

**Independent Review of evidence regarding selection of techniques for the suppression of Legionella in water supplies of hospitals and other healthcare premises**

**20<sup>th</sup> March 2009**

To: Professor Brian Duerden, Chief Inspector of Microbiology DH; Mr Rob Smith, Director of Gateway Reviews and Estates & Facilities DH; Mr Andrew Selous MP for South West Bedfordshire

Panel:

Dr A.P.R. Wilson, Chairman, Consultant Microbiologist, University College London Hospitals, London

Dr V. Gant, and Dr J Holton Consultant Microbiologists, University College London Hospitals, London

Dr A Fraise, Consultant Microbiologist, University Hospital Birmingham NHS Foundation Trust Microbiology Dept Queen Elizabeth Hospital, Queen Elizabeth Medical Centre, Birmingham

Mr H Gosling, Pool and Water Treatment Advisory group

Advisor

Mr G Hogben, Technical Manager, Feedwater Ltd., Moreton, Wirral

## Executive summary and recommendations

1. This independent review compares the relative quality and consistency of evidence for several techniques currently in use, or being considered for, the suppression of *Legionella* spp. in the water systems of healthcare premises in the UK.
2. The review has not formally taken into consideration the relative costs (either capital, or maintenance) of available systems. These will be commented on, but will not be used for purposes of recommendation.
3. Raising the temperature of the hot water system effectively reduces the viable concentration of *Legionella* spp., but organisms persist in cooler water in taps, showers and dead legs. (1b)
4. Temperatures above 60°C effectively produce and maintain negative cultures but carry a risk of scalding and organisms may still survive in biofilm. (2)
5. Pulsed superheating above 60°C with flushing effectively reverses outbreak-related problems but neither eradicates organisms, nor is long lasting. (1b)
6. The presence of copper (0.2-0.8 mg/L) and silver (0.02-0.08 mg/L) ions, without elevating hot water temperature, effectively and safely eradicates *Legionella* spp. provided ion concentrations are kept within the appropriate range, pH is below 7.6, and scale is removed (1b).
7. Chlorination effectively reduces, but does not eliminate, *Legionella* spp. (1b).
8. Installation costs are higher for ionisation but maintenance lower than thermal methods, which require a constant supply of energy. (2)
9. Comparative studies are retrospective but favour ionisation or chlorine dioxide over heat. Chlorine dioxide is more effective against biofilm.

10. A combination of ionisation and hot water above 50°C was a reliable method of control (2).
  
11. We conclude that thermal control, chlorine dioxide or copper-silver ionisation is effective in *Legionella* control in water systems. However, none are sufficiently robust to be effective in the absence of measures designed to control scale and biofilm.
  
12. We conclude that on the grounds of efficacy, reliability and energy costs, copper/silver ionisation or chlorine dioxide technologies should be recommended provided adequate monitoring is in place.
  
13. This conclusion is contingent upon a formal comparative cost/benefit analysis, which is beyond the brief of this review.

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## 1. Introduction

*Legionella* spp. are found commonly in fresh water and soil. The number of bacteria at the point of use is determining factor in the development of Legionnaire's disease. Hospital-acquired outbreaks of Legionnaire's disease have been reported repeatedly (>300 outbreaks by 2002) and are associated with potable water supplies rather than cooling towers.<sup>1</sup> A single diagnosed case may be accompanied by a number of others not diagnosed because the signs and symptoms are non-specific and most hospitals do not routinely test patients with hospital-acquired pneumonia. Detection of *Legionella* spp. in the water supply on routine testing increases the suspicion of legionnaire's disease and makes diagnosis more likely. Colonisation of water supplies in large buildings is common but showering is not a common means of transmission in hospitals. Most cases are due to aspiration of oropharyngeal secretions and hence patients with chronic lung disease or recent surgery are most at risk. High fever, diarrhoea, confusion, liver dysfunction, hyponatremia and haematuria are common features. Culture of respiratory secretions for Legionella requires specific media which have to be arranged for the purpose. Most diagnosis is by detection of antigen in the urine, although this is not effective for all serogroups of *Legionella pneumophila* or other *Legionella* spp.

To control growth of Legionella in water distribution systems, several methods have been recommended. The most common is keeping hot water tank temperatures at 50-60°C outside the normal growth range of the organism.<sup>1</sup> In an outbreak, heating and flushing with hyperchlorination can be used but only reduces levels for a few weeks. Close control of temperature in the entire system is difficult so hyperchlorination or a thermal shock followed by continuous chlorination may be more effective but prolonged hyperchlorination is expensive, corrosive and potentially toxic. Copper-silver ionisation systems are a widely used alternative and do not require elevation of the hot water temperature.

Following a series of Parliamentary Questions and a Parliamentary Debate, the Department of Health requested an independent review of the scientific evidence regarding methods of control of *Legionella* spp. in hospital water systems (hot, cold and drinking). In particular the review was to examine the recommendations in the Health Technical Memorandum 04-01, namely that the preferred system is the use of temperature controls on water supply systems rather than the use of chlorine dioxide or copper/silver ions. The Terms of Reference (20/11/08) are attached (Appendix 1). The Review is independent of the Department of Health, Department of Work and Pensions, Health and Safety Executive, the Health Protection Agency and employees and those connected with ProEconomy Ltd of Orca House, Leighton Buzzard.

The specific issue raised relates to HTM 04-01 Part B 7.84 and the use of the term 'preferred' rather than 'traditional' in respect of the temperature control regimen to maintain systems free of *Legionella* spp. and other waterborne

organisms. As a result, some hospitals using other methods and water temperatures between 20 and 50°C have considered returning to temperature control. They also have started monitoring *Legionella* spp. in the water systems monthly until confidence in efficacy has been established. Temperature controlled hot water systems require mixing valves to be fitted to avoid scalding which can themselves be a reservoir for *Legionella* spp. The energy cost of maintaining the higher water temperature is appreciable. However the Health and Safety code of practice (Legionnaire's disease: the control of Legionella bacteria in water systems) does not require a temperature control system to be used as long as proliferation of bacteria is prevented. It refers to temperature control as the traditional method of control and describes the alternatives.

