change in blood urea nitrogen, which the authors concluded was of doubtful physiological or toxicological significance. This exposure, equivalent to 0.036 mg/kg bw per day, can be considered a NOAEL (Lubbers et al., 1981).

In a prospective study of 197 persons, a portion of the population of a rural village exposed for 12 weeks to a chlorine dioxide-treated water supply (containing 0.25–1.1 mg chlorine dioxide/L and 0.45–0.91 mg free chlorine/L) experienced no significant changes in haematological parameters, serum creatinine or total bilirubin (CMA, 1989).

8.1.2 Reproductive Effects

A cross-sectional study was conducted of 548 births at Galliera Hospital in Genoa and 128 births at Chiavari Hospital in Chiavari (Italy) during 1988–1989 to mothers residing in each city. Women in Genoa were exposed to filtered water disinfected with chlorine dioxide (Brugneto River wells, reservoir and surface water) and/or chlorine (Val Noci reservoir). Women residing in Chiavari used untreated well water. Water source and type of disinfectant were recorded, as well as family income, mother's age, smoking, alcohol consumption, education level and birth outcomes (low birth weight, preterm delivery, body length, cranial circumference and neonatal jaundice). Neonatal jaundice was almost twice as likely (odds ratio 1.7; 95% confidence interval 1.1–3.1) in infants whose mothers used surface water disinfected with chlorine dioxide as in infants whose mothers used untreated well water. Chlorinated surface water did not produce a similar effect. Smaller cranial circumference and body length were associated with water from surface water sources disinfected with chlorine or chlorine dioxide. Risks of low birth weight ($\leq$2500 g) were also increased in infants whose mothers used drinking water disinfected with either chlorine or chlorine dioxide, but they were not statistically significant. For preterm delivery ($\leq$37 weeks), there were small but non-significant increased risks associated with chlorine or chlorine dioxide disinfection. This study suggests possible risks associated with surface water disinfected with either chlorine or chlorine dioxide, but the results should be interpreted very cautiously. No information was collected to assess the mothers' water consumption (including use of bottled water) or nutritional habits, and the age distribution of the mothers was not considered. In addition, there are concerns about incomplete ascertainment of births and whether the populations may be different in aspects other than the studied water system differences. Exposures to surface water and groundwater sources are compared in this study; however, no information is presented about other possible water quality differences. No conclusion can be drawn from this study, since some of the effects were not statistically significant and also because numerous biases were found (Kanitz et al., 1996).

8.2 Effects on Experimental Animals and *In Vitro*

8.2.1 Acute Toxicity

For sodium chlorite, oral LD_{50}s reported in rats, mice and guinea pigs were 165, 350 and 300 mg/kg bw, respectively (Pis'ko et al., 1980). Oral LD_{50}s of 105 and 493 mg/kg bw have been reported in rats and quail, respectively (Musil et al., 1964; Fletcher, 1973).

Sodium chlorate is moderately toxic in laboratory animals, with oral LD_{50}s of 1200, 8350 and 7200 mg/kg bw (for chlorate ion) identified in rats, mice and rabbits, respectively (RTECS, 2000b).

One hour after dogs ingested 0.5–2 g sodium chlorate/kg bw, the dogs vomited and their methaemoglobin levels increased. Chlorate ion was observed in the blood and urine. Dogs who received the highest dose (between 1 and 2 g/kg bw) developed tachycardia and depression. They also exhibited cyanosis and died between 12 and 24 hours later (Sheahan et al., 1971).

An oral LD_{50} of 292 mg chlorine dioxide/kg bw was identified for rats. At this dose, chlorine dioxide causes somnolence and respiratory stimulation (Abdel-Rahman et al., 1982b).

8.2.2 Short-term Exposure

8.2.2.1 Chlorite

Single doses of sodium chlorite administered orally to cats produced methaemoglobinaemia. A dose of 1.5 mg chlorite/kg bw caused up to 32% of the haemoglobin to be in the methaemoglobin state and was considered to be the lowest-observed-adverse-effect level (LOAEL) (Heffernan et al., 1979).

In a more recent study, doses of 0, 10, 25 or 80 mg sodium chlorite/kg bw per day were administered daily by gavage to male and female Crl: CD (SD) BR rats (15 per sex per group) for 13 weeks (equivalent to 0, 7.4, 18.6 or 59.7 mg chlorite/kg bw per day). The highest dose produced death in a number of animals. It also resulted in morphological changes in erythrocytes and significant decreases in haemoglobin concentrations. A non-significant reduction in red blood cell counts was observed at 10 mg/kg bw per day in male rats, with further decreases being observed at 80 mg/kg bw per day. Red blood cell counts were significantly depressed in female rats at doses of 25 mg/kg bw per day and above. As would be expected where haemolysis is occurring, splenic weights were increased. Adrenal weights were increased in females at 25 and 80 mg/kg bw per day, whereas statistically significant changes were observed only at 80 mg/kg bw per day in males. Histopathological examination of necropsied tissues revealed squamous cell epithelial hyperplasia, hyperkeratosis, ulceration, chronic inflammation and oedema in the stomach of 7 of 15 males and 8 of 15 females given 80 mg/kg bw per day doses. This effect was observed in only 2 of 15 animals at the 25 mg/kg bw per day dose and not at all at the 10 mg/kg bw per day dose. The NOAEL for this study was determined to be 7.4 mg chlorite/kg bw per day for stomach lesions and increases in spleen and adrenal weights (Harrington et al., 1995).

In an study of oxidative damage to erythrocytes, rats were exposed to chlorite ion at 0, 1, 5, 10, 25 or 50 mg/kg bw per day for 30–90 days in their drinking water. Haematological parameters were monitored, and the three highest concentrations produced transient anaemia. At 90 days, red blood cell glutathione levels in the 10 mg/kg bw per day group were 40% below those of controls, and there was at least a 20% reduction in rats receiving 5 mg/kg bw per day. A NOAEL of 1 mg/kg bw per day was identified (Heffernan et al., 1979). While providing useful information on the toxicity of chlorite, the design of this study would not make it suitable as a basis for setting a drinking water guideline, because the effects were transient and occurred at only two dose levels.

Both A/J and C57L/J mice were exposed to sodium chlorite at about 0.15, 1.5 or 15 mg/kg bw per day in their drinking water for 30 days. At a dose of 15 mg/kg bw per day, increases in glucose-6-phosphate dehydrogenase, mean corpuscular volume and osmotic fragility were observed; however, no increases were seen at lower doses. There was a significant difference between strains for both glucose-6-phosphate dehydrogenase and osmotic fragility (Moore and Calabrese, 1982). The NOAEL for this study was 1.5 mg/kg bw per day, based on blood changes.

African green monkeys (five males and seven females) were used to study the thyroid effects of sodium chlorite when administered for 30–60 days as chlorite at concentrations of 4, 7.5, 15, 30 or 58.4 mg/kg bw per day (U.S. NRC, 1987). Chlorite did not induce thyroid depression. Chlorite induced a dose-dependent oxidative stress, which resulted in a decrease in haemoglobin and erythrocyte count and an increase in methaemoglobin, which is interpreted as oxidative stress on haematopoiesis. There was a statistically significant dose-dependent increase in alanine aminotransaminase, but the authors indicated that the change was not clinically important. The blood changes during the study reversed before the end of the administration of chlorite, further indicating that only mild clinical changes had occurred. No NOAEL or LOAEL was determined in this study. However, based on a review by the U.S. EPA (2000), the data were not presented in a manner that would allow identification of threshold doses for these effects.

In another study, male rats and white leghorn chickens were given chlorite in drinking water at approximately 4.28, 42.8 and 428 mg/kg bw per day (chickens) and 3.42, 34.2 and 342 mg/kg bw per day (rats) for 4 months. A decrease in osmotic fragility of erythrocytes and in the morphology of erythrocytes was observed in both species in all treatment groups (Abdel-Rahman et al., 1980a)

8.2.2.2 Chlorate

No evidence of adverse toxicity except for minor signs of anaemia at the highest dose was observed in rats orally administered sodium chlorate by gavage at doses of 10, 100 or 1000 mg/kg bw per day for 13 weeks (Bio/Dynamics, Inc., 1987b).

Beagle dogs (four per sex per dose) were exposed by gavage to sodium chlorate at doses of 0, 10, 60 or 360 mg/kg bw per day for 3 months. Haematological changes were limited to a slight elevation in methaemoglobin level in high-dose animals, but this appeared to be within normal limits and was not judged to be treatment-related. No other effects were observed. A NOAEL of 360 mg/kg bw per day in dogs was identified (Bio/Dynamics, Inc., 1987a).

Sprague-Dawley rats (14 per sex per dose) were exposed by gavage to sodium chlorate at doses of 0, 10, 100 or 1000 mg/kg bw per day for up to 3 months. At the highest dose, haematological changes indicative of anaemia included decreases in erythrocyte count, haemoglobin concentration and erythrocyte volume fraction (haematocrit). No other effects were observed. A NOAEL of 100 mg/kg bw per day was identified (Bio/Dynamics, Inc., 1987b).

In a 90-day study, concentrations of chlorate at 30, 100 or 510 mg/kg bw per day in males and 42, 164 or 800 mg/kg bw per day in females in drinking water were provided to Sprague-Dawley rats. Body weight gain was sharply curtailed in both sexes at the highest concentration. These effects were generally paralleled by smaller organ weights (except for brain and testes). Some decreases in haemoglobin, haematocrit and red blood cell counts were observed at this same dose. Pituitary lesions (vacuolization in the cytoplasm of the pars distalis) and thyroid gland colloid depletion were observed in both the mid- and high-dose groups of both sexes. A NOAEL of 30 mg/kg bw per day was identified (McCauley et al., 1995).

African green monkeys (five males and seven females) were used to study the thyroid effects of sodium chlorate when administered for 30–60 days as chlorate at concentrations of 4, 7.5, 15, 30 or 58.4 mg/kg bw per day (U.S. NRC, 1987). Chlorate did not induce thyroid depression. Chlorate did not induce a dose-dependent oxidative stress, as was observed in the case of chlorite. No NOAEL or LOAEL was determined in this study. However, based on a review by the U.S. EPA (2000), the data were not presented in a manner that would allow identification of threshold doses for these effects.

