IV. Recommended Limits for the Disinfectant Chlorine Dioxide

The following Immediate Action Levels are recommended for those systems disinfecting with chlorine dioxide:

Measured Parameter	Immediate Action Level, mg/L	Applicable to:
chlorine dioxide	2 mg/L	women of childbearing age, infants and young children
	72 mg/L	other healthy members of the population
chlorite	2 mg/L	women of childbearing age, infants and young children
	72 mg/L	other healthy members of the population
pH, free chlorine	<4.5 (low pH) >11.0 (high pH) 25 mg/L (free chlorine)	all
pH, ORP*(sample location on chlorine dioxide delivery line)	employ facility-specific limits.	all

* ORP = oxidation-reduction potential

Treatment and Monitoring Systems

Chlorine dioxide can be generated at water treatment plants by a number of processes which Gates (1998) has characterized as generally involving reaction of sodium chlorite ($NaClO_2$) or chlorate solutions with oxidizing agents such as: gaseous or aqueous chlorine alone; a mineral acid by itself or with chlorine; or acid in combination with a hypochlorite salt solution.

Six water treatment plants in MassDEP's Northeast Region employ chlorine dioxide as a disinfectant. Three means of generating chlorine dioxide are utilized onsite at these facilities:

i. a two chemical process involving combining chlorine gas and sodium chlorite;

ii. a three-chemical process involving the combination of sodium chlorite, sodium hypochlorite and sulfuric acid; and

iii. a three chemical process involving a commercial preparation called Purate (sodium chlorate and hydrogen peroxide) plus sulfuric acid.

A conceptualized process flow diagram for drinking water disinfection using chlorine dioxide through drinking water plants from source water through delivery to the point of entry into the distribution system is shown in Figure 2. Only the chlorine dioxide disinfection portions of the treatment process are indicated along with representation of monitoring that is conducted on the system.

Monitoring is performed for two reasons: to determine compliance with state drinking water standards; and for monitoring the operational status of the water treatment system.

Background and Existing Drinking Water Standards

Chlorine dioxide in water is unstable and readily dissociates primarily into chlorite and chloride, secondarily into chlorate (US EPA 2000b).

$$ClO_2 \rightarrow ClO_2^- + ClO_3^{--} + Cl^-$$

There is also interconversion between forms in the water and the human gut. Because of this chemistry and similarities in toxicities, chlorine dioxide and chlorite have been reviewed together by other groups such as the US EPA (2000b) and ATSDR (2004).

A federal drinking water standard (MRDL) for chlorine dioxide of 0.8 mg/L was established by US EPA in its Stage 1 Disinfectants and Disinfectants Byproducts Rule in 1998. The MCL for the byproduct, chlorite is 1.0 mg/L. The 1- and 10-day Health Advisory (HA) values for both chlorine dioxide and chlorite are 0.84 mg/L and are set to protect the most sensitive group, children.

The critical study that is the basis of all of the above criteria for both chlorite and chlorine dioxide is a two-generation developmental study in rats exposed to chlorite (CMA, 1996).

Sampling and Compliance With Chlorine Dioxide MRDL and Chlorite MCL

Sampling for compliance with the chlorine dioxide MRDL and chlorite MCL is described in US EPA (1998) and consists of daily sample monitoring at the entrance to the distribution system. In addition, for chlorite, a monthly sampling of three samples on the same day at designated locations within the distribution system must also be taken.

Compliance with the MCL for chlorite is determined as follows. If the daily sample result at the entrance of the distribution system is greater than the MCL of 1.0 mg/L for chlorite, then 3 samples must be taken the next day at 3 designated locations within the distribution system. The system will be out of compliance with the MCL if the arithmetic average of any three sample set within the distribution system is greater than the MCL.