The CDC/Hospital Infection Control Practices Advisory Committee (HICPAC) system for categorizing recommendations were used to grade recommendations according to scientific evidence and economic considerations. Consideration is given to the practicality and maintainability of systems in a hospital and healthcare premises environment with a reasonable number of trained engineers and infection control specialists. :

*Category 1a. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical or epidemiological studies.*

*Category 1b. Strongly recommended for implementation and strongly supported by certain experimental, clinical or epidemiological studies and a strong theoretical rationale.*

*Category 1c. Required for implementation, as mandated by federal or state regulation or standard. The UK equivalent is to operate within European Union or UK Health & Safety Legislation.*

*Category 2. Suggested for implementation and supported by suggestive clinical or epidemiological studies or a theoretical rationale.*

*No recommendation. Unresolved issue. Practices for which insufficient evidence exists or for which there is no consensus regarding efficacy*

## **2. Background**

*Legionella* sp are widespread in freshwater and in building systems such as cooling towers and plumbing. The organism proliferates at temperatures of 20-45°C. When disseminated as an aerosol inhaled organisms can infect alveolar macrophages and epithelium causing severe pneumonia (Legionnaire's disease) or a 'flu-like illness (Pontiac fever). The reported prevalence is 0-4-0.6 per 100,000 population<sup>3</sup> but this probably represents less than 1 in 20 of the actual number of cases. Outbreaks are commonly related to drinking water systems but most cases are sporadic. Infection rates in healthcare premises are higher than

in the community. Nosocomial cases have been associated with aerosols from contaminated shower heads and hot water taps. Up to 60% of samples have been reported to be positive at these sites with as many as 1000 colony forming units/mL.<sup>2</sup> Lower water temperature and stagnation in these distal areas can allow proliferation of large numbers of organisms. Hydrotherapy pools, whirlpool baths and spa pools are sources of Legionellae and have to be carefully maintained and disinfected. Trolley washing must be supplied direct from potable water with an air gap to prevent backflow.

The type of Legionella, the means of transmission and the susceptibility of the host are important factors in the development of disease. *Legionella pneumophila* accounts for 90% of cases and serogroup 1 is the most virulent. In the immune suppressed patient up to 20% of cases are due to other species which are not detected by the urinary antigen test. Hospital water systems are colonized with various species. Inhalation of a contaminated aerosol transmits the infection when the bacteria are in an aerosol of droplets of 1-5 µm, which can be generated by nebulisers and showers.<sup>3</sup> Water hitting a hand wash basin, shower or bath generates aerosols and the concentration of bacteria in the water and the amount of water dispersed are critical to the risk of causing disease. Sources such as cooling towers provide much longer exposure times than baths or showers. Smaller particles (<5µm) remain airborne for long periods and penetrate the lungs but larger ones contain more bacteria. Smoking, male sex, alcoholism, chronic obstructive pulmonary disease, cancer, diabetes, immune suppression, surgery and organ transplantation all increase the risk of the disease.<sup>3</sup> The risk of a single high level exposure may be similar to that of multiple low level exposures. In nosocomial outbreaks, the potable water supply is usually implicated. Disinfectants used for drinking water must be safe in terms of concentration and nature.

Of 4402 cases of Legionnaire's disease between 1980 and 2002, 264 were hospital-acquired<sup>3</sup> but the diagnosis is often missed in complicated cases or when seroconversion is delayed. Guidelines on the control of *Legionella* spp. in water systems form the basis for preventative maintenance to limit the level of colonization and prevent outbreaks. Methods of control include heat, ultraviolet light, sonication, compressed air, use of chemicals to prevent scale, biocides and charcoal filters, elimination of dead legs, and regular flushing of outlets. Colonization can be prevented by maintaining the temperature of the water below 20°C or above 55° C.<sup>3</sup> Several studies have failed to show a correlation between the numbers of Legionellae present in the water and cases of legionellosis. Nevertheless it is necessary to suppress the organism when it is found. In some cases a different source such as a cooling tower has been implicated in the absence of positive sites in the hot water system.

Survival of *Legionella* spp. in water depends on temperature, nutrients and the presence of protozoa. The most favourable temperatures for growth are between 20 and 45°C and this range is likely where the water flow is slow, or in a dead leg

or mixing valve. Bacteria adhere to metal or plastic by producing slime and together with fungi, algae, protozoa and debris form a biofilm.<sup>4</sup> A suitable temperature and presence of nutrients such as sediment, sludge, scale or rust, are needed for biofilm to develop. Legionella is predominately (98%) localised in biofilm on the surface of the pipe.<sup>5</sup> Biofilms facilitate interaction between different microorganisms and *Legionella* spp. are frequently located within amoebae as facultative intracellular parasites, providing protection from many disinfection processes.<sup>6</sup> *Legionella* spp. can survive exposure to silver at 0.1 mg/L and copper at 1 mg/L for one week within *Acanthamoeba polyphaga* cells compared with only 30 minutes in the planktonic phase.<sup>7</sup> Colonization of biofilm in hot water systems also renders *Legionella* spp. resistant to halogenation and ionisation. Resistance to iodine is 100 fold greater in sessile than free floating organisms and disinfection also takes four times longer.<sup>8</sup> Legislation, however, is directed towards eradication of free organisms. Thermal treatment will disinfect biofilm but can also increase its formation.

