

This study evaluated the safety and efficacy of chlorine dioxide (ClO<sub>2</sub>) fed into the incoming main water line to control *Legionella* bacteria in two hospital water systems. In both hospitals A and B, positivity of all distal outlets (sinks and showers) for *Legionella* decreased from 60% to ≤ 10% after the ClO<sub>2</sub> treatment. In hospital B, the heterotrophic plate count bacteria in hot water were reduced from 15,400 cfu/mL to 2,900 cfu/mL after ClO<sub>2</sub> treatment. Mean concentrations of ClO<sub>2</sub> and chlorite (ClO<sub>2</sub><sup>-</sup>) in cold and hot water did not exceed the maximum residual disinfection level of 0.8 mg/L and the maximum contaminant level of 1.0 mg/L, respectively. No cases of healthcare acquired legionellosis have been identified in the postdisinfection period in these two hospitals. The study indicates that ClO<sub>2</sub> is a promising disinfectant for controlling not only *Legionella*, but also other microorganisms in drinking water.

# *Legionella* control by chlorine dioxide in hospital water systems

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**L**egionnaires' disease is caused by *Legionella* bacteria, which colonize 12–70% of hospital water systems (Lin et al, 1998b). Of the Legionnaires' disease cases reported to the Centers for Disease Control and Prevention (CDC), 25–45% were hospital-acquired (Benin et al, 2002). *Legionella* and other opportunistic pathogens colonize water systems; cause pneumonia, wound, and bloodstream infections in hospitalized patients; and cause approximately 25% of all hospital-acquired infections (Anaisse et al, 2002). These infections could be prevented through active and supplemental disinfection of hospital water systems.

Disinfection methods that have been used by hospital water systems to control *Legionella* include thermal eradication, hyperchlorination, copper–silver ionization, and point-of-use (POU) filters. Thermal eradication is a short term solution that is time-consuming and labor-intensive to implement. High levels of free chlorine in distribution systems from hyperchlorination will cause excessive pipe corrosion problems. Although copper–silver ionization has been an effective disinfection method, a recent study showed that *Legionella* could develop resistance to copper and silver ions (Mietzner et al, 2005). POU filters do not provide disinfectant residual protection for the entire water distribution system.

Chlorine dioxide (ClO<sub>2</sub>) is a promising alternative disinfectant for hospital water systems to prevent Legionnaires' disease. Chlorine dioxide has been effectively used to control *Legionella* in European hospitals (Hill et al, 2000; Hood et al, 2000; Hamilton, et al, 1996). However, chlorine dioxide has not been extensively evaluated in the United States for its disinfection efficacy and safety to control hospital-acquired Legionnaires' disease (Bova et al, 2004; Sidari et al, 2004; Srinivasan et al, 2003). Chlorine dioxide has long been considered an alternative drinking water disinfectant in the United States (Aieta & Berg, 1986).

ClO<sub>2</sub> exists as a stable free radical with an unpaired electron and reacts with organic and inorganic compounds mainly through a one-electron transfer reaction. Unlike chlorine, ClO<sub>2</sub> does not react with natural organic matter to form trihalomethanes or haloacetic acids. ClO<sub>2</sub> is a highly selective oxidant with respect to specific functional groups, such as phenolic moieties or tertiary amino groups (Hoigné & Bader, 1994). The biocidal efficiency of ClO<sub>2</sub> equals or is superior to chlorine (Gates, 1998; Korich et al, 1990; Aieta & Berg, 1986). ClO<sub>2</sub> is effective against viruses, bacteria, protozoan cysts, biofilm, and waterborne pathogens in public drinking water systems (Radziminski et al, 2002; Chauret et al, 2001; Walker & Morales, 1997; Walker et al, 1995; Olivieri et al, 1986). Moreover, ClO<sub>2</sub> is an effective biocide over a wide pH range and is effective for removing iron and manganese and for controlling taste and odor.

*Legionella* is considered to be a continuing risk and the single most common etiologic agent associated with outbreaks involving drinking water (WSTB, 2006). Healthcare facilities are increasingly faced with the decision of choosing a *Legionella* disinfection method. It is recommended that any such methods undergo a four-step evaluation process to ensure the method's safety and efficacy (Stout & Yu, 2003). These steps are: (1) demonstrate disinfectant efficacy in vitro, (2) document anecdotal experience in preventing disease outbreaks in individual hospitals, (3) implement controlled studies of sufficient duration in single hospitals, and (4) validate confirmatory reports from multiple hospitals over a prolonged period. The study presented in this article represents step three of the process for chlorine dioxide—a controlled prospective full-scale study in two hospitals.

A previous field study showed that an extended time (i.e., 1.75 years) was required for complete *Legionella* eradication from a hospital distribution system and that the ClO<sub>2</sub> residual in the hot water system was significantly lower than in the cold water system (Sidari et al, 2004). This hospital also had a unique secondary distribution system that included a 520,000-gal reservoir where ClO<sub>2</sub> was injected and a 10,000-ft pipeline to 23 buildings across 60 acres. On the basis of this field study, it can be hypothesized that the efficacy of ClO<sub>2</sub> for controlling *Legionella* might be improved for hospitals with smaller secondary distribution systems in which ClO<sub>2</sub> is injected into the incoming water.

Therefore, to verify this hypothesis, the objectives of this study were

- to evaluate the efficacy of ClO<sub>2</sub> for controlling *Legionella* and total heterotrophic plate count (HPC) bacteria in two hospitals with smaller secondary water distribution systems and
- to monitor the levels of ClO<sub>2</sub>, chlorite (ClO<sub>2</sub><sup>-</sup>), and chlorate (ClO<sub>3</sub><sup>-</sup>) to ensure that the maximum residual disinfection level (MRDL) and maximum contaminant level (MCL) were not exceeded.

## MATERIALS AND METHODS

**Study hospital A.** Healthcare-acquired legionellosis caused by *Legionella pneumophila* was diagnosed in an immunocompromised patient in hospital A. Following the initial case, steps were taken to control *Legionella* in the water distribution system, and ClO<sub>2</sub> was chosen to treat the hospital water system. Hospital A has 364 patient beds and 74 skilled nursing beds, and comprises two buildings: building 1 (referred to as B1) and building 2 (referred to as B2). Both buildings have eight floors. Hospital water is supplied by the city water department.