Compliance with the chlorine dioxide MRDL is somewhat more complicated. There are acute violations and non-acute violations of the MRDL. If the daily sample result at the entrance to the distribution system is greater than the MRDL, then the system must sample at three designated locations within the distribution system on the next day. If the chlorine dioxide concentration for any sample at the entrance to the distribution system is greater than the MRDL AND the result for one or more of the three samples from the distribution system taken on the following day are greater than the MRDL, the system is in acute violation of the MRDL. The system will have to take immediate corrective action to lower the occurrence of chlorine dioxide below the MRDL and issue the required acute public notification (US EPA, 1998).

Health Advisory (HA) values are non-regulatory concentrations associated with no adverse health effects from ingestion exposures for periods up to the duration associated with the particular HA (e.g., 1-day). There is therefore no required sampling regimen associated with determining compliance with the HA values. They are not immediate "DO NOT DRINK" type of values.

Compliance with the drinking water standards for chlorine dioxide and chlorite is determined differently than for other disinfectant and disinfectant byproduct chemicals because the critical health effect used for setting the standard is a developmental endpoint, rather than a chronic toxicity endpoint. Chemicals which produce developmental or reproductive toxicity generally exert their toxicity within shorter time frames than occurs with chronic toxicity. These critical windows of exposure necessitate that potential shorter-term excursions in concentrations be minimized. This is done with short duration compliance determinations such as exists for chlorine dioxide. However, this monitoring is not of sufficient frequency to quickly pick up an upset condition, unless the daily grab sample coincidentally was taken at the same time or just after the start of an upset condition

Operational status monitoring is performed to document that the water quality is being maintained within defined limits and that treatment systems are functioning correctly. Ideally, online chlorine dioxide monitors could be used to determine if chlorine dioxide concentrations exceed any acute health-based concentration limits when an upset event occurs. However, only one of the six facilities in northeastern Massachusetts presently employing chlorine dioxide disinfection has an online chlorine dioxide monitor. We therefore are identifying limits for several operational parameters monitored continuously in these systems as alternatives to online chlorine dioxide monitoring. Because of the rapid conversion of chlorine dioxide to chlorite and chlorate, chlorite concentrations would be an alternative indicator of upset conditions. While real-time chlorite monitors exist, none of these six facilities reportedly has online chlorite monitors.

Other operational status online monitoring instruments employed at all facilities include pH and oxidation/reduction potential meters on the chlorine dioxide feed line and pH and free (or residual) chlorine online meters on finished water at the point of entry into the distribution system. The readings provided by these instruments provide good indications of upset conditions involving chlorine dioxide and its precursors. Table 1 shows each of the process chemicals that are being used to generate chlorine dioxide at public water supplies in northeastern Massachusetts and their relationships to each of these three indicators.

Table 1. Real-Time Monitoring for Chlorine Dioxide Generation Process Chemical Upset Conditions

ClO_2 Preparation Method	Chemical	Formula	Possible Real-Time Indicator and Relationship to Chemical Concentration		
			pH	**ORP***	**chlorine**
A. “Purate”	sodium chlorate	$NaClO_3$	1/α	α	α
	hydrogen peroxide	H_2O_2		α	
	sulfuric acid	H_2SO_4	1/α	α	
B. Two-Chemical	chlorine gas	Cl_2	1/α	α	α
	sodium chlorite	$NaClO_2$		α	α
C. Three-Chemical	sodium chlorite	$NaClO_2$			α
	sodium hypochlorite	NaClO	1/α	α	α
	sulfuric acid	H_2SO_4	1/α	α	

Key: α means proportional to; 1/ α means inversely proportional to;
* ORP = oxidation-reduction potential

For meters located on the chlorine dioxide feed lines, optimal operating ranges for pH and ORP are used by some of the plants to indicate when the chlorine dioxide generation process is functioning normally. When values for either pH or ORP go beyond the optimal operating range, this is an indication of some problem with the relative amounts of inputs of precursor chemicals. For online pH and chlorine meters at the point of entry to the distribution system, the health-based indicator values for pH and chlorine residual provided elsewhere in this guidance should provide additional checks on upset conditions.