The prevention of *Legionella* outbreaks requires identification of the sources of risk, preparation of adequate risk assessments and action plans that are executed. Treatment regimes must be properly monitored and maintained and staff who apply control measures must be trained in the risks the organisms pose. Engineering issues such as dead legs in the systems have to be addressed. The risk of infections is reduced by the correct application of the chosen water treatment method by all levels of the healthcare organization. The goal is only to reduce numbers of bacteria as elimination is very difficult except in small scale carefully controlled systems.

### 3. Health Technical Memorandum 04-01 2006

HTM 04-01 superseded HTM 2027 and HTM 2040 in 2006 and is designed to give guidance to managers in healthcare, estate and operations on the legal requirements and the maintenance, storage and distribution of water supplies. Both hot and cold water supplies to healthcare premises are considered potable and any addition must not breach the Water Supply Regulations (2000). Continuous chlorination after initial disinfection is not recommended because of the poor penetration of chlorine into biofilm but chlorine dioxide or copper/silver ionization can be used. Copper concentrations above 1 mg/L can stain laundry and cause corrosion of iron and steel even though up to 2 mg/L is allowed in drinking water.

Cold water supply below 20°C and hot water supply above 50°C is recommended to prevent multiplication of *Legionella* spp. and monthly monitoring is required. A temperature of 55°C is needed for fail-safe mixing devices and the temperature in the most distant outlets should be at this level. Sentinel outlets (closest and furthest from the storage tank) have to be tested monthly and shown to be below 20°C or above 50°C following 2 and 1 minutes draw-offs respectively. Similar tests have to be performed annually at representative outlets (rolling 20% of all

outlets). These temperatures are expected in practice to be achieved well before the end of the draw-off period. Dead legs have to be kept as short as possible. Hand washing is best performed under a running tap into a sink without plug and is essential to prevent spread of nosocomial infection. A thermostatic mixer valve is used at the point of use to prevent scalding. Taps and showers should be flushed at least twice a week.

The guidance does recognise that given the complexity of water systems, it may not be possible to maintain the correct hot and cold water temperatures and additional biocide may be necessary. Copper/silver or chlorine dioxide can be used as well as but not instead of temperature control. In these circumstances, monthly testing for Legionellae is recommended until there is confidence in the efficacy of the biocide when testing can be less frequent. Poor maintenance and control are the major cause of outbreaks related to water systems.

Chlorine dioxide is an oxidising biocide that binds amino acids and can destroy biofilm but requires careful monitoring and dose control in cold water. Concentration must not exceed 0.5 mg/L in water used for drinking preventing the use of feedback control at distant outlets. In hot water systems it may be lost as gas in open vented systems and the rate of loss increases with rise in water temperature. If there are copper pipes, high levels of copper may be detected. The effect on Legionellae in shower heads is temporary and scale should be removed at least quarterly.

Copper and silver ionisation is effective at 400 µg/L and 40 µg/L respectively in hot water systems against floating legionellae if properly managed. *Legionella* spp. within biofilm are also inhibited. Copper and silver ions are released from pairs of electrodes in running water and attach to bacterial cell wall, causing damage that allows silver ions to enter the cell. The silver ions inhibit nucleic acid, enzymes and protein causing cell death. Anti-scaling electrode cells and weekly pH monitoring are needed to maintain effectiveness as the level of ion release must be kept constant. Maintaining silver concentration can be difficult above pH 7.6 or if scale builds up in hard water. The chemical composition of the water to be treated has to be considered before selecting the method of treatment. Silver concentration at sentinel outlets must be monitored monthly and representative outlets annually to ensure it is over 20 µg/L. Silver should be kept at 0.01 to 0.08 ppm and copper at 0.2 to 0.8 ppm, Silver is monitored by a dipslide following neutralization of chlorine. Copper requires a colorimetric test. Legionellae are controlled but continuous dosing of drinking water with silver is not recommended.

Cleaning of pipeworks before commissioning requires dosing of the entire system, for example with high dose of sodium hypochlorite, and following by flushing and microbiological testing.

#### 4. Thermal disinfection

Raising the temperature of hot water was the first method used to suppress *Legionella* spp. in hospital water hot water systems.<sup>9</sup> *Legionella* spp. are inhibited at water temperatures over 60°C and inactivated above 70°C.<sup>8</sup> To reduce a *Legionella* population ten-fold takes 2500 minutes at 45°C, 380 minutes at 50°C, 5 minutes at 60°C and 1 minute at 70°C.<sup>10</sup> Legionellae grow between 20 and 43°C and inactivation starts above 50°C, accelerating with rising temperature.<sup>11</sup> However it is difficult to raise the water temperature at the same time in all parts of the system so eradication frequently fails. Furthermore heat exchange with the cold water system may occur increasing the risk of cold water transmission. The superheat method is useful to reduce Legionellae following an outbreak but requires temperature above 60°C even at distal outlets and recolonization is common.<sup>12</sup> There is a risk of scalding so access has to be limited. The whole system must reach 60°C and draw-off from taps must be for at least 5 minutes, starting with the outlet furthest away and then towards the calorifier. The method is labour intensive and costs have been estimated between \$20,000 and \$31,000.

Hot water systems maintained above 50°C all the time are less at risk of colonization with *Legionella* spp.<sup>12</sup> If temperature is kept above 60°C, cultures can be kept negative. However, average hot water temperatures of 45-50°C together with a nutrient rich and protective slime may be ideal conditions for colonization.<sup>12</sup> Chlorine levels of 1.5-2.0 mg/L did not affect isolation of legionella in one hospital where hot water temperatures were 43-45°C whereas other buildings with a temperature of 58-60°C were consistently negative. Raising the temperature at these sites to 60°C did not eradicate Legionellae although flushing at 70-75°C was effective.<sup>13</sup> In a survey of domestic water heating systems, there was an inverse association between positive samples and water temperature in range 52-62°C.<sup>14</sup> Maintaining water temperatures above 55°C (>65°C at tank outlet) as the only control measure was associated with 12% of water samples being positive during a 10 year period in which 4 patients developed Legionnaire's disease.<sup>15</sup> *Legionella* spp. was isolated from taps and showers in one system when the mains temperature was at 54°C but not at 60°C.<sup>16</sup> In another hospital Legionellae were repeatedly isolated from sink faucets and shower units until faucets and showers were flushed with water at 55°C plus 0.5 mg/L chlorine every morning for one hour.<sup>17</sup> Thirteen subsequent samples did not show any *Legionella* bacteria. Old vertical tanks were most likely to be colonized, probably due to accumulation of scale.