*Legionella* has been detected in the hot water systems of both buildings of hospital A since October 2002. The extent of *Legionella* colonization is expressed as percent *Legionella* positivity, which is the percentage of all sampling sites that tested positive for *Legionella*. The risk of Legionnaires' disease in hospitalized patients has been shown to be better predicted by the percentage of water system sites testing positive for *Legionella* than by the concentration of *Legionella* bacteria in individual samples (Stout & Yu, 2003; Kool et al, 1999). In January 2003, the hospital began operating a ClO<sub>2</sub> generating system to control *Legionella* in the water system. Before installation of the ClO<sub>2</sub> system, the percentage of *Legionella*-positive hot water outlets was 67% (six out of nine samples).

**Study hospital B.** From March 2001 to January 2002, three cases of hospital-acquired *Legionella pneumophila* pneumonia occurred in hospital B. Cultures from the water distribution system reflected the presence of *Legionella pneumophila* serogroup 5 and were identical to *Legionella* cultured from one of the identified patients. Following the initial cases, steps were taken to eliminate *Legionella* in the water distribution system, including superheating and flushing the hot water system and replacing a water tank found to be colonized with *Legionella*. Despite these measures, another case of hospital acquired *Legionella pneumophila* pneumonia was identified in January 2002. The optimal method for long-term disinfection has not yet been identified and no recommendations for long-term treatment exist at this time (CDC, 2004). To investigate the effectiveness of ClO<sub>2</sub>, this method was chosen to treat the hospital water system and was installed in April 2004. In hospital B, the single 12-floor building that is treated with ClO<sub>2</sub> has 672 operating patient beds. Predisinfection baseline cultures were collected from 2002 to 2004.

**ClO<sub>2</sub> generation systems.** One ClO<sub>2</sub> generating unit<sup>1</sup> was installed in each of the two buildings of hospital A by a private contractor.<sup>2</sup> Another ClO<sub>2</sub> generator<sup>3</sup> was installed in hospital B by a different private contractor.<sup>4</sup> Examples of ClO<sub>2</sub> generators are shown in the photos on page 119. The generators use modular electrochemical cassettes to generate a solution with approximately 500 mg/L of ClO<sub>2</sub> using a 25% sodium chlorite solution. ClO<sub>2</sub> is injected into the incoming cold water main at the

target  $\text{ClO}_2$  concentration of 0.5–0.7 mg/L based on the flow rate of the incoming cold water.

**Sample collection and analyses.** Sampling locations for *Legionella* and HPC bacteria were selected throughout the distribution systems in hospitals A and B. In hospital A, 13 sampling locations in B1 and seven sampling locations in B2 were located on the second, fourth, fifth, sixth, and eighth floors of each building. In hospital B, 17 sampling locations were located on the third through the twelfth floors. Hot and cold water samples were collected from distal outlets (sinks and showers) at each sampling location. The hot water storage tank was also sampled at both hospitals.

Sampling in hospital A was performed every two months from June 2004 to August 2005 and then extended to June 2006. Sampling in hospital B was performed from August 2003 to June 2005 and then extended to February 2006. *Legionella* testing was performed in a laboratory,<sup>5</sup> as described in an earlier study (Sidari et al, 2004).

For *Legionella* cultures, 120-mL water samples were collected immediately after the outlet taps were turned on. Distal outlets were then flushed for 1 min to collect representative water samples for  $\text{ClO}_2$  analysis. Temperature measurements were taken directly from the flow stream after the flush. A 10-mL sample was taken for  $\text{ClO}_2$  analysis at the time of collection and 100 g/L of glycine was added to eliminate free chlorine interference. Levels of  $\text{ClO}_2$  were analyzed in both hot and cold water samples using the DPD method for  $\text{ClO}_2$  (0.00–5.00 mg/L; Hach, 2000) and using a glycine reagent and a DPD free chlorine reagent.<sup>6</sup> Colorimetric measurements were performed using a spectrophotometer.<sup>7</sup>

Hospital personnel also monitored  $\text{ClO}_2$  residual in cold water throughout the distribution system every month in hospital A. Hospital personnel performed  $\text{ClO}_2$  residual measurements with a pocket colorimeter<sup>8</sup> following method 10126 (Hach Co., 2000) with the same reagents as the study samples.

Samples for  $\text{ClO}_2^-$  and  $\text{ClO}_3^-$  analysis were chosen to represent various distances from the  $\text{ClO}_2$  injection point (closest, midpoint, and farthest sites). In hospital A, a total of seven hot water samples and five cold water samples were collected for  $\text{ClO}_2^-$  and  $\text{ClO}_3^-$  analysis every two months from five locations in B1 and two locations in B2. In hospital B, a total of six hot water samples and four cold water samples was collected for  $\text{ClO}_2^-$  and  $\text{ClO}_3^-$  analysis every two months from six locations.

Samples for  $\text{ClO}_2^-$  and  $\text{ClO}_3^-$  analysis were sparged with nitrogen gas for 10 min immediately following the collection to remove  $\text{ClO}_2$  residual. Next, 30 mL of the sample was filtered through a 0.2- $\mu\text{m}$  filter, followed by the addition of 50 mg/L of ethylenediamine to each sample.  $\text{ClO}_2^-$  and  $\text{ClO}_3^-$  were measured by ion chromatography<sup>9</sup> with suppressor and conductivity detectors according to method 300.1 (USEPA, 1997). Two samples



The chlorine dioxide ( $\text{ClO}_2$ ) generators (above) in this study use an electrical source and membrane technology to produce  $\text{ClO}_2$  from a sodium chlorite precursor. The membranes are housed in removable cassettes in the upper portion of the unit (left). The generators eliminate the need for handling hazardous chlorine gas or strong acids.

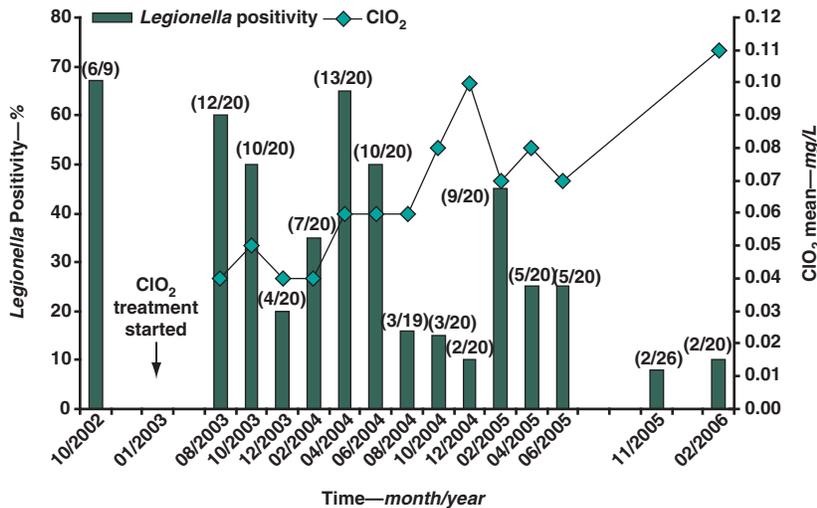


Monitoring for chlorine dioxide is conducted using method 10126 (Hach Co., 2000).