In another study, male rats and white leghorn chickens were given chlorate in drinking water at approximately 4.28, 42.8 and 428 mg/kg bw per day (chickens) and 3.42, 34.2 and 342 mg/kg bw per day (rats) for 4 months. A decrease in osmotic fragility of erythrocytes and in the morphology of erythrocytes was observed in both species in all treatment groups (Abdel-Rahman et al., 1980a).

8.2.2.3 Chlorine Dioxide

Drinking water containing chlorine dioxide at 0, 1.5 or 15 mg/kg bw per day was administered to mice (10 per dose) for 30 days with no apparent effects on blood parameters. The NOAEL for this study was 15 mg/kg bw per day (Moore and Calabrese, 1982).

Twelve African green monkeys were exposed to water containing chlorine dioxide at doses of 0, 30, 100 or 200 mg/L (0, 3.5, 9.5 or 11 mg/kg bw per day) using a rising-dose protocol. Each dose was maintained for 30–60 days. A slight suppression of thyroid function (decreased thyroxine) was observed in monkeys receiving the two highest doses. No other effects were noted. The NOAEL, according to the authors, was 3.5 mg/kg bw per day (Bercz et al., 1982). A review by IPCS (2002) found that the two highest concentrations were both equivalent to about 9 mg/kg bw per day due to impaired palatability leading to reduced water intake. Treatment at the highest dose was stopped due to signs of dehydration. The suppression of thyroid function was not supported by the few data available. Overall, at 200 mg/L, there were clear indications of irritation of the oral cavity, leading to palatability problems. At 100 mg/L (approximately 9 mg/kg bw per day) or less, there were no clear effects among these primates over an 8-week exposure period (IPCS, 2002).

Six monkeys were treated for 8 weeks with drinking water containing chlorine dioxide at 4.6 mg/kg bw per day. Thyroxine level was reduced after 4 weeks of treatment but rebounded after a further 4 weeks. In the same study, drinking water containing chlorine dioxide was administered to male rats (12 per dose) at 0, 10 or 20 mg/kg bw per day. A dose-dependent decrease in thyroxine levels was observed after 8 weeks of treatment; there was no rebound. The LOAEL in this study was identified as 10 mg/kg bw per day (Harrington et al., 1986). According to IPCS (2002), there was no consistent pattern for effects on the thyroid.

Sprague-Dawley rats (10 per sex per dose) were exposed to chlorine dioxide in drinking water for 90 days at dose levels of 0, 2, 4, 6 or 12 mg/kg bw per day for males and 0, 2, 5, 8 or 15 mg/kg bw per day for females. Water consumption was decreased in both sexes at the three highest dose levels, probably because of its reduced palatability. Food consumption was decreased in males receiving the highest dose. Goblet cell hyperplasia was significantly increased in the nasal turbinates of females given 8 or 15 mg/kg bw per day and of males at all doses. Inflammation of the nasal cavity was observed in males at 2 mg/kg bw per day and in both sexes at higher doses. However, the authors mentioned that these lesions were likely caused by inhalation of chlorine dioxide vapours at the drinking water sipper tube or from off-gassing of the vapours after drinking rather than by ingestion of the drinking water. The authors concluded that the lowest dose (2 mg/kg bw per day) was a LOAEL (Daniel et al., 1990).

In another study, male rats and white leghorn chickens were given chlorine dioxide in drinking water at approximately 4.28, 42.8 and 428 mg/kg bw per day (chickens) and 3.42, 34.2 and 342 mg/kg bw per day (rats) for 4 months. A decrease in osmotic fragility of erythrocytes and in the morphology of erythrocytes was observed in both species in all treatment groups (Abdel-Rahman et al., 1980a).

8.2.3 Long-term Exposure and Carcinogenicity

A one year study was conducted to examine the effects of chlorine dioxide and its metabolites on the formation of chloroform, H-thymidine incorporation in organs, and hepatic microsomal enzyme activities in rats. Male Sprague-Dawley rats were given double-distilled water containing chlorine dioxide at 0, 1, 10 or 100 mg/L (corresponding to 0, 0.1, 1 and 10 mg/kg bw per day), chlorite at 1 or 10 mg/L (corresponding to 0.1 and 1 mg/kg bw per day) or chlorate at 1 or 10 mg/L (corresponding to 0.1 and 1 mg/kg bw per day) for 1 year . Blood chloroform levels were decreased in the chlorine dioxide-treated groups at 2, 10 and 12 months treatment. In addition, the chlorite and chlorate treatment groups showed similar decreases in blood chloroform concentration after 1 year of treatment. However, no significant chloroform values in liver, kidney, spleen, testes, and brain were observed in any treatment group in the same time period. I (Suh et al., 1984).

Sprague-Dawley rats (four males per group) were given different concentrations of chlorine dioxide (0, 1, 10, 100 or 1000 mg/L), chlorite ion (10 or 100 mg/L) or chlorate ion (10 or 100 mg/L) in double-distilled water 20 hours per day, 7 days per week, for a year. Control animals received double-distilled water. Rats were administered methyl 1',3'-^{3}H-thymidine at 0.5 μCi/g bw intraperitoneally after treatment with 10 and 100 mg chlorine dioxide/L, 10 and 100 mg chlorite/L and 10 mg chlorate/L in daily drinking water. Nuclei of liver, kidney, testes and mucosa of small intestines were taken for determination of thymidine incorporation. Decreased osmotic fragility in the red blood cells was observed in all treatment groups. At 2 months, blood glutathione content decreased significantly in all treatment groups except the 100 mg chlorine dioxide/L group. At 4 months, glutathione content decreased only in the 1 and 10 mg chlorine dioxide/L groups and in the 100 mg chlorite/L group. At 9 months, decreased glutathione was observed in both the chlorite and chlorate groups, while it was significantly increased in the 100 mg chlorine dioxide/L groups. Changes were observed in the blood cell compartment after 7 months, but not before this period. The red blood cell counts were significantly increased in the 100 mg chlorine dioxide/L group, while they were decreased in the 10 mg chlorate/L group. Haematocrit was increased in the 100 and 1000 mg chlorine dioxide/L treatment groups and decreased in the 10 mg chlorate/L group. The mean corpuscular haemoglobin concentration was increased in the 10 mg chlorine dioxide/L and the 10 and 100 mg chlorite/L groups. After 9 months, red blood cell counts, haematocrit and haemoglobin were decreased in all treatment groups. All three compounds inhibited the incorporation of ^{3}H-thymidine into nuclei in rat testes, whereas chlorite inhibited its incorporation in the liver and chlorine dioxide (100 mg/L) in the kidney. The incorporation of ^{3}H-thymidine in small intestinal nuclei was increased at both 10 and 100 mg chlorine dioxide/L and at 10 mg chlorite/L. The treatment with all three compounds decreased rat body weights in all groups after 10 and 11 months of treatment (Abdel-Rahman et al., 1984a).

8.2.3.1 Chlorite

The effect of sodium chlorite in drinking water at 0, 0.09, 0.18, 0.35, 0.7, 9.3 or 81 mg/kg bw per day on the survival and postmortem pathology of albino rats (seven per sex per dose) was examined in a 2-year study. The life span of the animals was not significantly affected at any dose. No effects were observed in animals exposed to 0.7 mg/kg bw per day or less. Animals exposed to 9.3 or 81 mg/kg bw per day exhibited treatment-related renal pathology; the author concluded that this was the result of a non-specific salt effect (Haag, 1949). Based on renal effects, this study identifies a NOAEL of 0.7 mg/kg bw per day. This study has limited value, however, since an insufficient number of animals was tested per group, pathology was conducted on a small number of animals and the author did not adequately evaluate more sensitive parameters.

In a carcinogenicity study in which sodium chlorite was administered to B6C3F1 mice (50 per sex per dose) at concentrations of 0, 250 or 500 mg/L (equivalent to 0, 36 or 71 mg chlorite ion/kg bw per day) in drinking water for 85 weeks, there was no significant increase in tumours compared with controls at a dose of 36 mg chlorite ion/kg bw per day. Although treated male mice exhibited an increased incidence of lung and liver tumours, tumour rates were within historical ranges for control mice, increases in the liver tumours did not display a typical dose–response pattern and significant increases were seen only for benign tumours (Kurokawa et al., 1986). This study was not conducted for the entire life span of the animals and was not considered adequate based on Organisation for Economic Co-operation and Development (OECD) guidelines.

Chlorite ion was given to Sprague-Dawley rats (four males per group) in drinking water for 12 months (7 days per week) at dose levels of 0, 1 or 10 mg/kg bw per day, based on a reference body weight of 0.523 kg and a drinking water intake of 0.062 L/day. There were significant decreases in body weight gain at 10 mg/kg bw per day at all measuring periods; body weight gain was also decreased in the 1 mg/kg bw per day group at 10 and 11 months. No changes were observed in erythrocyte count, haematocrit or haemoglobin levels. Mean corpuscular haemoglobin concentration was increased at both exposure levels after 7 months of exposure, but not after 9 months. Osmotic fragility was significantly decreased at 1 and 10 mg/kg bw per day after 7 and 9 months of exposure. DNA synthesis (as measured by ^{3}H-thymidine incorporation) was decreased in the liver and the testes at 1 and 10 mg/kg bw per day, decreased in the intestinal mucosa at 10 mg/kg bw per day and increased in the intestinal mucosa at 1 mg/kg bw per day. Blood glutathione reductase activity was significantly increased at 1 and 10 mg/kg bw per day after 6 months of exposure and decreased at 1 mg/kg bw per day after 12 months. Blood glutathione peroxidase was not altered after 6 months of exposure, but was decreased in both groups after 12 months. Significant decreases in blood glutathione levels were observed in both groups. Blood catalase activity was decreased after 6 months of exposure in the 1 and 10 mg/kg bw per day groups and increased in the 1 mg/kg bw per day groups after 12 months. The lack of consistent dose–response, small numbers of animals and small magnitude of effects complicate the interpretation of the results (Couri and Abdel-Rahman, 1980; Abdel-Rahman et al., 1984b).

8.2.3.2 Chlorate

There are no studies of the carcinogenic potential of chlorate administered alone. Sodium and potassium chlorate were evaluated as promoters of renal tumours in N-ethyl-N-hydroxyethyl-nitrosamine-initiated F344 rats. Sodium but not potassium chlorate caused an increase in the number of renal tumours, but the effect was not statistically significant due to the small number of animals used (Kurokawa et al., 1986).