Identification of Health-Based Immediate Action Levels for Chlorine Dioxide and Chlorite

For those water systems disinfecting with chlorine dioxide and having real-time monitoring capabilities for chlorine dioxide and/or chlorite, health-based acute exposure limits may be used as direct indicators of potential toxicity associated with “upset” concentrations of these chemicals.

The derivation of acute exposure limits should ideally be based on the acute toxicity database for these chemicals. The limited acute toxicity information available for chlorine dioxide and chlorite has been summarized in the US EPA and ATSDR toxicological reviews noted above. Ingestion of high concentrations of chlorine dioxide or chlorite could produce irritation in the mouth, esophagus, or stomach. The chlorine dioxide data however are not sufficiently extensive to use for setting an Immediate Action Level, as most of the observations concern mortality.

Since chlorine dioxide is rapidly converted to chlorite in water systems and there appears to be more extensive literature on chlorite toxicity, the chlorite database was used to identify a health-based acute exposure limit that may apply to both chlorite and chlorine dioxide. This approach is consistent with EPA's approach for deriving the RfD, the HA and MRDL for chlorine dioxide.

The critical toxicological endpoints identified from the literature reviews for chlorite are neurodevelopmental and neurobehavioral effects seen in animals from exposures before birth or during early development after birth. We therefore can look to the developmental and reproductive study results to provide a basis for setting an acute exposure limit for this chemical.

The 2-generation rat study used as the basis for development of US EPA's NOAEL[1] (CMA, 1996) included the finite phases of the animal's lifecycle when they would be susceptible to developmental or reproductive effects. From the chlorite study results, it is not possible to determine how long of an exposure during pre- or post-natal development is needed to produce adverse effects. We therefore make the conservative assumption for this derivation that any short duration exposure level at which effects have been seen in humans or animals during the developmental period could be capable of producing those effects in humans with only very short-term (e.g., hours) exposures such as could occur after an upset condition at a water treatment plant.

A study LOAEL[1] of 6 mg/kg/d chlorite was identified from the CMA (1996) rat study. Our objective is to protect customers of the water companies from any significant adverse health effects as a result of short-term exposures to chlorine dioxide or chlorite as a result of treatment plant upset conditions. We therefore chose a starting point based upon observed neurobehavioral effects (LOAEL) associated with exposures (in animals) during prenatal development. This number was the basis for the derivation of a "do not drink" action level for water treatment plants.

[1] NOAEL – no observed adverse effects level; LOAEL – lowest observed adverse effects level