Multiple chlorine dioxide generators can be installed to accommodate larger demand or to provide backup units.

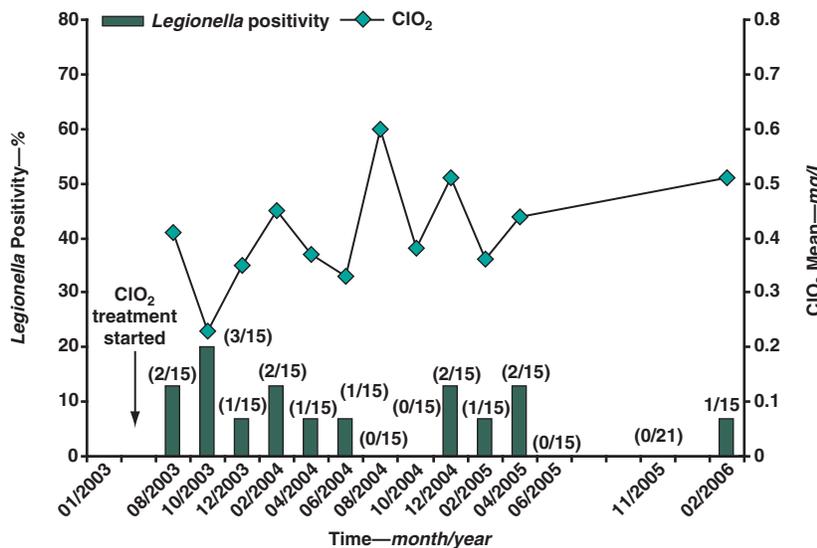
**FIGURE 1** Percent distal site *Legionella* positivity and mean ClO<sub>2</sub> concentrations in the hot water of hospital A over 40 months



ANOVA—analysis of variance, ClO<sub>2</sub>—chlorine dioxide

Within the figure, numbers in parentheses represent positive *Legionella* samples/total samples for month indicated. A significant reduction in percent *Legionella* positivity (ANOVA,  $p < 0.05$ ) was observed after the first 18 months of ClO<sub>2</sub> treatment (Zhang et al, 2007).

**FIGURE 2** Percent distal site *Legionella* positivity and mean ClO<sub>2</sub> concentrations in the cold water of hospital A over 40 months



ClO<sub>2</sub>—chlorine dioxide

Within the figure, numbers in parentheses represent positive *Legionella* samples/total samples for month indicated. *Legionella* positivity was maintained below 20% with ClO<sub>2</sub> residual of 0.3–0.5 mg/L.

were also sent to a reference laboratory<sup>10</sup> each time as a quality control measure to ensure the accuracy of ClO<sub>2</sub><sup>-</sup> and ClO<sub>3</sub><sup>-</sup> analysis.

Water quality of the municipal water supply was evaluated in October 2003 and June 2004. Water samples from the city water supply were collected and stored at 4°C before transfer to the Pittsburgh Water and Sewer Authority for analysis using standard laboratory procedures.

**Statistical analysis.** Statistical software<sup>11</sup> was used for statistical analysis. Significant differences were evaluated by student's *t*-tests and analysis of variance (ANOVA), and a *p* value below 0.05 was considered indicative of a significant difference.

## RESULTS AND DISCUSSION

**Hospital A. Water quality parameters.** Water quality of the municipal water supply was monitored in October 2003 and June 2004. The mean values of water quality parameters were as follows: hardness was 127 mg/L as calcium carbonate, alkalinity was 83 mg/L as calcium carbonate, pH was 7.70, total iron was 0.03 mg/L, total manganese was 0.01 mg/L, total organic carbon (TOC) was 1.96 mg/L, and turbidity was 0.40 ntu. The ClO<sub>2</sub> demand of the drinking water was determined to be 0.20 mg/L after 6 h contact time at 24°C and pH 7.9 using method 2350 C (Standard Methods, 1998).

**Legionella positivity.** *Legionella* positivity in hot water was reduced from 60% (12 out of 20 samples) in August 2003 to 10% (two out of 20 samples) in February 2006 (Figure 1). Significant reduction in hot water *Legionella* positivity (ANOVA,  $p < 0.05$ ) occurred in 18 months (Figure 1) because of the ClO<sub>2</sub> residual. The authors believe that this decline can be attributed to an increase in ClO<sub>2</sub> residual in the hot water. ClO<sub>2</sub> residual in the hot water increased significantly from 0.04 mg/L in August 2003 to 0.11 mg/L in February 2006 ( $p < 0.05$ ) as shown in Figure 1. The decline in *Legionella* positivity in the hot water cannot be attributed to the

variation of the hot water temperatures because hot water temperatures below 60°C do not affect *Legionella* colonization (Lin et al, 1998b; Zacheus & Martikainen, 1996; Darelid et al, 1994). The mean distal site hot water temperature was 44°C during the study (range from 27 to 52°C). The mean distal site cold water temperature was 18°C (range from 4 to 31°C). *Legionella* positivity in cold water samples was below 20% with 0.3–0.5 mg/L of ClO<sub>2</sub> residual (Figure 2). The increase in ClO<sub>2</sub> with time in the cold water was not significant ( $p > 0.05$ ).

In February 2005, *Legionella* positivity of hot water samples unexpectedly increased from 10% (in December 2004) to 45%. No malfunction of the ClO<sub>2</sub> generator was found prior to this increase, and the mean ClO<sub>2</sub> residual remained at 0.36 mg/L in the cold water on the sampling day. The reason for the increase in *Legionella* positivity remained unclear. The feed concentration of ClO<sub>2</sub> was increased to 0.58 mg/L in B1 in April 2005. Samples collected in April and June 2005 showed that *Legionella* positivity returned to 25% (Figure 1).