However, a survey of 16 US hospitals showed no significant difference in the numbers of positive samples between hot water systems where the lowest temperatures in patient rooms were above or below 43°C.<sup>18</sup> Surprisingly, the energy costs of maintaining systems above 60°C can be lower than at a temperature of 43°C because less hot water is used.<sup>12</sup>

In a study in hotels and hospitals in Greece, the temperature in the hot water storage tank was raised to 70–80°C and then circulated throughout the system for 3 days.<sup>9</sup> Temperatures in taps were above 65°C. After the first disinfection one of four hospitals requiring treatment remained positive but a second disinfection was effective in all samples. *Legionella pneumophila* was more resistant to treatment than other species. The failure to eradicate the organism was probably related to biofilm in which most of the organisms are non-culturable and available to repopulate the system following disinfection. Heating may be uneven in some parts of the system and recolonization can develop from populations in taps and shower heads within a few weeks of disinfection. Thermal disinfection is not effective beyond thermostatic mixer valves. A five minute flush may be inadequate and dismantlement and removal of scale may be necessary. To eliminate Legionellae, heat disinfection would have to be applied repeatedly together with extended flushing and chlorine disinfection of faucets.

Another hospital reported persistence of Legionellae after superheat and flush, when water temperatures between flushes were 13-48°C.<sup>19</sup> Another noted failure of disinfection at 80°C (5 min flush) to eradicate Legionellae on the background of normal hot water tank temperature of 55°C.<sup>20</sup> With one exception, all negative samples were at 57.8°C or higher. A third hospital reported persistence of different clones of *Legionella pneumophila* serogroup 6 in a hot water system at a temperature of 55-56°C associated with two proven cases of infection (another three seroconversions were observed).<sup>21</sup> The system was superheated twice during 6 years to > 65°C and flushed for 15 minutes.

After cases of legionnaire's disease in one hospital,<sup>22</sup> Legionellae were isolated from inside the faucet spout at the room sinks, the shower mixing valve and from 9 of 18 aerators in taps throughout the building. A second hospital found the organisms in 73 of 78 tap aerators. Hot water valve seats were more often positive than cold water valve seats. Legionellae were detected in hot water tanks at 31-54°C but not in those at 71-77°C. Low temperatures and sediment at the base of hot water tanks were thought to be the source.

Hot water held at 60-65°C carries a risk of scalding so one university hospital piped hot water into a separate tank where it was mixed with cold water to give outlet water temperature of 40-45°C.<sup>23</sup> During 6 years, 15 cases of hospital-acquired legionnaire's disease were reported, all being immune compromised patients. All samples from hot water taps in patients' rooms showed Legionellae, two thirds with more than  $2 \times 10^5$  cfu/L. Heating tanks were also positive but cold water was negative. Chlorination of the mixer tank (45°C) was not effective even at 6 ppm. When water in the heating tanks was raised to 80°C, they were cleared but most samples taken at the taps (45°C) remained positive. Removing the mixer tank, rendering outlet temperature to 50-55°C, and annually heating the system to 95°C for 10 minutes resulted in a reduction of positive samples to 23 of 40 taken but these still contained  $10^4$ - $10^5$  cfu/L. Increasing the flow rate through the tanks resulted in a further reduction but not elimination of the bacteria.

When a heating element was used to maintain a temperature of 50°C in a mixer valve and dead leg of a shower in the absence of chlorine, *Legionella* counts were significantly reduced in stand pipes and the hot feed but it could still be isolated, particularly in shower water.<sup>24</sup> On two occasions hot water temperatures fell to 43-48°C. After five months, Legionellae was still found in large numbers in the stand pipe samples next to the uninsulated mixer valve. Legionellae can proliferate in the cold water system, especially if warmed by proximity to hot pipes. Legionnaire's disease has been reported associated with >100cfu/L in a hospital cold water supply. Hot water (>70°C) was flushed through to clear the system.<sup>25</sup>

## 5. Copper-silver ionisation

Copper-silver ionisation has been reported to be effective in suppressing *Legionella* spp. in water systems. Water is channelled through a device applying low potential electricity to copper and silver electrodes.<sup>26</sup> Most studies have used both copper and silver ions to disinfect water systems in hospitals. These ions form bonds with negatively charged sites on the bacterial cell wall altering permeability.<sup>12</sup> They interfere with enzymes necessary for cellular respiration and bind to DNA at specific sites, causing cell lysis and death. Chlorine enhances this inactivation.<sup>27</sup> Ions can be added electrolytically or in salt.<sup>8</sup> Early laboratory studies showed Legionella was inactivated after 2.5 h exposure to copper at 0.1 mg/L and that the two ions were synergistic. Accumulation of copper and silver in the hot water tanks resulted in long term inhibition.<sup>28</sup> In warm water, silver at 0.003 mg/L was adequate to inhibit Legionella but the organism remained in showers and taps.<sup>29</sup> Copper concentrations below 0.3 mg/L and silver below 0.03 mg/L have been reported not to be effective in hot water systems.<sup>30</sup>

A copper level of 0.2-0.8 mg/L and a silver level of 0.02-0.08 mg/l are recommended but may cause safety concerns if drinking water supply is treated so lower concentrations may be advised. Nevertheless, the WHO suggests 2mg/L for copper and 0.1 mg/L of silver can be used in drinking water.<sup>31</sup> The maximum silver intake should be less than 0.0005 mg/kg/day. In a German hospital, ionisation produce a 3.8 log-reduction in *Legionella* spp. isolated from hot water when silver concentrations were 2.3-20.8 µg/L and copper 0.2 mg/L, i.e. usually below recommended levels.<sup>32</sup> However after three years, the positive sample rate was 78% and a 5-fold increase in silver level reduced counts by only 1 log. Hot water temperature explained 27% of the variance but legionella was probably not eradicated because ion concentrations were inadequate. In an earlier study, the same authors found that for contaminated water systems at 45°C 0.04-0.08 mg/L silver and 0.4-0.8 mg/L copper were needed, although lower levels were sufficient for maintenance.<sup>33</sup> Higher levels were needed for inhibition at 22°C.