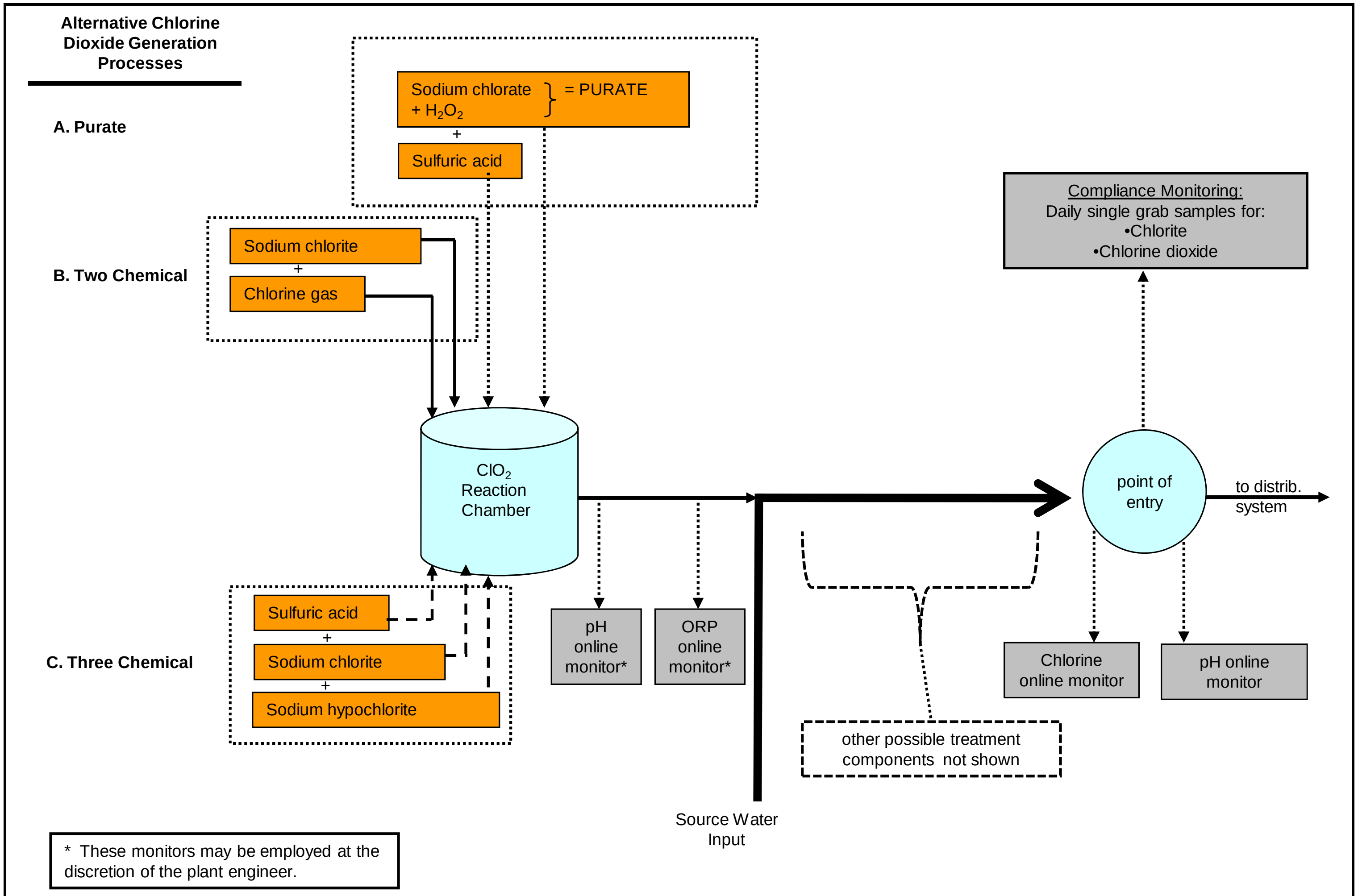

Figure 2. Hypothetical Chlorine Dioxide Generation and Monitoring in a Water Treatment Plant

An Immediate Action Level can be derived from the LOAEL of 6 mg/kg/d by dividing the value by default uncertainty factors of: a) 10 for interspecies extrapolation of the results from rats to humans, and b) 10 for sensitive individuals within the population. This operation gives an acute dose of 0.06 mg/kg/d.

This value can be translated into an equivalent concentration in drinking water of **2 mg/L** by using the default adult exposure parameters of 70 kg body weight and 2 L/d drinking water ingestion.

We considered employing either an additional uncertainty factor of 2 in the derivation of the RfD or using children's exposure parameters for the translation of the RfD to the drinking water concentration to reflect the greater exposures that children experience relative to adults. However, US EPA provided their perspective on these additional considerations with the final rule: "*The MCLG and MRDLG presented for chlorite and chlorine dioxide"* (0.8 mg/L for each) "*are considered to be protective of susceptible groups, including children, given that the RfD is based on a NOAEL derived from developmental testing, which includes a two-generation reproductive study. A two-generation reproductive study evaluates the effects of chemicals on the entire developmental and reproductive life of the organism. Additionally, current methods for developing RfDs are designed to be protective for sensitive populations. In the case of chlorite and chlorine dioxide a factor of 10 was used to account for variability between the average human response and the response of more sensitive individuals. In addition, the important exposure is that of the pregnant and lactating female and the nursing pup. The 2 liter per day water consumption and the 70 kg body weight assumptions are viewed as adequately protective of all groups.*" (US EPA, 1998).