Although the overall distal site positivity declined during the study, the authors did not observe a significant decrease in the concentration of *Legionella* (mean cfu/mL) in positive samples ( $p > 0.05$ ). No cases of hospital-acquired Legionnaires' disease have been detected in this hospital since the ClO<sub>2</sub> system was installed in January 2003.

The feed pump of the ClO<sub>2</sub> generator was changed on June 8, 2004, to allow for additional feed capacity. As shown in Figure 3, the mean monthly ClO<sub>2</sub> residual in the cold water increased significantly ( $p < 0.001$ ) from 0.41 mg/L to 0.54 mg/L after the pump replacement. The changes and variability in mean monthly ClO<sub>2</sub> residual are attributed to operational adjustments and maintenance.

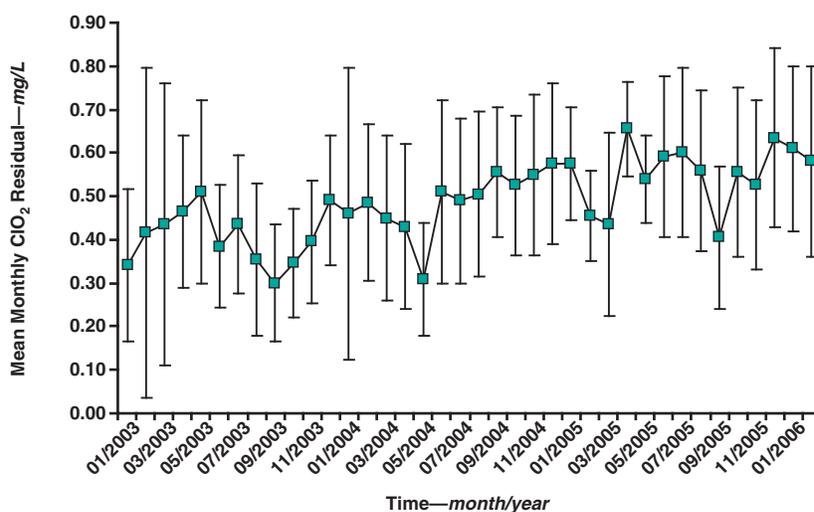
After the ClO<sub>2</sub> system was installed, a significant decrease in *Legionella* percent positivity was observed in the hot water system ( $p < 0.05$ ). However, an extended period (18 months) was needed to achieve this reduction in positivity, which is most likely due to the low concentration of ClO<sub>2</sub> in the hot water. This is significant because *Legionella* species proliferate in hot water (Lin et al, 1998b). It is clear that maintaining sufficient ClO<sub>2</sub> residual in the hot water system is challenging. Elevated water temperature hastens the conversion of ClO<sub>2</sub> to ClO<sub>2</sub><sup>-</sup> through the reactions with organic compounds in the water distribution system

(Zhang et al, 2006). This is consistent with the observation that ClO<sub>2</sub> was consumed and converted to ClO<sub>2</sub><sup>-</sup> to a greater extent in hot water, because the mean ClO<sub>2</sub><sup>-</sup> concentration in hot water was higher than it was in cold water (Figure 4, part A). However, this study and other studies have demonstrated that zero positivity is not necessary to prevent hospital acquired Legionnaires' disease (Stout & Yu, 2003).

It may be possible to reduce this lag period by performing shock ClO<sub>2</sub> treatment (Bova et al, 2004). Makin reported (1998) that the successful application of ClO<sub>2</sub> in hot water systems for controlling *Legionella* required increasing the ClO<sub>2</sub> level to 3–5 mg/L in hot water systems. Alternatively, daily flushing of sinks and showers in patient rooms may also be effective (Bova et al, 2004). However, both of these measures need to be evaluated in a controlled study. Another possible approach to achieving a higher ClO<sub>2</sub> residual in hot water includes adding a ClO<sub>2</sub> injection point to the line after the hot water tanks. This may shorten the time needed to achieve a measurable ClO<sub>2</sub> residual at distal outlets. The effect of injecting ClO<sub>2</sub> directly into the hot water for controlling *Legionella* has yet to be evaluated.

**ClO<sub>2</sub> and its disinfection by-products.** ClO<sub>2</sub>, ClO<sub>2</sub><sup>-</sup>, and ClO<sub>3</sub><sup>-</sup> levels were monitored throughout the buildings during the study. The mean ClO<sub>2</sub> residual in the hot water was 0.07 mg/L; the residual rarely exceeded 0.1 mg/L. The mean ClO<sub>2</sub> residual in the cold water was 0.42 mg/L. The difference in the mean ClO<sub>2</sub> concentrations between the cold water distal outlets and hot water distal outlets was significant ( $p < 0.05$ ).

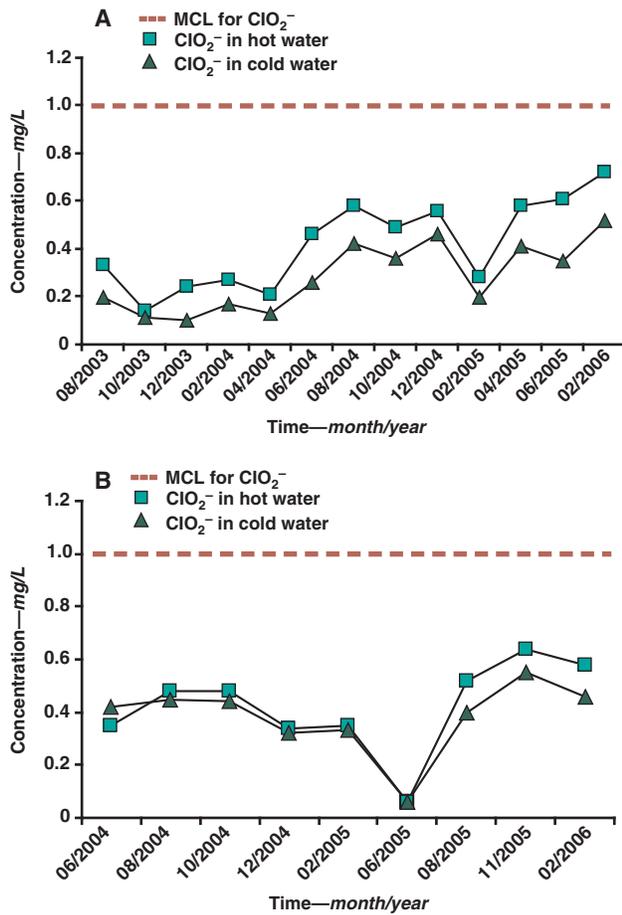
**FIGURE 3** Mean monthly ClO<sub>2</sub> residual in cold water samples of hospital A



ClO<sub>2</sub>—chlorine dioxide

Error bars represent standard deviation. The changes and variability in mean monthly residual are attributed to operational adjustments and maintenance.