Chlorate ion was administered to Sprague-Dawley rats (four males per group) in drinking water for 12 months (7 days per week) at dose levels of 0, 1 or 10 mg/kg bw per day based on a reference body weight of 0.523 kg and a drinking water intake of 0.062 L/day. After 6 months, blood glutathione peroxidase was increased in the 10 mg/kg bw per day group only. A decrease in catalase activity was observed in the 10 mg/kg bw per day group. After 6 and 12 months, a significant increase in blood glutathione levels was observed at both dose levels compared with the control groups (Couri and Abdel-Rahman, 1980).

8.2.3.3 Chlorine Dioxide

Chlorine dioxide was given to Sprague-Dawley rats (four males per group) in drinking water for 12 months (7 days per week) at dose levels of 0, 0.1, 1, 10 or 100 mg/kg bw per day, based on a reference body weight of 0.523 kg and a drinking water intake of 0.062 L/day. After 12 months of exposure, the erythrocyte glutathione reductase levels in treated rats were similar to those of the controls, but the levels of erythrocyte glutathione peroxidase were significantly increased at 10 and 100 mg/kg bw per day. Erythrocyte glutathione concentrations were significantly decreased at 0.1, 1 and 10 mg/kg bw per day after 6 months and at 100 mg/kg bw per day after 12 months of exposure. Erythrocyte catalase levels were increased in the 100 mg/kg bw per day group after 6 and 12 months of exposure and decreased in the 0.1 and 1 mg/kg bw per day group after 6 months of exposure (Couri and Abdel-Rahman, 1980).

Chlorine dioxide was also given to Swiss mice in drinking water for 12 months (7 days per week) at dose levels of 0, 0.18, 1.8, 18 or 180 mg/kg bw per day. Glutathione peroxidase levels were decreased at 18 mg/kg bw per day and increased at 180 mg/kg bw per day after 12 months of exposure, and glutathione levels were decreased at 1.8 and 18 mg/kg bw per day after 12 months. Catalase levels were increased in the 1.8, 18 and 180 mg/kg bw per day groups after 12 months of exposure. The inconsistent relationship between the dose and the magnitude of the alterations in the glutathione-dependent system makes interpretation of the results of this study difficult. In addition, it is not clear if these effects are biologically significant. Therefore, no NOAEL or LOAEL could be determined (Couri and Abdel-Rahman, 1980).

Chlorine dioxide was given to white male leghorn chicken (four per group) in drinking water for 10 months (7 days per week) at concentrations of 0, 10, 100 or 1000 mg/L. An increase of 70% in the activity of glutathione reductase was observed at all concentrations. Glutathione peroxidase activity was significantly decreased at the highest concentration; however, catalase activity was increased in the same group. Glutathione peroxidase activity varied inversely with the concentration of chlorine dioxide in drinking water (Couri and Abdel-Rahman, 1980).

Chlorine dioxide was administered in drinking water to rats (seven per sex per dose) at concentrations of 0, 0.5, 1, 5, 10 or 100 mg/L (equivalent to dose levels of 0, 0.07, 0.13, 0.7, 1.3 and 13 mg/kg bw per day) for 2 years. At the highest dose level, survival rate was substantially decreased in both sexes, and mean life span was reduced compared with that for control animals. No correlation was observed between treatment and histopathological findings. A NOAEL of 1.3 mg/kg bw per day was identified (Haag, 1949), although it should be noted that this 1949 study has serious limitations.

8.2.4 Mutagenicity/Genotoxicity

8.2.4.1 Chlorite

Sodium chlorite produced an increase in revertants in *Salmonella typhimurium* strain TA100 in both the presence and absence of metabolic activation (Ishidate et al., 1984). No chromosomal abnormalities were seen in either the mouse micronucleus test or a cytogenetic assay in mouse bone marrow cells following gavage dosing with chlorite (Meier et al., 1985).

A positive result was obtained in a micronucleus test in bone marrow from male ddY mice after a single intraperitoneal injection of sodium chlorite at 0, 7.5, 15, 30 or 60 mg/kg bw. A statistically positive response was observed at 15 and 30 mg/kg bw only: 0.38% and 1.05%, respectively, compared with 0.18% for the control group (Hayashi et al., 1988).

8.2.4.2 Chlorate

Chlorate has long been known to select nitrate reductase-deficient mutants of *Aspergillus nidulans* (Cove, 1976). However, it has been demonstrated that there is also a mutagenic effect of chlorate in *Chlamydomonas reinhardtii* and *Rhodobacter capsulatus*. Chlorate failed to induce mutations in the BA-13 strain of *Salmonella typhimurium*. The positive mutagenic effects were separated from simple selection of nitrate reductase mutants by incubating cells in nitrogen-free media; lack of nitrogen prevents cell division during the treatment period. In the case of *C. reinhardtii*, significant increases in mutants were observed at concentrations of 4–5 mmol/L and above (Prieto and Fernandez, 1993).

No chromosomal abnormalities were seen in either the micronucleus test or a cytogenetic assay in mouse bone marrow cells following gavage dosing with chlorate (Ishidate et al., 1984).

8.2.4.3 Chlorine Dioxide

In vitro, chlorine dioxide was mutagenic in *Salmonella typhimurium* strain TA100 in the absence of a metabolic activation system (S9) (Ishidate et al., 1984). No sperm head abnormalities were observed in male mice following chlorine dioxide gavage (Meier et al., 1985). In an *in vitro* cytogenetics assay, Chinese hamster ovary (CHO) cells were treated with 0, 2.5, 5, 10, 15, 30 or 60 µg 0.2% chlorine dioxide/mL in phosphate-buffered saline solution without metabolic activation (-S9). A second experiment was conducted with CHO cells treated at 0, 6, 13, 25, 50 or 75 µg/mL with metabolic activation (+S9). In the first experiment (without metabolic activation), cell toxicity was observed at 60 µg/mL, and there was an absence of mitotic cells at 30 µg/mL. At 2.5–15 µg/mL, there was a dose-related, statistically significant increase in the number of metaphases with chromosome aberrations. In the second experiment (with metabolic activation), cell toxicity and absence of mitotic cells were observed at 75 µg/mL. A statistically significant increase in the number of metaphases with chromosome aberrations was noted at 50 µg/mL (Ivett and Myhr, 1986). In a mouse lymphoma forward mutation assay (using L5178Y $TK^{+/-}$), cells were treated with 0–65 µg chlorine dioxide/mL in phosphate-buffered saline with and without metabolic activation (S9). Without S9, marked toxicity was observed at the highest concentration used, 37 µg/mL. The relative growth at the next two concentrations (15 and 24 µg/mL) was 13–18%. There was a dose-related increase in mutant frequency. With S9, marked toxicity was observed at the highest concentration, 65 µg/mL, and there was also a dose-related increase in mutant frequency, indicating positive results both with and without metabolic activation in this test system (Cifone and Myhr, 1986).

In *in vivo* studies, no chromosomal abnormalities were seen in either the micronucleus test or a cytogenetic assay in mouse bone marrow cells following gavage dosing with chlorine dioxide (Meier et al., 1985). CD-1 mice (five per sex) received a single intraperitoneal injection of 0, 2, 5 or 15 mg chlorine dioxide/kg bw in a bone marrow cytogenetic assay. Bone marrow cells were analysed for chromosome aberrations at 6, 24 and 48 hours. There were no clear effects on the mitotic index, but two males receiving approximately 15 mg chlorine dioxide/kg bw died, and other signs of toxicity were also observed at the highest dose level. There were no increases in the frequency of chromosome aberrations among treated animals at any of the sacrifice times compared with controls (Ivett and Myhr, 1984). Groups of five male ICR mice received a single intraperitoneal injection of approximately 0, 9, 21, 28 or 39 mg aqueous chlorine dioxide/kg bw. Following subcutaneous implantation of bromodeoxyuridine and 26 hours after chlorine dioxide administration, approximately 25 bone marrow metaphase cells from each animal were assessed for sister chromatid exchange. All animals showed hyperactive behaviour after administration of chlorine dioxide. Overall, there were no significant increases in sister chromatid exchange among any of the chlorine dioxide-treated groups (Ivett and Myhr, 1984).

In a dominant lethal assay in rats administered up to 20 mg aqueous chlorine dioxide/kg bw intraperitoneally, no mutagenic effects on male germ cells were observed (Moore and Myhr, 1984).

8.2.5 Reproductive and Developmental Toxicity

8.2.5.1 Chlorite

Female A/J mice (10 per dose) were treated with sodium chlorite in drinking water at doses equivalent to 0 and 22 mg/kg bw per day (U.S. EPA, 2000) from day 1 of gestation and throughout lactation. Conception rates were 56% for controls and 39% for treated mice. The body weights of pups at weaning were reduced (14% below the controls) in treated mice (Moore and Calabrese, 1982), so that 22 mg/kg bw per day (the only dose tested) is the LOAEL for this study (U.S. EPA, 2000).

In a series of three experiments, sodium chlorite was administered to male rats (12 per dose) in drinking water for 66–76 days at concentrations of 0, 0.075, 0.75, 7.5 or 27 mg chlorite/kg bw per day. No compound-related abnormalities were observed on histopathological examination of the reproductive tract. Abnormal sperm morphology and decreased sperm motility were seen at the two highest dose levels, but no sperm effects were observed at 0.75 mg/kg bw per day, which can be identified as the NOAEL (Carlton et al., 1987).

In another part of the same study, male rats were bred with female rats treated at 0, 0.075, 0.75 or 7.5 mg chlorite/kg bw per day dose levels. Males were exposed for 56 days and females for 14 days prior to breeding and throughout the 10-day breeding period. Females were also exposed throughout gestation and lactation until the pups were weaned on day 21. There was no evidence of any adverse effects on conception rates, litter size, day of eye opening or day of vaginal opening. Decreases in the concentrations of triiodothyronine and thyroxine in blood were observed on postnatal days 21 and 40 in male and female pups exposed to 7.5 mg/kg bw per day. Based on reproductive effects, the NOAEL was 0.75 mg/kg bw per day (Carlton et al., 1987).