We therefore choose a chlorite concentration of 2 mg/L as an upper do not use/do not drink value applicable to pregnant women, infants and young children. If faced with the need to issue emergency notifications to the public in the face of upset conditions with systems employing chlorine dioxide for disinfection, water suppliers may wish to direct their notification to the identified sensitive subgroups: pregnant women (prudent to include all women of child-bearing age to capture those who may unknowingly be pregnant), infants and young children.

In order to provide guidance to adults, the work of the World Health Organization (WHO, 2005) provides a useful starting point. They concluded from their review of the toxicity of chlorine dioxide and chlorite that "humans are probably not sensitive to the concentrations of chlorite that are likely to be found in water disinfected with chlorine dioxide. Some safety factor is present in these data, because it is unlikely that concentrations of chlorite would exceed 1 mg/L". They also noted that the studies "provide little information relative to the actual margin of safety that exists between those concentrations seen or administered and concentrations that would lead to clear adverse effects. Consequently, these studies do not imply that the concentrations of chlorite in drinking-water should be without limits". Highest one-time exposure concentrations to chlorite in healthy human volunteers of from 5-24 mg/L have not been associated with any demonstrable adverse clinical effects on hematology and blood chemistry (see

Lubbers et al. 1981,1982, 1984; Lubbers and Bianchine 1984; all cited in (WHO, 2005). Another perspective on chlorine dioxide and chlorite acute toxicity is provided from chlorine dioxide's use as a water disinfectant in tablet form for campers, hikers and those needing to make potable water from natural water sources. These tablets generally contain 6.4% sodium chlorite and 1% sodium dichloroisocyanurate dihydrate. Users are instructed to add the tablet to one liter of water. The manufacturer of the tablets indicates that they generate solutions with from 3-5 mg/L chlorine dioxide and a small amount of unreacted chlorite ion[2]. The labels carry no warnings about potential adverse health effects, and presumably most users are healthy individuals engaged in outdoor activities. In light of this widespread use and the human exposure studies, an upper limit of something in the range of 5 mg/L on chlorite exposures for healthy adults would seem to be too conservative for a do not drink action level. Since the highest exposure level reported with no adverse effects was 24 mg/L, this level might serve as an upper limit do not drink level for healthy adults. Alternatively, the standard uncertainty factor of 10 could be applied to this NOAEL to extrapolate it to a LOAEL to give a concentration of 240 mg/L (using concentrations, rather than doses as a mathematical shortcut for these calculations). This value seems high. We recommend the alternative application of an uncertainty factor of 3 instead of 10 to give an upper limit of 72 mg/L to indicate when notices should be issued to also warn healthy adults not to drink the water.

Statistical Reality Check

To provide some perspective on the feasibility of using the health-based value in the context of a typical water treatment plant utilizing chlorine dioxide disinfection, a statistical approach was used to identify "outlier" concentrations of chlorite and chloride dioxide that might be indicative of an upset condition. The approach used is borrowed from the industrial process control literature and is used to identify concentrations that fall outside the range of normal operating conditions. Daily monitoring data over a period of one year from six public water supplies in Massachusetts that use chlorine dioxide disinfection were used for this evaluation. These data were summarized in a database that contained over 1400 daily concentrations each for chlorine dioxide and chlorite. The distributions of values were described using standard statistics of mean and standard deviation. In general, these concentrations were lognormally distributed. Most values were quite low, with chlorine dioxide concentrations lower than chlorite concentrations, and there were many non-detect values (i.e., approximately 13% of the chlorite values and 66% of the chlorine dioxide values were "ND" or censored). Both Kaplan-Meier survival analysis and Maximum Likelihood Estimation (MLE) statistical methods were employed to better characterize the distributional characteristics of these heavily censored data sets. The Kaplan-Meier method is a non-parametric approach that is recommended with data sets containing less than 50% censored data. The MLE method is a parametric method that is recommended with data sets containing between 50-80% censored data. Based on these recommendations, the summary statistics describing the distributions of chlorite and chlorine dioxide for both of these chemicals

[2] Personal Communication 12/28/07 from Mr. Barry Speronello, Research Fellow, BASF Catalysts LLC.

were determined using the Kaplan-Meier method (using Statistica® software) for the chlorite data and the MLE method (using Minitab® software) for the chlorine dioxide data (Table 2).