**FIGURE 4** Mean  $\text{ClO}_2^-$  level in hot and cold water of hospital A (A) and hospital B (B)



$\text{ClO}_2^-$ —chlorite, MCL—maximum contaminant level

$\text{ClO}_2^-$  level in hot and cold water systems of hospitals A and B did not exceed the MCL.

A total of 91 hot water samples and 65 cold water samples were analyzed for  $\text{ClO}_2^-$  and  $\text{ClO}_3^-$ . The average  $\text{ClO}_2^-$  concentrations in the hot and cold water were 0.42 and 0.28 mg/L, respectively. The  $\text{ClO}_2^-$  concentrations measured in this study were in agreement with those obtained by the reference laboratory<sup>10</sup> (data not shown), because the mean difference was 8% ( $p > 0.05$ ). The mean  $\text{ClO}_2^-$  concentrations in cold and hot water were below the MCL of 1.0 mg/L (Figure 4). The mean  $\text{ClO}_3^-$  concentrations in hot and cold water were below the detection limit of 0.10 mg/L.

In Figure 5, parts A and B show the mean  $\text{ClO}_2$  and  $\text{ClO}_2^-$  concentrations among the different sampling locations in hospital A over two years. Chlorine dioxide concentration ranged from 0 to 0.70 mg/L, whereas chlorite concentration ranged from 0 to 0.82 mg/L. No significant differences ( $p > 0.05$ ) occurred in mean  $\text{ClO}_2$  and  $\text{ClO}_2^-$  concentrations among the sampling locations

that represent various distances from the injection point in the hot water (Figure 5, part A) and in the cold water (Figure 5, part B).

**Hospital B. Water quality parameters.** Water quality of the municipal water supply was monitored in June 2004. The values of water quality parameters were as follows: hardness was 124 mg/L as calcium carbonate, alkalinity was 69 mg/L as calcium carbonate, pH was 8.57, total iron was 0.04 mg/L, total manganese was 0.01 mg/L, TOC was 2.25 mg/L, and turbidity was 0.38 ntu. The  $\text{ClO}_2$  demand of the drinking water was determined to be 0.20 mg/L after 6 h contact time at 23°C and pH 7.8 using method 2350 C (*Standard Methods*, 1998).

**Legionella positivity.** Mean percent positivity of all distal outlets (both hot and cold) for *Legionella* was 60% before the  $\text{ClO}_2$  treatment (range from 35 to 88%,  $n = 72$ ). After the  $\text{ClO}_2$  treatment, mean percent positivity of all distal outlets for *Legionella* decreased from 60 to 8% (range from 0 to 24%,  $n = 165$ ,  $p < 0.05$ ) as shown in Figure 6. *Legionella* positivity in the hot and cold water was reduced to 0% after six months of  $\text{ClO}_2$  treatment and remained at 0% for three consecutive sampling events after August 2005 (Figure 6). *Legionella* positivity unexpectedly increased to 19% in June 2006. One possible explanation for the observed increase is that the  $\text{ClO}_2$  generator malfunctioned between the two sampling events. The  $\text{ClO}_2$  residual in hot and cold water was 0.09 and 0.29 mg/L, respectively, which was lower than the average values. No cases of healthcare-acquired legionellosis have been identified in the postdisinfection period.

The mean concentration of *Legionella* in positive hot water samples decreased from 166 cfu/mL (range from 10 to 520 cfu/mL) to 43 cfu/mL (range from 10 to 100 cfu/mL). The mean concentration of *Legionella* in positive cold water samples decreased from 20 (range from 10 to 20 cfu/mL) to 0 cfu/mL. The decrease in mean concentration of *Legionella* in positive samples was not significant, but the overall distal site positivity decreased significantly. The mean distal site water temperatures for the hot and cold water during the study were 43°C (range from 34 to 52°C) and 17°C (range from 4 to 25°C), respectively.

*Legionella* positivity in the hospital B water system was reduced to 0% in a much shorter period of time (six to 10 months) compared with hospital A. The mean  $\text{ClO}_2$  residual in the hot water system of hospital B reached above 0.10 mg/L in a much shorter time, and the mean  $\text{ClO}_2$  residual in hot water of hospital B was significantly higher than in hospital A (Table 1). The percentage of samples positive for *Legionella* in hot water has been shown to decrease as  $\text{ClO}_2$  residual increased to  $> 0.10$  mg/L (Zhang et al, 2007). It is hypothesized that reducing the time it takes to achieve  $\text{ClO}_2$  residual in hot water  $> 0.10$  mg/L leads to faster reduction of *Legionella* positivity.