Fetuses from maternal Sprague-Dawley rats exposed to chlorite ion via drinking water at levels of 1 or 10 mg/L for 2.5 months prior to mating and throughout gestation were examined. There was an increase in the incidence of anomalies at both concentrations; however, because the treatment groups were small (6–9 females per group), the effects were not considered statistically significant (Suh et al., 1983).

Groups of female Sprague-Dawley rats (12 per group) were exposed for 9 weeks to drinking water containing 0, 3 or 6 mg chlorite/kg bw per day beginning 10 days prior to breeding with untreated males and until the pups were sacrificed at 35–42 days post-conception. From day 31 to day 42 post-conception, six litters of each treatment group were assessed for the development of exploratory activity. Pups exposed to a dose of 6 mg/kg bw per day exhibited a consistent and significant depression in exploratory behaviour on post-conception days 36–39, but not on day 40. Exploratory activity was comparable between treated and control groups after post-conception day 39. Based on behavioural effects, the NOAEL and LOAEL were identified as 3 and 6 mg/kg bw per day, respectively (Mobley et al., 1990).

In a two-generation study, Sprague-Dawley rats (30 per sex per dose) received drinking water containing 0, 35, 70 or 300 mg sodium chlorite/L for 10 weeks and were then paired for mating. Males were exposed throughout mating, then sacrificed. Exposure for the females continued through mating, pregnancy and lactation until necropsy following weaning of their litters. Twenty-five males and females from each of the first 25 litters to be weaned in a treatment group were chosen to produce the F_1 generation. The F_1 pups were continued on the same treatment regimen as their parents. At approximately 14 weeks of age, they were mated to produce the F_{2a} generation. Because of a reduced number of litters in the 70 mg/L F_1–F_{2a} generation, the F_1 animals were remated following weaning of the F_{2a} generation to produce the F_{2b} generation. Doses for the F_0 animals were 0, 3.0, 5.6 or 20.0 mg chlorite/kg bw per day for males and 0, 3.8, 7.5 or 28.6 mg chlorite/kg bw per day for females. For the F_1 animals, doses were 0, 2.9, 5.9 or 22.7 mg chlorite/kg bw per day for males and 0, 3.8, 7.9 or 28.6 mg chlorite/kg bw per day for females. There were reductions in water consumption, food consumption and body weight gain in both sexes in all generations at various times throughout the experiment, primarily in the 70 and 300 mg/L groups; these were attributed to lack of palatability of the water. At 300 mg/L, reduced pup survival, reduced body weight at birth and throughout lactation in F_1 and F_2, lower thymus and spleen weights in both generations, lowered incidence of pups exhibiting a normal righting reflex, delays in sexual development in males and females in F_1 and F_2 and lower red blood cell parameters in F_1 were noted. Significant reductions in absolute and relative liver weights in F_0 females and F_1 males and females, reduced absolute brain weights in F_1 and F_2 and a decrease in the maximum response to auditory startle stimulus on postnatal day 24 but not on postnatal day 60 were noted in the 70 and 300 mg/L groups. Minor changes in red blood cell parameters in the F_1 generation were seen at 35 and 70 mg/L, but these appear to be within normal ranges based on historical data. The NOAEL and LOAEL in this study were 35 mg/L (2.9 mg/kg bw per day) and 70 mg/L (5.9 mg/kg bw per day), based on lower auditory startle amplitude, decreased absolute brain weight in the F_1 and F_2 generations and altered liver weights in two generations (CMA, 1997; TERA, 1998).

New Zealand white rabbits (16 per group) were treated with 0, 10, 26 or 40 mg chlorite ion/kg bw per day in their drinking water from day 7 to day 19 of pregnancy to study developmental toxicity. The animals were necropsied on day 28. Food consumption was depressed at the two highest doses, and water consumption was depressed at all doses, but more notably at the two highest doses. Mean fetal weights were slightly lower at the two highest doses as well, with a slightly higher incidence of incomplete ossification of some bones. There were no dose-related increases in defects identified. Minor skeletal anomalies were observed as the concentration of chlorite in water was increased and maternal food consumption was depressed (Harrington et al., 1995).

8.2.5.2 Chlorate

No studies were available examining the reproductive or embryotoxic potential of chlorate. Sodium chlorate was administered to pregnant CD rats by gavage at doses of 0, 10, 100 or 1000 mg/kg bw per day on days 6–15 of gestation. There were no maternal deaths in treated animals or treatment-related effects on maternal body weight gain, food consumption, clinical observations, number of implantations or gross necropsy. Examination of fetuses on day 20 revealed no effects on fetal weight or sex ratio, and no external, visceral or skeletal abnormalities were detected. In this study, a developmental NOAEL of 1000 mg/kg bw per day in rats was identified (Bio/Dynamics, Inc., 1987c).

8.2.5.3 Chlorine Dioxide

A one-generation study was carried out with chlorine dioxide administered to Long-Evans rats by gavage at doses of 2.5, 5 or 10 mg/kg bw per day to male rats (12 per group) for 56 days prior to and through mating to female rats (24 per group) that were dosed from 14 days prior to mating and through pregnancy. Fertility measures were not significantly different among the dose groups. There were no dose-related changes in sperm parameters (i.e., concentration, motility, progressive movement or morphology). Thyroid hormone levels were altered significantly, but not in a consistent pattern. The only significant difference was depressed vaginal weights in female pups whose dams had been treated with 10 mg/kg bw per day. Based on this one change, the NOAEL was considered to be 5 mg/kg bw per day (Carlton et al., 1991).

The developmental neurotoxic potential of chlorine dioxide was evaluated in a study in which it was administered to male and female Sprague-Dawley rat pups by oral intubation at 14 mg/kg bw per day on postnatal days 1–20. Forebrain cell proliferation was decreased on postnatal day 35, and there were decreases in forebrain weight and protein content on postnatal days 21 and 35. Cell proliferation in the cerebellum and olfactory bulbs was comparable to that in untreated controls, as were migration and aggregation of neuronal cells in the cerebral cortex. Histopathological examination of the forebrain, cerebellum and brain stem did not reveal any lesions or changes in these tissues. In this study, a LOAEL of 14 mg/kg bw per day (the only dose tested) was identified (Toth et al., 1990).

Female Sprague-Dawley rats (13–16 per dose) were supplied with drinking water containing 0, 1, 3 or 14 mg/kg bw per day from 2 weeks before mating through gestation and lactation until pups were weaned on postnatal day 21. No significant effect on the body weight of either the dams or the pups was observed at any dose tested. At 14 mg/kg bw per day for the pregnant dams, a significant depression of serum thyroxine and an increase in serum triiodothyronine were observed in the pups at weaning, but not in the dams. Neurobehavioural exploratory and locomotor activities were decreased in pups born to dams exposed to 14 mg/kg bw per day but not in pups born to those exposed to 3 mg/kg bw per day, which was considered a NOAEL (Orme et al., 1985).

In a companion study, Sprague-Dawley rat pups were exposed directly (by gavage) to 14 mg chlorine dioxide/kg bw per day on postnatal days 5–20. In this study, serum thyroxine levels were depressed, a somewhat greater and more consistent delay in the development of exploratory and locomotor activity was seen and pup body weight gain was reduced. The decrease in serum triiodothyronine levels was not statistically significant. Based on decreased pup development and decreased thyroid hormone levels, a LOAEL of 14 mg/kg bw per day (the only dose tested) was identified (Orme et al., 1985).

Cell number was significantly depressed in the cerebellum of 21-day-old rat pups born to Sprague-Dawley dams supplied during gestation and lactation with water containing about 14 mg chlorine dioxide/kg bw per day. A group of 12 rat pups dosed directly by gavage with 14 mg/kg bw per day had depressed cell numbers in both the cerebellum and forebrain at postnatal day 11 and displayed decreased voluntary running-wheel activity at postnatal days 50–60, despite the fact that chlorine dioxide treatments were terminated at 20 days of age. These data suggest that chlorine dioxide is capable of influencing brain development in neonatal rats. In this study, a LOAEL of 14 mg/kg bw per day, the only dose tested, was identified (Taylor and Pfohl, 1985).

Female Sprague-Dawley rats received chlorine dioxide at approximately 0, 0.07, 0.7 or 7 mg/kg bw per day in drinking water. After approximately 10 weeks of exposure, females were mated with untreated males and continued to receive chlorine dioxide throughout gestation. On day 20 of gestation, the dams were euthanized, their uteri were removed and weighed and fetuses were examined; half of the fetuses were examined for skeletal and half for visceral abnormalities. There were no clinical signs of toxicity and no exposure-related mortalities among the dams. There was a slight, but statistically significant, reduction in body weight gain among dams at 0.7 and 7 mg/kg bw per day during pregnancy (about 14% reduction compared with controls). There was a slight reduction in the mean number of implants per dam in the two highest dose groups, which was statistically significant at 7 mg/kg bw per day (10.3 per dam compared with 12.3 per dam in controls), with a similar change in the number of live fetuses. This may be related to maternal toxicity at these two exposure levels, as there was a slight reduction in body weight gain among dams. The incidence of litters with anomalous fetuses was unaffected by treatment (5/6, 4/6, 6/6 and 7/8 among animals receiving 0, 0.07, 0.7 and 7 mg/kg bw per day, respectively) (Suh et al., 1983).

9.0 Classification and Assessment

9.1 Chlorite

Based on the available data, chlorite has been classified in Group VIA (inadequate data for evaluation of carcinogenicity to humans) (Health Canada, 1994). This concurs with the conclusions by IARC (1991) — Group 3, not classifiable as to its carcinogenicity to humans — and the U.S. EPA (1996) — not classifiable as to human carcinogenicity because of inadequate data in humans and animals.

Subchronic studies in animals (cats, mice, rats and monkeys) indicate that chlorite and chlorate cause haematological changes (osmotic fragility, oxidative stress, increase in mean corpuscular volume), stomach lesions and increased spleen and adrenal weights (Heffernan et al., 1979; Bercz et al., 1982; Moore and Calabrese, 1982; Bio/Dynamics, Inc., 1987b; Harrington et al., 1995; McCauley et al., 1995).

No carcinogenicity studies were found for chlorite in the literature. The chronic study on mice with chlorite (Kurokawa et al., 1986) was not conducted for the entire life span of the animals and was not considered adequate based on OECD guidelines. Although haematological effects were observed in the rat study (Couri and Abdel-Rahman, 1980; Abdel-Rahman et al., 1984b), a consistent dose–effect relationship was not found; a small number of animals and the small magnitude of effects complicate the interpretation of the results. Minor blood changes were observed in the two-generation study used to derive the guideline, confirming the effects found in subchronic studies with rats (CMA, 1997; TERA, 1998).