Table 2. Summary Statistics for Chlorine Dioxide Data

PARAMETER	Chlorite	Chlorine Dioxide
Total # data points	1454	1482
Percent Censored Data	13%	66%
Mean	*---	0.072 mg/L
Standard Deviation	*---	0.077 mg/L
Median	0.14 mg/L	0.049 mg/L
First Quartile	0.33 mg/L	0.027 mg/L
Third Quartile	0.1 mg/L	0.089 mg/L
Interquartile Range	0.22 mg/L	0.061 mg/L

* The mean and standard deviation using the Kaplan-Meier method may not be useful measures due to the skewness of most survival data and thus they were not calculated.

A variety of definitions of "outlier" concentrations were identified from the process control literature (included in Table 3). Using the information in Table 2 together with these definitions, a series of outlier concentrations for each chemical (on the high end of each distribution) were determined (Table 3).

The estimated outlier concentrations are all well within the typical range of chlorite and chlorine dioxide concentrations seen at normally operating chlorine dioxide treatment plants. They are also all below the respective MCL/MRDL for chlorite/chlorine dioxide as well as the acute exposure limit developed in the above sections for these compounds. Several factors could explain why these calculated "outlier" values were not so extreme. The disinfection process with chlorine dioxide is fairly well-controlled and thus the database of monitored concentrations may not provide a good basis for identifying a usable outlier. This particular database had a very high percentage of censored data, thus resulting in a highly skewed database and many very low concentrations. Finally, it is very possible that the lognormal curve fit to the data by MLE did not provide a good fit as a result of the highly skewed data set.

The health-based value derived above was compared to the calculated "outlier" concentrations presented in Table 3. There was concern that the value of 2 mg/L developed for sensitive subpopulations was perhaps too low as it was not too far off in magnitude from the MCL and MRDL for these chemicals. However, the above exercise supports the observation that there is not much variation in a normally operating chlorine dioxide treatment process. We therefore conclude that 2 mg/L is a reasonable health-based level for identifying potential "upset" conditions at facilities employing chlorine dioxide treatment.

Table 3. Calculated Outliers

Type	Mathematical definition	Outlier Concentration (mg/L)		Probability of Getting (%)	
		Chlorite	**Chlorine dioxide**	**Chlorite**	**Chlorine dioxide**
Outlier	$>$ or $<$ $\pm 2\sigma$ from the mean	-----	0.16	-----	8.8
Mild outlier	$< Q_{0.25} - 1.5$ * Interquartile range(IQR) or **$> Q_{0.75} + 1.5$ * IQR** (Occurring about 1 out of 150 values in a normally distributed population)	0.43	0.18	-----	6.8
Extreme outlier	$< Q_{0.25} - 3$*IQR or **$> Q_{0.75} + 3$*IQR** (occurring about 1 in 425,000 values)	0.76	0.27	-----	2.5

Summary of Monitoring Parameters for Chlorine Dioxide

Table 4 summarizes the alternative Acute Exposure Limits discussed above for different indicator chemicals associated with the use of chlorine dioxide for disinfection of drinking water.

Table 4. Immediate Action Levels for Chlorine Dioxide Disinfection-Associated Parameters

Measurement	Immediate Action Level, mg/L	Applicable to:
chlorine dioxide	2 mg/L	women of childbearing age, infants and young children
	72 mg/L	other healthy members of the population
chlorite	2 mg/L	women of childbearing age, infants and young children
	72 mg/L	other healthy members of the population
pH residual chlorine	<4.5 (low pH) >11.0 (high pH) 25 mg/L (free Cl)	all
pH ORP*(sample location on chlorine dioxide delivery line)	employ facility-specific limits	all

* ORP = oxidation-reduction potential

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