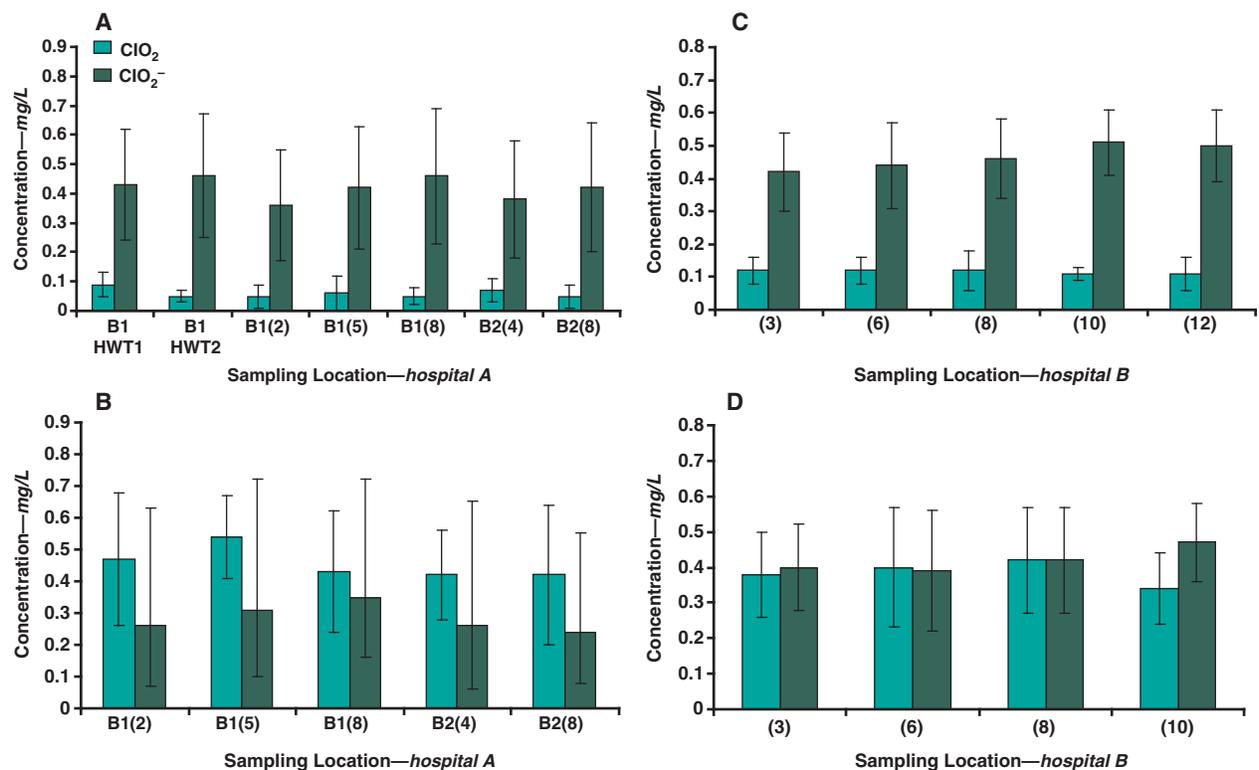
It was also found that the incoming drinking water in hospital B contained high levels of free chlorine (range

from 0.75 to 1.02 mg/L) because the hospital was close to the water treatment plant. The mean chlorine in the incoming water of hospital B was higher than in hospital A (Table 1). It can be hypothesized that the coincident reaction of two disinfectants (chlorine and chlorine dioxide) provided synergistic effects in controlling *Legionella* in the water distribution system. It is also possible that the high levels of free chlorine in the drinking water could meet some oxidant demand so that  $\text{ClO}_2$  injected in this healthcare facility can be maintained at a stable residual concentration in both hot and cold water systems. Katz and colleagues (1994) showed that the combination of two disinfectants (chlorine dioxide and chlorine) applied to the effluent from a municipal sewage treatment plant produced a relatively stable high residual of both disinfectants and reduced the concentration of the undesirable disinfection by-product (i.e., chlorite ion) despite increasing chlorine dioxide concentration. Several studies showed that mechanically mixed oxidants achieved considerable disinfection efficiency for selected microorganisms (Son et al, 2005). However, the level of the enhanced disinfection efficiency remains unclear, and the synergistic effect

of the mixed oxidants also needs to be confirmed. One study (Cho et al, 2006) showed that sequential disinfection with chlorine dioxide followed by free chlorine is an effective approach to treating *Bacillus subtilis* spores whereas another study (Corona-Vasquez et al, 2002) found no such synergy for treating *Cryptosporidium parvum* oocysts. The synergistic effect of sequential treatment may be caused by the unique activity of each disinfection agent reacting with specific chemical groups of the cell walls and needs to be investigated further in the case of chlorine dioxide, free chlorine, and *Legionella*.

**HPC bacteria.** The efficacy of  $\text{ClO}_2$  for controlling HPC bacteria in the hot water system was also evaluated in hospital B. Although most of the HPC bacteria in drinking water are not human pathogens, HPC bacteria in drinking water may include bacterial species, such as *Pseudomonas* species and different fungi, that are pathogenic for immunocompromised patients in hospitals (Glasmacher et al, 2003). The efficacy of  $\text{ClO}_2$  for controlling HPC bacteria in hospital B was also evaluated to assess the potential for reducing the risk of infection from waterborne opportunistic patho-

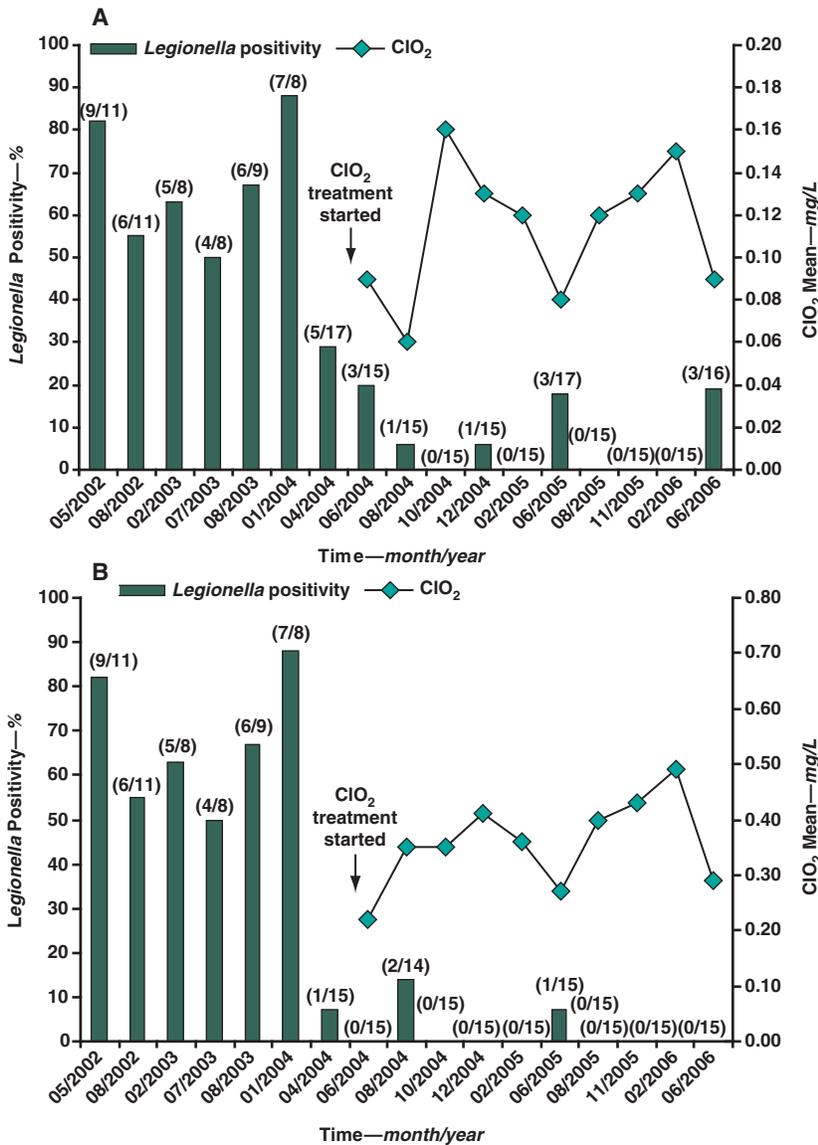
**FIGURE 5**  $\text{ClO}_2$  residual and  $\text{ClO}_2^-$  level in hot water (A and C) and cold water (B and D) at different locations in hospitals A and B