Neurobehavioural effects (lowered auditory startle amplitude, decreased brain weight and decreased exploratory activity) are the most sensitive endpoints following oral exposure to chlorite (Mobley et al., 1990; CMA, 1997). The LOAEL identified in both the Mobley et al. (1990) developmental toxicity study and the CMA (1997) two-generation study is approximately 6 mg chlorite/kg bw per day. Mobley et al. (1990) also found significant decreases in exploratory activity at 3 mg/kg bw per day, but the difference between activity in this group and the controls was small. Nevertheless, the NOAEL for neurobehavioural effects from this study is 3 mg chlorite/kg bw per day. These studies were conducted using the drinking water route, which makes them relevant for the present assessment.

The CMA (1997) study was selected for a number of reasons. It was conducted with sufficient numbers of animals of both sexes at multiple dose levels showing a range of effects and with numerous endpoints. The endpoint is toxicologically significant, and the rat species is widely used to parallel reproductive and developmental effects in humans. In this study, the male rats were also exposed to sodium chlorite during the mating period. Therefore, a more complete assessment of the adverse effects is covered in this study, which makes it more appropriate to select as the critical study for the development of a guideline.There are sufficient data available to estimate a tolerable daily intake (TDI) for chlorite, based on this two-generation study.

In this two-generation study in rats, a NOAEL of 2.9 mg/kg bw per day was identified based on lower startle amplitude, decreased absolute brain weight in the F_1 and F_2 generations and altered liver weights in two generations (CMA, 1997; TERA, 1998). The TDI has been derived based on this study as follows:

$$\text{TDI} = \frac{2.9 \text{ mg/kg bw per day}}{100} = 0.029 \text{ mg/kg bw}$$

where

- 2.9 mg/kg bw per day is the NOAEL based on lower startle amplitude, decreased absolute brain weight and altered liver weights in a two-generation study in rats,
- 100 is the uncertainty factor (×10 for interspecies variation; ×10 for intraspecies variation).

This TDI is consistent with results from human volunteer studies.

Because chlorite is classified in Group VIA, the MAC for chlorite in drinking water is derived from the TDI as follows:

$$\text{MAC} = \frac{0.029 \text{ mg/kg bw} \times 70 \text{ kg bw} \times 0.80}{1.5 \text{ L/day}} = 1.083 \text{ mg/L (rounded to 1 mg/L)}$$

where:
- 0.029 mg/kg bw is the TDI, as calculated above,
- 70 kg bw is the average body weight of an adult,
- 0.80 is the proportion of total daily intake allocated to drinking water (as drinking water is the major source of exposure),
- 1.5 L/day is the average daily consumption of drinking water for an adult.

9.2 Chlorate

There are no data available to assess the carcinogenicity of chlorate; as such, chlorate has been classified in Group VIB — no data available for evaluation of carcinogenicity to humans (Health Canada, 1994). IARC has not classified the carcinogenicity of chlorate. The chronic and carcinogenicity studies and the developmental and reproductive studies do not provide sufficient information to derive a guideline for chlorate.

A chlorate dose of 0.036 mg/kg bw per day for 12 weeks did not result in any adverse effects in human volunteers (Lubbers et al., 1981). Although the database for chlorate is less extensive than that for chlorite, a well-conducted 90-day study in rats is available, which identified a NOAEL of 30 mg/kg bw per day based on thyroid gland colloid depletion at the next higher dose of 100 mg/kg bw per day (McCauley et al., 1995).

A TDI for chlorate can therefore be derived as follows:

$$\text{TDI} = \frac{30 \text{ mg/kg bw per day}}{1000} = 0.03 \text{ mg/kg bw}$$

where:
- 30 mg/kg bw per day is the NOAEL based on thyroid gland colloid depletion in a 90-day study in rats,
- 1000 is the uncertainty factor (×10 for interspecies variation; ×10 for intraspecies variation; ×10 to account for the short duration of the study).

This TDI is consistent with results from human volunteer studies.

Because chlorate is classified in Group VIB, the MAC for chlorate in drinking water is calculated from the TDI as follows:

$$\text{MAC} = \frac{0.03 \text{ mg/kg bw} \times 70 \text{ kg bw} \times 0.80}{1.5 \text{ L/day}} = 1.12 \text{ mg/L (rounded to 1 mg/L)}$$

where:
- 0.03 mg/kg bw is the TDI, as calculated above,

- 70 kg bw is the average body weight of an adult,
- 0.80 is the proportion of total daily intake allocated to drinking water (as drinking water is the major source of exposure),
- 1.5 L/day is the average daily consumption of drinking water for an adult.

9.3 Chlorine Dioxide

Chlorine dioxide has been shown to impair neurobehavioural and neurological development in rats exposed perinatally. Significant depression of thyroid hormones has also been observed in rats and monkeys exposed to it in drinking water studies. However, a MAC has not been proposed for chlorine dioxide because of its rapid hydrolysis to chlorite (and, to a lesser extend, chlorate). As well, the MAC for chlorite is considered adequately protective for potential toxicity from chlorine dioxide; the NOAEL of 2.9 mg/kg bw per day used to derive the TDI for chlorite is similar to the lowest NOAELs observed for effects of chlorine dioxide on neurobehavioural and neurological development and on thyroid hormone levels.

The taste and odour threshold for chlorine dioxide is 0.4 mg/L (U.S. NRC, 1987), which is lower than the MACs derived for chlorite and chlorate.

10.0 Rationale

Chlorite, chlorate and chlorine dioxide can be found in drinking water that is treated using chlorine dioxide instead of the much more commonly used chlorine. Chlorate can also be found in drinking water that has been treated with hypochlorite solutions (as a source of chlorine) that have been inadequately stored or used or that fail to meet quality specifications. Both disinfection methods are very effective in reducing waterborne disease; however, both also have the potential to produce harmful by-products, and these should be minimized without compromising the effectiveness of disinfection of the water.

Because chlorine dioxide is used by very few Canadian water treatment plants, the risk of exposure to chlorine dioxide, chlorite and chlorate is not expected to be significant for the average Canadian. Although more Canadians could be exposed through the use of hypochlorite solutions, the quality of the solution, as well as its appropriate storage and use, can greatly reduce any potential exposure. There is no epidemiological or experimental evidence to show that chlorite, chlorate and chlorine dioxide are human carcinogens. However, other health effects were observed in rigorous experimental and epidemiological studies, which warrant the establishment of guidelines for chlorite and chlorate. Despite neurological and hormonal effects observed in experimental animals, a guideline for chlorine dioxide was deemed unnecessary because of its rapid hydrolysis to chorite, making human exposure via drinking water unlikely.

10.1 Chlorite

Decreased brain weight, decreased reaction to loud noise and altered liver weights in the first two generations of offspring in Sprague-Dawley rats were considered significant effects of chlorite exposure in one study. This study was used to derive the TDI of 0.029 mg/kg bw and is consistent with results from human volunteer studies. The subsequently derived MAC of 1 mg/L can be easily measured using a number of U.S. EPA analytical methods. Although it is possible to remove chlorite from treated drinking water using methods such as activated carbon and sulphur and iron reducing agents, the recommended approach is to reduce the production of chlorite in the disinfection process by tuning the chlorine dioxide generator to work as efficiently as possible. Chlorite levels of 1 mg/L are considered achievable using these strategies.

10.2 Chlorate

Subchronic chlorate exposure was associated with smaller body and organ weights, blood abnormalities and pituitary and thyroid abnormalities in one study using Sprague-Dawley rats. The TDI derived from this study was very close to that of chlorite, at 0.03 mg/kg bw, and is consistent with results from human volunteer studies. The proposed MAC of 1 mg/L is easily measured using several U.S. EPA analytical methods, including variations of the methods used to detect chlorite. Unlike the case with chlorite, however, there are no known treatments available to reduce chlorate ion once it has been formed in drinking water. Furthermore, excess chlorite can react to produce additional chlorate, so it is important to carefully tune and maintain the chlorine dioxide generator to work as efficiently as possible to reduce the production of chlorite and chlorate. Excess chlorite must be removed before adding post-chlorine. The chlorate MAC of 1 mg/L is considered achievable using this method.

11.0 References

Abdel-Rahman, M.S. 1985. Pharmacokinetics of chlorine obtained from chlorine dioxide, chlorine, chloramine and chloride. In: Water chlorination. Vol. 5. Chemistry, environmental impact and health effects. R.L. Jolley (ed.). Lewis Publishers, Chelsea, MI. pp. 281–293.

Abdel-Rahman, M., Couri, D. and Bull, R.J. 1980a. Kinetics of ClO_2 and effects of ClO_2, ClO_2^- and ClO_3^- in drinking water on blood glutathione and hemolysis in rat and chickens. J. Environ. Pathol. Toxicol., 3: 431–449.

Abdel-Rahman, M.S., Couri, D. and Jones, J.D. 1980b. Chlorine dioxide metabolism in rat. J. Environ. Pathol. Toxicol., 3: 421–430.

Abdel-Rahman, M.S., Couri, D. and Bull, R.J. 1982a. Metabolism and pharmacokinetics of alternate drinking water disinfectants. Environ. Health Perspect., 46: 19–23.

Abdel-Rahman, M.S., Gerges, S.E. and Alliger, H. 1982b. Toxicity of alcide. J. Appl. Toxicol., 2(3): 160–164 [cited in RTECS, 2000a].

Abdel-Rahman, M.S., Couri, D. and Bull, R.J. 1984a. Toxicity of chlorine dioxide in drinking water. J. Am. Coll. Toxicol., 3(4): 277–284.

Abdel-Rahman, M.S., Couri, D. and Bull, R.J. 1984b. The kinetics of chlorite and chlorate in the rat. J. Am. Coll. Toxicol., 3(4): 261–267.

Abdel-Rahman, M.S., Couri, D. and Bull, R.J. 1985. The kinetics of chlorite and chlorate in rats. J. Environ. Pathol. Toxicol. Oncol., 6(1): 97–103.