Copper-silver ionisation is efficient without raising water temperatures. Installation can cost \$60,000-\$100,000 and maintenance \$1500-\$4000 per annum.<sup>12</sup> Legionellae are killed not suppressed and recolonization takes 6-12 weeks when the system is disabled.<sup>12</sup> Resistance has not arisen. However scale has to be regularly removed from the electrodes and levels of ions must be monitored to avoid staining of water and sinks. Ionisation is affected by pH so monitoring is required. In a US hospital, Legionella control failed despite adequate copper and silver levels.<sup>34</sup> The on site pH was found to be 8.5-8.9. The predominant form of copper ion was copper carbonate rather than copper bicarbonate which was found at pH 7. Bacterial killing was only 10-fold in 72h at pH 8.5-8.9 rather than 10<sup>6</sup>-fold in 1.5h at pH 7. The action of silver ions was unaffected. Water hardness did not affect bactericidal activity.

A review of 32 studies<sup>26</sup> involving copper-silver ionisation found them heterogeneous and of low quality. Some treatments were mixed, control systems were not similar to intervention systems, consecutive applications at different doses were made and controls were historical. Chlorination was not considered although it can alter effectiveness. Outcomes were given in terms of percentage of positive samples, Legionellosis cases, and the level of *Legionella* in samples. The effect of biofilm and different methods of culture were not considered. High temperature could increase effectiveness of copper-silver but high pH (>8) impaired it. Different conditions were used in different studies. In general copper-silver ions were effective in suppressing *Legionella* spp. and were safe provided ion levels were kept within recommended levels.

A survey of 16 hospitals over 10 years indicated the system was effective.<sup>35</sup> Before installing the systems, 7 of 15 hospitals found Legionellae in more than 30% of distal sampling sites despite using superheat and flush (not temperature control), hyperchlorination or ultraviolet light. Following installation there were no positive samples in 8 of 16 hospitals. All but one hospital monitored copper and silver concentrations and that was still the case five years later in 7 hospitals. There was only one case of hospital-acquired Legionnaire's disease after installation. Maintenance was considered average or easy by 88% of hospital engineers. Discoloured hot water (44%) was reported in the initial stages when silver concentrations were 20-40 µg/L.

Most studies relate to ionisation systems installed at hot water recirculation points rather than the point of entry of water into the system. In tropical countries both hot and cold systems must be treated. Following a hospital outbreak of Legionnaire's disease, samples from distal water sites in wards remained positive in 14% of cases and in ICU in 66% of cases despite chlorination, superheating and flushing.<sup>36</sup> When copper silver ionisation was activated, the rate of positivity did not change significantly after 3 months although they were below 30%. Measured concentrations were copper 0.094-0.114 mg/L and silver 0.007-0.02 mg/L. Only when concentrations were increased to 0.143-0.212 mg/L copper and 0.008-0.017 mg/L silver did rates fall to 5% and 16% respectively

compared with 50% in another building. After month 7 there were no Legionellae found in the water to wards, although one site remained positive in ICU. The mean copper ion concentration in ICU was lower than the wards (0.094 vs. 0.145 mg/L) but that of silver was not significantly different. There were no further nosocomial cases.

Domestic point of use carbon filters have been tested as a possible means of reducing exposure from taps or shower heads. However they can provide a substrate for bacterial growth. The filters reduced effluent levels by >99% immediately but over a six week period there was no significant reduction in the total throughput of bacteria. Copper ions in the filter did not reduce levels but copper and silver together did. After challenge with seeded tap water at  $4 \times 10^{11}$  cfu/filter, the number of organisms in the effluent was reduced to  $4.5 \times 10^3$  cfu/mL in the presence of copper and silver ions in the filter compared with  $1.3 \times 10^4$  cfu/mL with a filter containing copper only.<sup>2</sup> However a single challenge at  $5 \times 10^9$  cfu showed no significant difference in the effluent levels for a carbon filter with or without copper. Legionellae persisted in the effluent for 6 weeks as organisms were shed from the filter.

## 6. Hyperchlorination

Hyperchlorination is not a method of long term suppression but is used during commissioning or during an outbreak. Legionella is inactivated in 15 minutes by a concentration of 0.4 mg/L free chlorine but organisms in biofilm require higher levels.<sup>12</sup> Chlorine is lost at high water temperatures. Shock hyperchlorination requires 20-50 ppm followed by dilution back to 1 ppm with incoming water. Continuous hyperchlorination can be achieved by calcium hypochlorite, sodium hypochlorite or gas. Concentrations will vary and stagnant areas may have insufficient concentrations to inactivate Legionellae. Chlorination at 2-6 ppm for 6 weeks has been reported to reduce positive cultures from 43% to 8% .<sup>12</sup> The main disadvantage is corrosion of the pipes and a 30-fold increase in leaks can be expected. Chlorination may only be suppressive and organisms in cysts of Acanthamoebae can survive 50 ppm chlorine. Recolonization after shock hyperchlorination occurs after 2-5 months. There are epidemiological correlations between chlorination and the development of rectal and bladder cancer. Costs of \$75800 for installation plus \$48000 consultant fees and \$7000 operating costs have been reported.