ANOVA—analysis of variance, B—building,  $\text{ClO}_2$ —chlorine dioxide,  $\text{ClO}_2^-$ —chlorite, HWT—hot water tank

Error bars represent standard deviation. Numbers in parentheses indicate hospital floor. Hospital A has two buildings. Distance from the  $\text{ClO}_2$  injection point did not significantly affect mean concentrations of  $\text{ClO}_2$  and  $\text{ClO}_2^-$  in hot and cold water of hospitals A and B (ANOVA,  $p > 0.05$ ).

**FIGURE 6** Percent distal site *Legionella* positivity and mean ClO<sub>2</sub> concentrations in hot water (A) and cold water (B) of hospital B



Within the figure, numbers in parentheses represent positive *Legionella* samples/total samples for month indicated. Legionella positivity from May 2002 to January 2004 represents average positivity for both hot and cold water sites. Significant reduction in *Legionella* positivity (ANOVA,  $p < 0.05$ ) was accomplished after six months of ClO<sub>2</sub> treatment.

gens. The average concentration of HPC bacteria was significantly reduced ( $p < 0.05$ ) from 15,400 cfu/mL before chlorine dioxide treatment to 2,900 cfu/mL after treatment (Figure 7). This suggests that ClO<sub>2</sub> may be an effective disinfectant not only for controlling *Legionella* but also against opportunistic bacteria. Further study would be needed to evaluate the effects of chlorine dioxide on specific opportunistic bacteria in hospital water systems.

*ClO<sub>2</sub> and its disinfection by-products.* The mean ClO<sub>2</sub> residuals in the hot and cold water samples from hospital B were 0.11 and 0.36 mg/L, respectively (Table 1). The difference in mean ClO<sub>2</sub> concentrations between the cold water distal outlets and hot water distal outlets was significant ( $p < 0.05$ ). A total of 54 hot water samples and 36 cold water samples were analyzed for ClO<sub>2</sub><sup>-</sup> and ClO<sub>3</sub><sup>-</sup>. The mean ClO<sub>2</sub><sup>-</sup> concentrations in cold and hot water were 0.42 and 0.38 mg/L, respectively (Figure 4, part B). The ClO<sub>2</sub><sup>-</sup> concentrations measured in this study were in agreement with those obtained by the reference laboratory<sup>10</sup> (data not shown) because the mean difference was only 8% ( $p > 0.05$ ). The mean ClO<sub>3</sub><sup>-</sup> concentrations in hot and cold water were below 0.10 mg/L.

In Figure 5, parts C and D show mean ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> concentrations on different floors in the hot and cold water system of hospital B during the two-year study. Chlorine dioxide concentration ranged from 0.04 to 0.74 mg/L, whereas chlorite concentration ranged from 0.19 to 0.66 mg/L. ANOVA analysis showed that there was no significant difference in ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> levels between different sampling locations representing various distances from the injection point in the hot water and cold water ( $p > 0.05$ ).

Srinivasan and co-workers (2003) compared the ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> levels at different sampling locations between two time points in a hospital water system. The ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> levels at the lower floor were higher than the ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> levels at the higher floor one month after treatment started. The differences disappeared after 17 months. One explanation for this phenomenon was that the background ClO<sub>2</sub> demand in the system had been met after 17 months. In the authors' study, no significant difference was found for the mean ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> concentrations in the hot water among sampling locations that represented various distances from the ClO<sub>2</sub> injection point in hospitals A and B (Figure 5, parts A and C). Also, no significant difference was found in ClO<sub>2</sub> and ClO<sub>2</sub><sup>-</sup> levels with increasing distance from the point of

injection in the cold water in hospitals A and B (Figure 5, parts B and D). The change in  $\text{ClO}_2$  and  $\text{ClO}_2^-$  levels with time could be attributed to mechanical modifications to the  $\text{ClO}_2$  feed system and operational adjustments. For hospital A, the study began six months after the installation and operation of the  $\text{ClO}_2$  unit. The initial demand may have been met, and the system may have reached equilibrium within the first six months of continuous treatment with  $\text{ClO}_2$ . For hospital B, the high level of free chlorine in the incoming cold water may have met some of the oxidant demand and helped to maintain the  $\text{ClO}_2$  residual at relative stable levels.

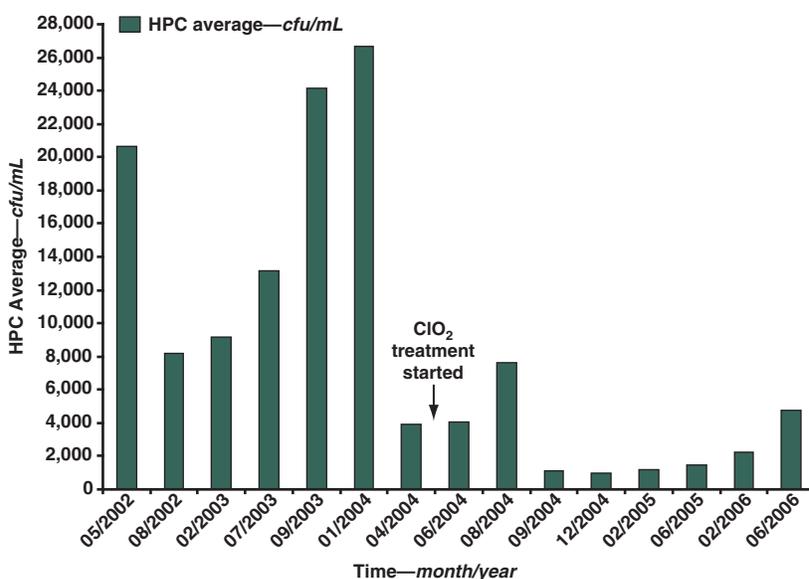
The operation of the  $\text{ClO}_2$  system for controlling *Legionella* in two hospital water systems was found to be safe, based on the MRDL for  $\text{ClO}_2$  and MCL for  $\text{ClO}_2^-$ .  $\text{ClO}_3^-$  is currently not regulated, but its levels in hot and cold water never exceeded 0.30 mg/L. Users of chlorine dioxide systems must comply with current regulations for municipal water systems. These monitoring requirements address concerns that chlorine dioxide and its disinfection by-products (chlorite and chlorate ions) may pose health risks to consumers. Chlorite may cause congenital cardiac defects and hemolytic anemia through oxidative damage to the red blood cell membrane (Condie, 1986). US Environmental Protection Agency (USEPA) has set the MRDL for  $\text{ClO}_2$  at 0.8 mg/L and the MCL for  $\text{ClO}_2^-$  at 1.0 mg/L (USEPA, 1998). Chlorate is currently not regulated because of the lack of health data.  $\text{ClO}_2$  and the persistence of its disinfection by-products in water treatment plants and large distribution systems has been studied (Hoehn et al, 2003; Baribeau et al, 2002); however, few data exist for small secondary water systems.