Aieta, E.M., Berg, J.D., Robert, P.V. and Cooper, R.C. 1980. Comparison of chlorine dioxide and chlorine in wastewater disinfection. J. Am. Water Pollut. Control Fed., 52(4): 810–822.

APHA (American Public Health Association), American Water Works Association and Water Environment Federation. 1998. Standard methods for the examination of water and wastewater. 20th edition. American Public Health Association, Washington, DC.

AWWA (American Water Works Association). 2004. AWWA standard hypochlorites. American Water Works Association, Denver, CO (ANSI/AWWA B300-4).

Bercz, J.P., Jones, L., Garner, L., Murray, D., Ludwig, D. and Boston, J. 1982. Subchronic toxicity of chlorine dioxide and related compounds in drinking water in the non-human primate. Environ. Health Perspect., 46: 47–55.

Bio/Dynamics, Inc. 1987a. A subchronic (3-month) oral toxicity study in the dog via gavage administration with sodium chlorate. Bio/Dynamics, Inc., East Millstone, NJ (Report No. 86-3114; prepared for Sodium Chlorate Task Force, Oklahoma City, OK) [cited in WHO, 1996].

Bio/Dynamics, Inc. 1987b. A subchronic (3-month) oral toxicity study of sodium chlorate in the rat via gavage. Bio/Dynamics, Inc., East Millstone, NJ (Report No. 86-3112; prepared for Sodium Chlorate Task Force, Oklahoma City, OK) [cited in WHO, 1996].

Bio/Dynamics, Inc. 1987c. A teratogenicity study in rats with sodium chlorate. Bio/Dynamics, Inc., East Millstone, NJ (Report No. 86-3117; prepared for Sodium Chlorate Task Force, Oklahoma City, OK) [cited in WHO, 1996].

Budavari, S. (ed.). 1976. The Merck index: an encyclopedia of chemicals and drugs. 9th edition. Merck and Co., Rahway, NJ.

Budavari, S. (ed.). 1996. The Merck index — Encyclopedia of chemicals, drugs and biologicals. 12th edition. Merck and Co., Rahway, NJ.

Budavari, S., O'Neil, M. and Smith, A. (eds.). 1989. The Merck index. An encyclopedia of chemicals, drugs and biologicals. 11th edition. Merck, Rahway, NJ.

Carlton, B.D., Habash, D.L., Basaran, A.H., George, E.L. and Smith, M.K. 1987. Sodium chlorite administration in Long-Evans rats: reproductive and endocrine effects. Environ. Res., 42: 238–245.

Carlton, B.D., Basaran, A.H., Mezza, L.E., George, E.L. and Smith, E.K. 1991. Reproductive effects in Long-Evans rats exposed to chlorine dioxide. Environ. Res., 56: 170–177.

Cifone, M. and Myhr, B. 1986. Mutagenicity evaluation of chlorine dioxide in the mouse lymphoma forward mutation assay. Litton Bionetics Inc., Kensington, MD (Report No. 20989) [cited in IPCS, 2002].

CMA (Chemical Manufacturers Association). 1989. A review of the uses, chemistry and health effects of chlorine dioxide and the chlorite ion. Chemical Manufacturers Association, Washington, DC.

CMA (Chemical Manufacturers Association). 1997. Sodium chlorite: drinking water rat two-generation reproductive toxicity study. Chemical Manufacturers Association, Washington, DC (Quintiles Report CMA/17/96).

Cotton, F.A. and Wilkinson, G. 1980. Advanced inorganic chemistry. John Wiley and Sons, New York, NY.

Couri, D. and Abdel-Rahman, M.S. 1980. Effect of chlorine dioxide and metabolites on glutathione dependent system in rat, mouse and chicken blood. J. Environ. Pathol. Toxicol., 3: 451–460.

Cove, D.J. 1976. Chlorate toxicity in *Aspergillus nidulans*: Studies of mutants altered in nitrate assimilation. Mol. Gen. Genet., 146: 147–159.

Daniel, F.B., Condie, L., Robinson, M., Stober, J., York, R., Olson, G. and Wang, S. 1990. Comparative subchronic toxicity studies of three disinfectants. J. Am. Water Works Assoc., 82: 61–69.

Dixon, K. and Lee, R.G. 1991. The effect of sulfur-based reducing agents and GAC filtration on chlorine dioxide by-products. J. Am. Water Works Assoc., 83: 48–55.

Fletcher, D. 1973. Acute oral toxicity study with sodium chlorite in bobwhite quail. Industrial Bio-Test Laboratory (IBT No. J2119; report prepared for Olin Corporation) [cited in WHO, 1996].

Gallagher, D.L., Hoehn, R.C. and Dietrich, A.M. 1994. Sources, occurrence, and control of chlorine dioxide by-product residuals in drinking water. American Water Works Association Research Foundation, Denver, CO.

Gates, D.J. 1989. Improvements in chlorine dioxide use: A two-step method for determining residual oxidants in the presence of other chlorine species in finished water. In: Advances in water analysis and treatment: Proceedings of the American Water Works Association Water Quality Technology Conference, November 13–17, 1988, St. Louis, MO. American Water Works Association, Denver, CO. pp. 689–703.

Gordon, G. 2001. Is all chlorine dioxide created equal? J. Am. Water Works Assoc., 93: 163–173.

Gordon, G., Adam, L. and Bubnis, B. 1995. Minimizing chlorate formation in drinking water when hypochlorite ion is the chlorinating agent. American Water Works Association Research Foundation, Denver, CO.

Griese, M.H., Hauser, K.A., Berkemeier, M. and Gordon, G. 1991. Using reducing agents to eliminate chlorine dioxide and chlorite ion residuals in drinking water. J. Am. Water Works Assoc., 83: 56–61.

Griese, M.H., Kaczur, J.J. and Gordon, G. 1992. Combining methods for the reduction of oxychlorine residuals in drinking water. J. Am. Water Works Assoc., 84: 69–77.

Haag, H.B. 1949. The effect on rats of chronic administration of sodium chlorite and chlorine dioxide in the drinking water. Report to the Mathieson Alkali Works from the Medical College of Virginia.

Haller, J.F. and Northgraves, W.W. 1955. Chlorine dioxide and safety. TAPPI, 38: 199–202.

Harrington, R.M., Shertzer, H.G. and Bercz, J.P. 1986. Effects of chlorine dioxide on thyroid function in the African green monkey and the rat. J. Toxicol. Environ. Health, 19: 235–242.

Harrington, R.M., Romano, R.R. and Irvine, L. 1995. Developmental toxicity of sodium chlorite in the rabbit. J. Am. Coll. Toxicol., 14: 108–118.

Hayashi, M., Kishi, M., Sofuni, T. and Ishidate, M., Jr. 1988. Micronucleus tests in mice on 39 food additives and 8 miscellaneous chemicals. Food Chem. Toxicol., 26(6): 487–500.

Health Canada. 1994. Canadian Environmental Protection Act — Human health risk assessment for priority substances. Appendix B: Criteria for classification of carcinogenicity. Environmental Health Directorate, Health Canada, Ottawa.

Heffernan, W.P., Guion, C. and Bull, R.J. 1979. Oxidative damage to the erythrocyte induced by sodium chlorite, *in vivo*. J. Environ. Pathol. Toxicol., 2: 1487–1499.

Hurst, G.H. and Knocke, W.R. 1997. Evaluating ferrous iron for chlorite ion removal. J. Am. Water Works Assoc., 89: 98–105.

IARC (International Agency for Research on Cancer). 1991. Chlorinated drinking-water; chlorination by-products; some other halogenated compounds; cobalt and cobalt compounds. IARC Monogr. Eval. Carcinogen. Risks Hum., 52: 45–359.

Iatrou, A. and Knocke, W.R. 1992. Removing chlorite by the addition of ferrous iron. J. Am. Water Works Assoc., 84: 63–68.

IPCS (International Programme on Chemical Safety). 2002. Chlorine dioxide (gas). World Health Organization, Geneva (Concise International Chemical Assessment Document 37).

Ishidate, M., Sofuni, T., Yoshikawa, K., Hayashi, M., Nohmi, T., Sawada, M. and Matsuoka, A. 1984. Primary mutagenicity screening of food additives currently used in Japan. Food Chem. Toxicol., 22: 623–636.

Ivett, J. and Myhr, B. 1984. Mutagenicity evaluation of chlorine dioxide in the mouse bone marrow cytogenetic assay. Litton Bionetics Inc., Kensington, MD (Report No. 22202) [cited in IPCS, 2002].

Ivett, J. and Myhr, B. 1986. Mutagenicity evaluation of chlorine dioxide in an *in vitro* cytogenetic assay. Litton Bionetics Inc., Kensington, MD (Report No. 20990) [cited in IPCS, 2002].

Kanitz, S., Franco, Y., Patrone, V., Caltabellotta, M., Raffo, E., Riggi, C., Timitilli, D. and Ravera, G. 1996. Association between drinking water disinfection and somatic parameters at birth. Environ. Health Perspect., 104(5): 516–520.

Kurokawa, Y., Takayama, S., Konishi, Y., Hiasa, Y., Asahina, S., Takahashi, M., Maekawa, A. and Hayashi, Y. 1986. Long-term *in vivo* carcinogenicity tests of potassium bromate, sodium hypochlorite and sodium chlorite conducted in Japan. Environ. Health Perspect., 69: 221–235.

Lewis, R.J. 1993. Hawley's condensed chemical dictionary. 12th edition. Van Nostrand Reinhold, New York, NY.

Lubbers, J.R., Chauhan, S. and Bianchine, J.R. 1981. Controlled clinical evaluation of chlorine dioxide, chlorite and chlorate in man. Fundam. Appl. Toxicol., 1: 334–338.

McCauley, P.T., Robinson, M., Daniel, F.B. and Olson, G.R. 1995. The effects of subchronic chlorate exposure in Sprague-Dawley rats. Drug Chem. Toxicol., 18: 185–199.

Meier, J.R., Bull, R., Stober, J. and Cimino, M. 1985. Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice. Environ. Mutagen., 7: 201–211.

Meister, R. (ed.). 1989. Farm chemicals handbook. Meister Publishing Co., Willoughby, OH.

Michael, G.E., Miday, R., Bercz, J., Miller, R., Greathouse, D., Kraemer, D. and Lucas, J. 1981. Chlorine dioxide water disinfection: a prospective epidemiology study. Arch. Environ. Health, 36: 20–27.