## 7. Chlorine dioxide

Chlorine dioxide can be generated electrochemically from sodium chlorite but in the UK is usually formed from precursors. Unusually it is effective in removing biofilm and has some activity in dead legs, having a different mode of action from chlorination.<sup>6</sup> The injection of chlorine dioxide into hospital water systems can result in very low levels of *Legionella* after 1-2 years but, unless the calorifer is sealed, concentrations in the hot water are significantly lower than those in cold water.<sup>37</sup> In a 364 bed hospital, the use of chlorine dioxide resulted in the number

of hot water specimens showing *Legionella* falling from 12 (60%) of 20 to 2 (10%) of 20 over 18 months. Concentrations of chlorine dioxide and chlorite were within recommended limits. However, in hot water, residual chlorine dioxide levels increased significantly from 0.04 mg/L in August 2003 to 0.11 mg/L in February 2006. The distal site temperatures were between 27 and 52°C. In cold water (4-31°C), the residual level of chlorine dioxide increased from 0.3 to 0.5 mg/L. Another hospital that introduced chlorine dioxide reported a fall in sites positive for Legionella from 41% to 4% over 9 months at safe levels of chlorine dioxide and chlorite and without additional corrosion of the pipes.<sup>38</sup>

After a nosocomial outbreak, a large Italian hospital introduced chlorine dioxide to the warm water system to obtain a concentration of 0.2-0.5 ppm of residual free chlorine at the points of use. Over a period of 45 months, chlorine dioxide reduced mean counts of Legionellae by 95%.<sup>39</sup> However counts over 1000 cfu/L remained in 8% of the samples and continued monitoring was necessary. Some strains were tolerant to chlorine. Point of use filtration was also introduced on high risk wards such as haematology. Nevertheless no further clinical cases of legionnaire's disease developed.

In contrast, a hospital in Cardiff installed chlorine dioxide treatment of both hot and cold water systems at a cost of £25,000 per annum but found up to 20,000 cfu/L of *Legionella* remained in 50% of water samples with little change in the number of positive sites.<sup>40</sup> At least two cases of legionnaire's disease occurred as the result of aspiration of tap water. After three months the concentration of chlorine dioxide at hot water outlets was 0.3 ppm and was raised to 0.5 ppm, the maximum recommended level. The use of sterile water only in critical care was effective when practice was compliant. However details of attempts to remove dead legs and where chlorine dioxide was monitored were not clear.

## 8. Other agents

Bromine, iodine, chloramines, and ozone have been used to disinfect potable water.<sup>8</sup> Bromine is less effective than chlorine and is not recommended for drinking water. There is little information on the use of iodine. Although ultraviolet light irradiation can be applied to cold and as well as hot water systems, it is inadequate by itself to control *Legionella* spp as it does not provide biocidal action downstream of the point of application. Chloramination involves adding ammonia to chlorinated water. In a case control study hospitals using chloramination rather than chlorine alone experienced fewer outbreaks of legionella.<sup>2</sup> Monochloramines may have superior properties of penetration into biofilm and hospitals where it was used have been found to be legionella-free and the risk of legionnaire's disease was reduced.<sup>18,41</sup> However handling of chemicals can be problematic, they do not remove biofilm and cause copper and lead corrosion. Non-oxidising agents such as 2,2-dibromo-3-nitrilopro-pionamide (DBNPA) and Tetra kis hydroxymethyl phosphonium chloride (THPS) are toxic and can only be used in closed systems. Ozone has been reported to be more effective than chlorine at inactivating Legionella but it does not provide a residual

effect and therefore is sometimes used with chlorine.<sup>8</sup> Alone, it is not suitable for hot or cold water systems or for removing biofilm. Filtration at the point of use has been used to delay recolonization after a superheat and can be effective for several months.<sup>12</sup>

## 9. Comparison of the systems

Following two nosocomial cases of legionnaire's disease in a children's hospital, thermal treatment of a hot water system was undertaken by flushing with water over 60°C for 10 minutes.<sup>28</sup> After the fourth flush no legionellae were recovered, but the organisms returned to baseline within 29 days. Copper-silver ionisation was introduced by placing units before the hot water tanks and reduced recovery from 108 taps from 72% to 2% within a month and maintained a low level. There were 530-700 cfu/ml before ionization in one tank and at most 2 cfu/mL in the 22 months after ionization. However, of 24 samples from hot water tanks, 42% and 50% exceeded silver and copper level standards, although this was not reflected in samples from taps. The long term health effects of copper and silver exposure were a concern. Skin discoloration with silver and gastrointestinal upset and liver and kidney damage with copper are only seen at higher concentrations. However cold drinking water contained 5-140 parts per billion of copper and 1-30 ppb of silver. Hence copper and silver concentrations had to be monitored along with numbers of bacteria at distal sites.

Metal ions (0.17 mg/L copper, 0.04 mg/L silver at outlets) have been reported to be more effective than superheating (60-77°C) and flushing of the system (20-30 min) at intervals.<sup>42</sup> During 13 years when heat and flush was used there was an average of 6 cases of Legionnaires' disease a year compared with just two annually for the three years when copper-silver ionisation was used. Hot water tanks were only negative for Legionellae when ionization was used. Positive cultures at distal sites were reduced from 14% to 4%.