Monitoring of a hospital water system involves daily monitoring of  $\text{ClO}_2$  at no fewer than three sites, and monthly monitoring of  $\text{ClO}_2^-$  at no fewer than three sites.  $\text{ClO}_2^-$  monitoring can be reduced to quarterly monitoring after monthly monitoring results show that the  $\text{ClO}_2^-$  level in the distribution system has not exceeded the MCL of 1.0 mg/L for one year (USEPA, 1998). The authors' data suggest that the chlorite level in

hot and cold water of an open water distribution system is unlikely to exceed the MCL when 0.5–0.7 mg/L of  $\text{ClO}_2$  is injected in the incoming cold water. Less frequent monitoring of the disinfection by-products would satisfy the safety concerns in hospital water systems.

**Cost of *Legionella* control.** *Legionella* remediation efforts are not inexpensive. Cost estimates in the range of \$70,000–\$80,000 for continuous hyperchlorination, and \$60,000–\$100,000 for copper–silver ionization systems have been reported (Lin et al, 1998a). One hospital estimated the cost for engineering measures with chlorine dioxide at approximately \$50,000 per year (Hosein et al, 2005). For 438-bed hospital A, the annual cost for operation and maintenance of two chlorine dioxide units was

**FIGURE 7** HPC bacteria concentration in hot water of hospital B before and after  $\text{ClO}_2$  treatment



$\text{ClO}_2$ —chlorine dioxide, HPC—heterotrophic plate count

HPC bacteria concentration in hot water samples decreased significantly after  $\text{ClO}_2$  treatment (t-test,  $p < 0.05$ ).

**TABLE 1** Comparison of study parameters of two hospitals using  $\text{ClO}_2$  for *Legionella* control

Parameter	Hospital A	Hospital B
Hospital size	438 beds Two buildings	672 beds One building
$\text{ClO}_2$ injection point	Cold water main	Cold water main
Mean $\text{ClO}_2$ in hot water—mg/L	0.07	0.11 ( $p < 0.05$ )
Mean $\text{ClO}_2$ in cold water—mg/L	0.42	0.36 ( $p > 0.05$ )
Mean $\text{Cl}_2$ in cold water—mg/L	0.55	0.91 ( $p < 0.05$ )
Months to achieve 0% <i>Legionella</i> positivity	> 24 months	6–10 months

$\text{Cl}_2$ —chlorine,  $\text{ClO}_2$ —chlorine dioxide,  $p$ —probability ranging from 0 to 1 (unitless)

Mean  $\text{ClO}_2$  and  $\text{Cl}_2$  in hospitals A and B were compared by the student's t-test

approximately \$34,000 per year; installation costs are not included because the hospital leased the units. Hospital personnel installed the required flowmeters, filters, injection points, and piping. The annual cost for monitoring the chlorine dioxide residual and chlorite level in the hospital water system ranged from \$3,000 to \$5,000, which brings the total annual cost for the chlorine dioxide system in hospital A close to \$40,000. For hospital B, the capital cost for the chlorine dioxide unit was close to \$50,000.

## CONCLUSIONS

This study conducted in two hospitals showed that *Legionella* can be successfully controlled by chlorine dioxide. However, the exact amount of time needed to achieve requisite reduction in percent positivity is site-specific. Chlorine dioxide and its disinfection by-products were successfully maintained below the regulatory limits. Specifically, when  $\text{ClO}_2$  was injected into the cold water main at 0.5–0.7 mg/L, mean concentrations of  $\text{ClO}_2$  and  $\text{ClO}_2^-$  in cold and hot water samples did not exceed the MRDL of 0.8 mg/L for  $\text{ClO}_2$  and MCL of 1.0 mg/L for  $\text{ClO}_2^-$ , respectively. Distance from the  $\text{ClO}_2$  injection point did not significantly affect mean concentrations of  $\text{ClO}_2$  and  $\text{ClO}_2^-$  in both hot and cold water systems. In addition to controlling *Legionella*,  $\text{ClO}_2$  is also a promising disinfectant for controlling other opportunistic waterborne pathogens in hospital drinking water systems.

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## FOOTNOTES

- <sup>1</sup>Chlorine dioxide generator, Halox Inc., Bridgeport, Conn.
- <sup>2</sup>Environmental Hygiene Services, Nalco Co., Naperville, Ill.
- <sup>3</sup>Chlorine dioxide generator, Diox, Klenzoid Inc., Conshohocken, Pa.
- <sup>4</sup>Klenzoid Inc., Conshohocken, Pa.
- <sup>5</sup>Special Pathogens Laboratory, Pittsburgh, Pa.
- <sup>6</sup>Hach DPD Free Chlorine Reagent, Hach Co., Loveland, Colo.
- <sup>7</sup>Hach DR/2010 Spectrophotometer, Hach Co., Loveland, Colo.
- <sup>8</sup>Hach Pocket Colorimeter, Hach Co., Loveland, Colo.
- <sup>9</sup>DX-500, Dionex Inc., Sunnyvale, Calif.
- <sup>10</sup>Novachem Laboratories Inc., Oxford, Ohio
- <sup>11</sup>Stata 9.0, StataCorp, College Station, Texas

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