Ministère de l'Environnement du Québec. 2004. Personal communication from H. Tremblay, Ministère de l'Environnement du Québec, Quebec City, to D. Green, Health Canada, Ottawa.

Mobley, S.A., Taylor, D.H., Laurie, R.D. and Pfohl, R.J. 1990. Chlorine dioxide depresses T_3 uptake and delays development of locomotor activity in young rats. In: Water chlorination: Chemistry, environmental impact and health effects. Vol. 6. R.L. Jolley, L.W. Condie and J.D. Johnson (eds.). Lewis Publishers, Ann Arbor, MI. pp. 347–360.

Moore, G.S. and Calabrese, E.J. 1982. Toxicological effects of chlorite in the mouse. Environ. Health Perspect., 46: 31–37.

Moore, M. and Myhr, B. 1984. Evaluation of chlorine dioxide in the mouse dominant lethal assay. Litton Bionetics Inc., Kensington, MD (Report No. 22203) [cited in IPCS, 2002].

Musil, J., Knotek, Z. and Chalupa, J. 1964. Toxicologic aspects of chlorine dioxide application for the treatment of water containing phenols. Technol. Water, 8: 327–346.

Noack, M.G. and Doerr, R.L. 1976. Chlorine oxygen acids and salts (ClO_2, $HClO_2$). Olin Corporation, Norwalk, CT.

Novatek. 1991. Removal of chlorine dioxide by-products from drinking water. Report prepared by Novatek, Oxford, OH, for the U.S. Environmental Protection Agency under Contract 68D00033, April.

Orme, J., Taylor, D., Laurie, R. and Bull, R. 1985. Effects of chlorine dioxide on thyroid function in neonatal rats. J. Toxicol. Environ. Health, 15: 315–322.

Pis'ko, G.T., Tolstopiatova, G.V., Belianina, T.V., Samoilov, A.P. and Gupalo, I.M. 1980. Establishment of the maximum permissible concentration of sodium chlorite in the water of reservoirs. Gig. Sanit., 4: 6–8 (in Russian) [cited in RTECS, 1992].

Prieto, R. and Fernandez, E. 1993. Toxicity and mutagenesis by chlorate are independent of nitrate reductase in *Chlamydomonas reinhardtii*. Mol. Gen. Genet., 237: 429–438.

Rav-Acha, C. 1984. The reactions of chlorine dioxide with aquatic organic materials and their health effects. Water Res., 18: 1329–1341.

Rice, R.G. and Gomez-Taylor, M. 1986. Occurrence of by-products of strong oxidants reacting with drinking water contaminants — Scope of the problem. Environ. Health Perspect., 69: 31–44.

RTECS (Registry of Toxic Effects of Chemical Substances). 1992. Sodium chlorite. National Institute for Occupational Safety and Health, Cincinnati, OH.

RTECS (Registry of Toxic Effects of Chemical Substances). 2000a. Chlorine dioxide. National Institute for Occupational Safety and Health, Cincinnati, OH.

RTECS (Registry of Toxic Effects of Chemical Substances). 2000b. Chloric acid, sodium salt. RTECS # FO0525000. National Institute for Occupational Safety and Health, Cincinnati, OH.

Sheahan, B.J., Pugh, D.M. and Winstanley, E.W. 1971. Experimental sodium chlorate poisoning in dogs. Res. Vet. Sci., 12: 387–389.

Simpson, G.D., Kuykendall, C., Miller, J. and Averett, B. 1995. Biocides: The safe and effective use of chlorine dioxide. Ind. Water Treatment, 27(5): 48–54.

Suh, D.H., Abdel-Rahman, M.S. and Bull, R.J. 1983. Effect of chlorine dioxide and its metabolites in drinking water on fetal development in rats. J. Appl. Toxicol., 3: 75–79.

Suh, D.H., Abdel-Rahman, M.S. and Bull, R.J. 1984. Biochemical interactions of chlorine dioxide and its metabolites in rats. Arch. Environ. Contam. Toxicol., 13: 163–169.

Taylor, D.H. and Pfohl, R.J. 1985. Effects of chlorine dioxide on the neurobehavioral development of rats. In: Water chlorination. Vol. 5. Chemistry, environmental impact and health effects. R.L. Jolley (ed.). Lewis Publishers, Chelsea, MI. pp. 355–364.

TERA (Toxicology Excellence for Risk Assessment). 1998. Health risk assessment/characterization of the drinking water disinfection by-products chlorine dioxide and chlorite. Toxicology Excellence for Risk Assessment, Cincinnati, OH (Report 8W-0766-NTLX).

Toth, G.P., Long, R., Mills, T. and Smith, M. 1990. Effects of chlorine dioxide on the developing rat brain. J. Toxicol. Environ. Health, 31: 29–44.

Trevors, J.T. and Basaraba, J. 1980. Toxicity of benzoquinone and hydroquinone in short-term bacterial bioassays. Bull. Environ. Contam. Toxicol., 25: 672–675 [cited in Rav-Acha, 1984].

U.S. EPA (Environmental Protection Agency). 1983. Sodium chlorate: exemption from the requirement of a tolerance. Fed. Regist., 48: 19028.

U.S. EPA (Environmental Protection Agency). 1996. Proposed guidelines for carcinogen risk assessment. Fed. Regist., 61(79): 17959–18011.

U.S. EPA (Environmental Protection Agency). 1998. EPA Method 300.1. Determination of inorganic anions in drinking water by ion chromatography. Revision 1.0. U.S. Environmental Protection Agency, Washington, DC (EPA/600/R-98/118; available at http://www.epa.gov/OGWDW/methods/met300.pdf).

U.S. EPA (Environmental Protection Agency). 1999a. Alternative disinfectants and oxidants guidance manual. Office of Water, U.S. Environmental Protection Agency, Washington, DC, April (EPA 815-R-99-014; available at http://www.epa.gov/safewater/mdbp/alternative_disinfectants_guidance.pdf).

U.S. EPA (Environmental Protection Agency). 1999b. EPA Method 300.0, Revision 2.2. Determination of inorganic anions by ion chromatography. U.S. Environmental Protection Agency, Washington, DC, October (EPA-821-R-99-015; available at http://old.lib.ucdavis.edu/govdoc/EPA/300_0.pdf).

U.S. EPA (Environmental Protection Agency). 2000. Toxicological review of chlorine dioxide and chlorite, in support of summary information on the Integrated Risk Information System (IRIS). U.S. Environmental Protection Agency, Washington, DC, September (EPA/636/R-00/007).

U.S. EPA (Environmental Protection Agency). 2001a. Method 317.0. Determination of inorganic oxyhalide disinfection by-products in drinking water using ion chromatography with the addition of a postcolumn reagent for trace bromate analysis. Revision 2.0. U.S. Environmental Protection Agency, Washington, DC, July (EPA 815-B-01-001; available at http://www.epa.gov/safewater/methods/met317rev2.pdf).

U.S. EPA (Environmental Protection Agency). 2001b. Controlling disinfection by-products and microbial contaminants in drinking water. U.S. Environmental Protection Agency, Washington, DC, December (EPA/600/R-01/110; available at http://www.epa.gov/ordntrnt/ORD/NRMRL/Pubs/600R01110/600r01110completedocument.pdf).

U.S. EPA (Environmental Protection Agency). 2002. Method 326.0. Determination of inorganic oxyhalide disinfection by-products in drinking water using ion chromatography incorporating the addition of a suppressor acidified postcolumn reagent for trace bromate analysis. Revision 1.0. U.S. Environmental Protection Agency, Washington, DC, June (available at http://www.epa.gov/safewater/methods/met326_0.pdf).

U.S. EPA (Environmental Protection Agency). 2003a. Stakeholder discussion on the reassessment of PQL's. U.S. Environmental Protection Agency, Washington, DC, June 19.

U.S. EPA (Environmental Protection Agency). 2003b. Method 327.0. Determination of chlorine dioxide and chlorite ion in drinking water using Lissamine Green B and horseradish peroxidase with detection by visible spectrophotometry. Revision 1.0. Technical Support Center, Office of Ground Water and Drinking Water, U.S. Environmental Protection Agency, Cincinnati, OH (EPA 815-B-03-001; available at http://www.epa.gov/safewater/methods/met327_0.pdf).

U.S. EPA (Environmental Protection Agency). 2004. 40 CFR, Chapter I, Part 136, Appendix B: Definition and procedure for the determination of the method detection limit — Revision 1.11. U.S. Environmental Protection Agency, Washington, DC (available at http://ca.water.usgs.gov/pnsp/rep/interpret/def.html).

U.S. FDA (Food and Drug Administration). 1990. Food and drugs. Vol. 21. Parts 170–179. Office of the Federal Register, Washington, DC.

U.S. NRC (National Research Council). 1980. Drinking water and health. Vol. 3. National Academy Press, Washington, DC.

U.S. NRC (National Research Council). 1982. Drinking water and health. Vol. 4. National Academy Press, Washington, DC.

U.S. NRC (National Research Council). 1987. Drinking water and health. Vol. 7. National Academy Press, Washington, DC.

Volk, C.J., Hofmann, R., Chauret, C., Gagnon, G.A., Ranger, G. and Andrews, R.C. 2002. Implementation of chlorine dioxide disinfection: Effects of the treatment change on drinking water quality in a full-scale distribution system. J. Environ. Eng. Sci., 1: 323–330.

White, G.C. 1992. The handbook of chlorination and alternative disinfectants. 3rd edition. Van Nostrand Reinhold, New York, NY.

WHO (World Health Organization). 1996. Guidelines for drinking-water quality. 2nd edition. Vol. 2. Health and other supporting criteria. World Health Organization, Geneva.