A consecutive study in Switzerland compared the use of ozone and copper-silver ionisation in hot water distribution systems in different hospitals over 7 years.<sup>43</sup> Water was kept above 50°C in both cases. A superheat and flush was assessed in which the hot water was increased to 75°C for 48h and each outlet flushed for 20 min. Although this resulted in negative samples one week later, the organisms reappeared within one month. There was no significant difference in the proportion of positive water samples for *Legionella* spp following ozonization or ionization. Before ionization 124 of 138 (90%) water samples were positive and during ionization 28 of 30 (93%) were still positive. Only when the water temperature was increased to 65°C did this fall to 7 of 18 (39%). At this temperature all the outlets reached 50°C. Ionization may have been ineffective because the concentration of ions was insufficient (yet copper was 0.3 mg/L) or because the pH of the hot water was high (7.8-8.0). Others have suggested that trisodium phosphate added to the water system to prevent corrosion may have bound both copper and silver ions preventing bactericidal activity.<sup>44</sup>

A US hospital used copper-silver ionisation successfully for 12 years after a case of legionnaire's disease.<sup>45</sup> However the number of positive sites gradually increased possibly due to silver tolerance in the organisms. The replacement cost of the anodes was \$13,200 a month, such that with labour costs the hospital spent \$203,400 a year on the system. Installation of electrochemically generated chlorine dioxide was cost effective within 6 months and reduced legionella counts. The proportion of positive sites fell from 4.9% to under 1% within 2 years.

In a simulation of a domestic water supply system, parallel water supply loops received a disinfectant over three months, one loop being a control.<sup>46</sup> The comparators were sodium hypochlorite, electrochlorination and monochloramine (all providing chlorine 2 mg/L), chlorine dioxide, ozone (0.5 mg/L), and copper/silver (0.5 mg/L, 0.01 mg/l). In the control loop, *Legionella* remained stable at  $2.6 \times 10^5$  cfu/l. *Legionella* fell within 3 days to undetectable levels with all the disinfectants. However five of six samples from the copper/silver loop were later positive and by the end of the experiment 10,000 cfu/L were present. Sessile legionellae were only detected in biofilm from the copper/silver treated loop. The thickness of biofilm was unaltered by copper/silver but reduced by other methods except monochloramine. Copper deposits and corrosion developed in steel pipes with copper/silver whereas chlorine caused corrosion. Dead legs regained bacterial counts within 24h of flushing. Copper may have been present as insoluble complexes at pH 7.6 so the real concentration was unclear.

A similar simulation used an initial inoculation with *Legionella* and amoebae to provide biofilm.<sup>6</sup> Continuous application of chlorine dioxide (0.5 mg/L) or chlorine (2.5 mg/L) significantly reduced bacterial flora. Ozone (0.5 mg/L) was less effective and monochloramine (0.5 mg/L) and copper-silver ionization (0.8/0.02 mg/L) left higher levels of contamination and did not remove biofilm. *Legionella* also showed regrowth during copper-silver ionization. Chlorine dioxide showed a longer residual activity and showed some effect in dead legs. Amoebae could not be eliminated and remained as a reservoir so Legionellae returned to initial levels after withdrawal of each treatment.

## 10. Conclusions and Recommendations

Raising the temperature of the hot water system reduces the population of Legionellae but the organism persists in cooler water in taps, showers or dead legs. (1b)

Temperatures above 60°C are needed to maintain negative cultures but carry a risk of scalding and legionella may not be eradicated from biofilm (2)

Temporary superheating above 60°C is effective following an outbreak but does not eradicate organisms and benefit is temporary. (1b)

Ionization with copper (0.2-0.8 mg/L) and silver (0.02-0.08 mg/L) without elevation of the hot water temperature is effective and safe in eradicating Legionellae provided ion concentrations are kept within the appropriate range, pH is below 7.6 and scale is removed (1b).

Installation costs are higher for ionisation but maintenance lower than thermal methods. (2)

Chlorination is effective in reducing but not eliminating legionellae (1b). Chlorination has high installation and maintenance costs.(2)

Comparative studies are retrospective but favour ionisation or chlorine dioxide. Although a combination of ionisation and hot water above 50°C was most reliable method of control, chlorine dioxide appeared the more effective against biofilm in laboratory studies. (2)

Thermal control, chlorine dioxide or copper-silver ionisation is effective in *Legionella* control in water systems. On grounds of efficacy, reliability and energy costs, recent studies suggest that copper-silver ionisation or chlorine dioxide should be recommended over thermal disinfection provided monitoring and controls are applied. This should be reflected in the HTM guidance. In the case of ionisation, adequate monitoring of pH, ion concentrations and scale is essential.

Further research is needed on the use of oxidising agents such as ozone or hydrogen peroxide.<sup>8</sup> Ozone appears more effective than chlorine but dissipates too quickly. Methods to eradicate either amoebae or biofilm are needed as they are main reservoirs for *Legionellae*. The formation of aerosols by faucets should also be further studied. If water were supplied to hand wash sinks at 20°C, *Legionellae* would not be a concern but little is known of hand hygiene compliance in hospitals at such water temperatures.

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**Appendix 1****Terms of Reference for Independent Review of Evidence and the related HTM guidance**

These Terms of Reference (TOR) are for governance of an independent review of published literature and other evidence regarding the selection of techniques for the suppression of Legionella in the water supplies of hospitals and other healthcare premises.

The content of Health Technical Memorandum 04-01 “The control of Legionella hygiene, “safe” hot water, cold water and drinking water systems” Parts A and B (Appx 1) has been challenged in a series of Parliamentary Questions (PQs) and a Parliamentary Debate. It is essentially alleged that the guidance does not reflect the contents of the current learned literature and expresses a preference for Legionella suppression by the use of temperature controls on water supply systems, which is not justified by the evidence.

The independent review team are asked to evaluate the evidence currently available in relation to the suppression of the Legionella pathogen within water systems. A list of references is appended (Appx 2) drawn largely from the scientific literature. However, the team is free to evaluate not only the papers listed but also other peer reviewed publications from any area of the relevant literature including that relating to the engineering of water supplies and the Quality Systems used in that area.

Whilst the range of suppression techniques included in the review is left for the Chairman to determine, the scope of the PQs requires that at least techniques involving water temperature control and the use of copper / silver ions be considered. Both of these techniques are described in HTM 04-01.