Appendix 1: Analytical Methods for the Determination of Chlorite and Chlorate in Drinking Water

Methodology	Reference method[a]	MDL[b] (µg/L)	PQL[c] (µg/L)	Interferences	Comments	References
Amperometric	Standard Method 4500-ClO2-E	100 (ClO_2^-)	500 (ClO_2^-)	Manganese, copper, nitrate and other oxidants	Identify Cl_2, ClO_2, ClO_2^- and ClO_3^-; adequate for utility use in daily testing	APHA et al., 1998
Ion chromatograph/ conductivity	U.S. EPA Method 300.0 (1993B Revision 2.2)	10 (ClO_2^-) 3 (ClO_3^-)	50 (ClO_2^-) 15 (ClO_3^-)	Chloramine, ClO_2	Good sensitivity, high expertise required; cannot determine Cl_2 or ClO_2	U.S. EPA, 1999b
Ion chromatograph/ conductivity	U.S. EPA Method 300.1 (1997E Revision 1.0)	0.45 (ClO_2^-) 0.78 (ClO_3^-)	2.2 (ClO_2^-) 3.9 (ClO_3^-)	Chloramine, ClO_2	Good sensitivity, high expertise required; cannot determine Cl_2 or ClO_2	U.S. EPA, 1998
Ion chromatograph/ conductivity and ultraviolet/visible detectors	U.S. EPA Method 317.0, Revision 2.0*	1.6 (ClO_2^-) 0.24 (BrO_3^-)	8.0 (ClO_2^-) 1.2 (BrO_3^-)	ClO_2	Nearly identical to 300.1, but includes a post-column reactor with o-dianisidine dihydrochloride and an ultraviolet/visible detector that targets bromate	U.S. EPA, 2001a
Ion chromatograph/ conductivity and ultraviolet/visible detectors	U.S. EPA Method 326.0, Revision 1.0*	1.6 (ClO_2^-) 0.17 (BrO_3^-)	8.0 (ClO_2^-) 0.9 (BrO_3^-)	ClO_2	Nearly identical to 300.1, but includes a post-addition of KI and Mo(VI) and an ultraviolet/visible detector that specifically targets bromate	U.S. EPA, 2002
Ultraviolet/visible spectrophotometric Lissamine Green B	U.S. EPA Method 327.0, Revision 1.0*	MDL not available	100 (ClO_2) 100 (ClO_2^-)	Free Cl_2 (eliminated with glycine) and ClO_2 (removed by sparging with inert gas)	Adequate for utility use in conjunction with daily monitoring; two-step procedure	U.S. EPA, 2003b
Flow injection analysis — iodometric	Flow injection analysis	130 (ClO_2) 10 (ClO_2^-) 20 (ClO_3^-)	650 (ClO_2) 50 (ClO_2^-) 100 (ClO_3^-)	Specific interferences are removed using masking agents	Identify ClO_2, ClO_2^- and ClO_3^-; may be automated and on-line	Novatek, 1991

[a] Asterisk (*) indicates U.S. EPA proposed methods.

[b] Method detection limit: a measure of a method's sensitivity, defined as the minimum concentration of a substance that can be reported with 99% confidence that the analyte concentration is greater than zero (U.S. EPA, 2004).

[c] Practical quantitation limit: the lowest concentration of an analyte that can be reliably measured within specified limits of precision and accuracy during routine laboratory operating conditions. A PQL may be determined either through the use of interlaboratory study data or, in the absence of information, through the use of a multiplier of 5–10 times the MDL. A multiplier of 5 times the MDL was used in this methods table (U.S. EPA, 2003a).

Appendix 2: Provincial/Territorial Cost Estimates

Prince Edward Island
Chlorine dioxide is not currently used by any water supply system on PEI, while the use of hypochlorite solutions is wide-spread. As relatively simple management measures can address any concerns relating to the production of chlorate as a degradation product of these hypochlorite solutions, no economic impact is anticipated as a result of the proposed guidelines.

Newfoundland and Labrador
At present no public water supplies are disinfected through the use of chlorine dioxide and consequently, there is no expectation of finding chlorite or chlorate in finished drinking water in Newfoundland and Labrador as a result of this form of disinfection. Monitoring for chlorite or chlorate has not been required in this province and hence there is no data for these parameters.

Under the scenario that there may be chlorate introduced into finished water as a result of poor quality hypochlorite solutions, appropriate mitigation such as proper use and storage of hypochlorite is not considered a significant cost factor. Therefore, the proposed guideline of 1 mg/L for chlorite and chlorate will not have an economic impact on water supply systems in this province.

Nova Scotia
Based on the supporting documentation, chlorite and chlorate are disinfection by-products that are formed when using chlorine dioxide as a disinfectant. Chlorate can also be formed when using sodium hypochloride that does not meet quality standards or has been stored for a long period. As this is a new proposed guideline, no historical data on chlorite-chlorate levels in Nova Scotia is available. In light of the lack of data, the proposed guideline of 1 mg/L for chlorite and chlorate is projected to have the following impacts:

- There are currently no municipal water facilities in Nova Scotia using chlorine dioxide as a disinfectant at this time. As such, no cost impacts are expected due to the use of this disinfectant.
- There are approximately 44 municipal water systems currently using sodium hypochlorite as a disinfectant that could be impacted by the proposed chlorate guideline. Many of these are small systems that may have to revise their operational practices if sodium hypochlorite does not meet quality standards or is stored for long periods of time. No capital expenditures are expected to address this issue. There may be some increases in operating costs due to more frequent deliveries, water quality testing, etc. A number of registered public drinking water supplies (i.e. private supplies that serve the public) may also be impacted.

In addition to the above, the limited number of labs that are currently accredited to offer this test, none of which are in Atlantic Canada, may cause some initial inconvenience to municipal utilities and other public drinking water supplies in Nova Scotia.

New Brunswick
New Brunswick does not have any historical data, however it is not expected that any major impact with the proposed Guideline levels. There are no systems in New Brunswick using Chlorine Dioxide. Sodium hypochlorite use is high and an educational component will be required on the proper use and storage . There may be a requirement for public water systems using sodium hypochlorite to expand their water sampling plans to include chlorate as an additional parameter to be tested.

Quebec
Il y a présentement au Québec 11 stations de production d'eau potable qui utilisent du bioxyde de chlore dans le cadre de leur traitement. Ces stations desservent environ 435 000 personnes (6 % de la population québécoise) dans 27 municipalités. Jusqu'à maintenant, le Québec n'a pas exigé de suivi des chlorites/chlorates dans l'eau potable distribuée par les installations utilisant du bioxyde de chlore. Selon des données disponibles, une seule des stations utilisant actuellement le bioxyde de chlore au Québec serait susceptible de présenter un dépassement des concentrations maximales acceptables proposées. Cette station devrait apporter des ajustements au traitement appliqué. Outre ces ajustements techniques, le seul autre impact économique prévisible proviendrait des coûts de l'imposition éventuelle d'un suivi régulier des chlorites et chlorates dans les réseaux de distribution québécois utilisant du bioxyde de chlore.

Ontario
Less than 1% of all drinking water systems in Ontario generate chlorine dioxide for use as a disinfectant. Ontario in the past has not required monitoring for chlorite or chlorate. Recently, requirements to monitor are included in site specific certificates of approval and only when chlorine dioxide is identified as a disinfectant. The economic impact of a proposed guideline of 1 mg/L to owners and operators of drinking water systems in Ontario is expected to be minimal.

Manitoba
Manitoba currently has one facility that uses chlorine dioxide as the primary disinfectant. Its' operational performance is currently being monitored. As for hypochlorite solutions, municipal water systems follow good management practices such as minimising storage of product at water treatment facilities, proper on-site storage to minimise exposure to UV light, storage in a cooler place and, limited period for use of solution batch in the treatment facility. There is no anticipated economic impact on Manitoba municipal water systems as a result of the proposed new guidelines for chlorite and chlorate.

Saskatchewan
At present no communities in Saskatchewan use chlorine dioxide as a disinfectant. Hence, it is expected that there will be no occurrence of chlorite/chlorate levels in finished drinking water from chlorine dioxide disinfectant use. Chlorine dioxide has been employed in water disinfection in isolated instances in Saskatchewan in the past. In the past Saskatchewan has not required monitoring for these parameters and at present, information on the levels of chlorite/chlorate in finished drinking water is not available in our database. Until such time as

chlorine dioxide disinfectant use resumes and planned monitoring can be undertaken it is difficult to estimate any future treatment cost for potentially affected communities or waterworks owners. Chlorate in sodium hypochlorite solutions during extended, warm temperature storage has been known previously and is not expected to represent a significant exposure route. Monitoring for chlorite/chlorate levels in a set of Saskatchewan based drinking water supplies is planned. At present the proposed guideline of 1 mg/L for chlorite/chlorate will not have a known economic impact on communities or waterworks owners regulated by Saskatchewan Environment.

Alberta

No communities in Alberta, at present, use chlorine dioxide as the primary disinfectant. As for hypochlorite solutions, Alberta Environment's guidelines for waterworks systems require communities to follow good management practices such as storing in dark containers to cut the UV light, storing in a cooler place, limit the use to 3 month period, etc. There will be no economic impact on the communities as a result of the new guidelines for chlorite and chlorate.

British Columbia

The proposed guidelines for chlorite and chlorate are not expected to have any significant impact in British Columbia. The few data available for either chlorate or chlorite in British Columbia suggest the proposed guideline is well above levels to be expected in drinking water supplies. Chlorine dioxide is not a common disinfectant in British Columbia and proper storage of hypochlorite to prevent decomposition to chlorate also reduces the likelihood that levels will occur at or above the proposed guideline.

Yukon

Chlorine dioxide is not used for disinfection of public water supplies at this time. Most of the water treatment plants in Yukon use sodium hypochlorite solutions. It has yet to be determined if there is a problem in this area.

Northwest Territories

Chlorine Dioxide is not used for disinfection in any drinking water systems in the Northwest Territories. Therefore there is no predicted economic impact as a result of the new guideline for Chlorite-Chlorate. Disinfection by chlorine is required and all water treatment plants use either gas chlorine or sodium hypochlorite.

Nunavut

There are no communities in Nunavut using Chlorine dioxide for disinfection of drinking water supplies at this time. Hypochlorite solutions are the primary form of disinfection with one community using gas. The new chlorite-chlorate guidelines are not expected to have any economic impact at this time.

Appendix 3: List of Acronyms

ANSI	American National Standards Institute
bw	body weight
CHO	Chinese hamster ovary
CI	confidence interval
DNA	deoxyribonucleic acid
EPA	Environmental Protection Agency (U.S.)
GAC	granular activated carbon
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
MAC	maximum acceptable concentration
MDL	method detection limit
NOAEL	no-observed-adverse-effect level
OD	odds ratio
OECD	Organisation for Economic Co-operation and Development
PQL	practical quantitation limit
TDI	tolerable daily intake