The Chairman is asked to ensure that the review produce recommendations related to the validity of the HTM guidance in terms of the supporting evidence and the review shall not be constrained to observations and evidence précis only.

The terms extend to considerations of practicality and maintainability in a hospital and healthcare premises environment with a reasonable compliment of trained engineers and infection control specialists. However, no detailed cost comparison between the suppression techniques is requested. Cost observations may, however, be included if these contribute materially to the matter of suppression technique selection.

The review shall have no express duty to call for witnesses to the creation or implementation of the HTM. There shall be no duty to generate or record minutes except at the discretion of the Chairman.

**Review group constitution and members.**

The review group shall be independent of the Department of Health (DH), Department of Work and Pensions, Health and Safety Executive and the Health Protection Agency. This requirement does not exclude the review from asking for such support as the Chairman may see fit from these Government related organisations.

Equally the review shall be independent of those persons employed by or connected with ProEconomy of Orca House, Leighton Buzzard. However, the review may consult with these persons at the discretion of the Chairman. The review may also consult with such learned, professional or trade organisations as the Chairman may so direct.

The proposed Chairman is A.P.R (Peter) Wilson, Consultant Microbiologist, Windeyer Institute of Medical Sciences, University College London Hospitals NHS Trust. The Chairman may nominate up to 4 other members of the review group. The nominations are to be notified to the DH but the Department will not have the right to exclude nominees from membership of the review.

**Timescales and schedules.**

This exercise is classified as a short, literature based review. This would imply that the evidence gathering and evaluation should take not more than 4 weeks. The drafting of the report should extend to no more than a further 3 weeks. This would imply a total review period of 7 to 8 weeks though extensions to this time shall be at the Chairmans' discretion.

The start and completion dates are subject to discussion with the Chairman. However, the Department of Health would request that the exercise be completed and reported by the end of February 2009. No interim reports are envisaged.

**Reporting requirements.**

The report shall include a digest of the evidence considered (graded where appropriate) and giving indications regarding the risk reduction qualities of each technique when properly applied.

In relation to the preference expressed by the HTM for thermal control methods the review is asked to present conclusions regarding the appropriateness of this element within the guidance. The review should also present opinion related to the content of the HTM in regard of Copper / Silver ion based Legionella suppression techniques. There is no requirement for this to extend specifically to consideration of the guidance in the context of any specific commercial products.

The Chairman and members of the independent review shall have no duty to revise the report in light of the response from DH or other parties. An erratum may be produced at the discretion of the Chairman.

The completed report shall be addressed jointly to: Professor Brian Duerden, Chief Inspector of Microbiology DH; Mr Rob Smith, Director of Gateway Reviews and Estates & Facilities DH; Mr Andrew Selous MP for South West Bedfordshire.

### **Duties on the Department of Health.**

The Department shall be required to receive and formally review the report. The Director of Gateway Reviews and Estates & Facilities shall convene a formal review meeting of officers of the Department and such invited representatives of other Government Departments and Agencies as the Director may see fit.

Following the formal review of the report the Department shall be required to generate a written response and to provide this to the independent Chairman of the review for comment. The response shall include any proposed amendments to HTM 04-01 as the Department may wish to make. The report and response shall then be made available to other Government Departments as may be requested and to both Andrew Selous MP and the Managing Director of ProEconomy Ltd of Leighton Buzzard.

The review will be funded by the DH GR Estates and Facilities Directorate and this group will provide services, such as meeting rooms, catering etc as may reasonably be required. Secretariat services will be provided or funded by DH to meet the Chairmans' requirements.

### **Confidentiality and Conduct**

The proceedings of the review shall be confidential where the Chairman directs. Members are bound by a duty of confidentiality in respect of business discussed at the review. In addition, they are expected, at all times, to conduct themselves in an appropriate manner, i.e. the use of their positions cannot be reasonably construed to be for their private gain or that of any other person, company or organisation.

Confidential information or material provided by to the review may only be disclosed to third parties with the written authorisation of the DH Director Gateway Reviews and Estates & Facilities and the author of the material.

### **Conflicts of Interest**

Where, on a particular issue, a member's personal or organisational interests conflict, or are perceived to conflict with their responsibilities as a member of the

review, the member should disclose the potential conflict and the Chairman will decide whether or not a conflict exists and whether the member should participate in discussions or decisions on that issue.

The Chairman shall ascertain during any meetings the existence of any conflicts of interest and take appropriate action to e.g. request withdrawal of a particular member/members whilst issues causing the conflict of interest are being discussed. Any conflicts of interest identified and the actions taken should be noted in the review report.

**DH INFORMATION READER BOX**

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<b>Document Purpose</b>	For Information
<b>Gateway Reference</b>	12215
<b>Title</b>	Independent Review of evidence regarding selection of techniques for the suppression of Legionella in water supplies of hospitals and other healthcare premises.
<b>Author</b>	DH/FP&O/Gateway Review Estates & Facilities
<b>Publication Date</b>	13 Jul 2009
<b>Target Audience</b>	To be published on DH website as per agreed Terms of Reference
<b>Circulation List</b>	Andrew Selous MP, Mr N Bedford (MD of ProEconomy Ltd), Dr John V Lee (Health Protection Agency), John Newbold (Health & Safety Executive)
<b>Description</b>	Feedback will be provided by letter, or e-mail, by the Chief Engineer or their representative
<b>Cross Ref</b>	(see also) Response to Independent Review of evidence regarding selection of techniques for the suppression of Legionella in water supplies of hospitals and other healthcare premises
<b>Superseded Docs</b>	None
<b>Action Required</b>	N/A
<b>Timing</b>	<b>N/A</b>
<b>Contact Details</b>	Philip Ashcroft GREFD 3N11 Quarry House Quarry Hill, Leeds LS2 7UE 0113 2545794
<b>For Recipient's Use</b>	