A review of drinking water standards for copper and investigation of copper levels in drinking water in institutional buildings

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ABSTRACT

Copper (Cu) has been used for centuries in the house, in industry and in agriculture. As a transition metal, it can adopt distinct redox states, which allows it to function as a catalytic cofactor in many enzymatic reactions essential to living organisms. Although copper is an essential nutrient, elevated levels of copper can be toxic. Indian Childhood Cirrhosis is a well-known epidemic of copper toxicity. Once recognized as a public health concern, daily recommended intakes were assessed at 0.3 to 3.0 mg/day for adults and at 0.1 to 2.0 mg/day for infants and young children, while the maximum safe levels for adults ranges from 0.8 to 30 mg/day and cannot be determined, due to insufficient data, for infants and young children.

One of the main sources of copper ingestion is drinking water due to the extensive use of copper pipes for plumbing, although copper is more often recognized as an aesthetic concern rather than a health concern. Many countries, including Canada, have not yet established health-based drinking water standards for copper. Currently, the WHO has the most referenced health-based guideline value for copper at 2 mg/L. However, the supporting evidence for this guideline value has been questioned due to high uncertainty, insufficient data and questionable interpretation of data. Exposure studies for copper in drinking water have not considered ingestion at work or school, where the majority of waking time is spent, which may underestimate the associated health risks.

First, the strength of the evidence and the science used to set the drinking water guideline values for copper is reviewed. Guideline levels, developed only for acute copper toxicity, rarely occur due to the low taste threshold of copper. There are irregularities in the reported levels of copper exposure for acute effects and the calculation of levels is not conservative. Second, copper concentrations have been measured in large institutional buildings to assess potential exposure levels. The results of the field study reveal that drinking water in these large buildings can provide a significant contribution to daily copper intakes ranging from 50% to almost 100% of the recommended daily intake values (0.7-0.8 mg Cu/day) proposed by the WHO. The field survey also shows that flushing in large building can reduce copper levels in the water by 40%. Lastly, the results confirm higher copper levels in newer or recently renovated buildings, likely due to the lack of time to develop a protective scale (due to oxidization of the copper) reducing dissolution of the pipes.

ABRÉGÉ

Le cuivre (Cu) a été utiliser pour des centaines d'années à la maison, dans l'industrie et dans l'agriculture. Étant un métal de transition, il put adopter des différents états redox. Cela lui permet d'agir comme un cofacteur catalytique dans des réactions enzymatiques essentielles au êtres vivants. Bien que le cuivre est un nutriment essentiel, des hauts niveaux de cet élément peut s'avérer toxique. Le cirrhose Indien d'enfants est une maladie bien connue de toxicité de cuivre. Une fois reconnu comme menace potentielle à la santé publique, la consommation quotidienne recommandé a été établi à 0.3 - 3.0 mg/jour pour adultes et à 0.1 - 2.0 mg/jour pour les nourrissons et les jeunes enfants. Le niveau maximal pour éviter les effets toxique est dans l'intervalle de 0.8 - 30 mg/jour pour adultes, mais ne peut pas être déterminé pour les nourrissons et les jeunes enfants dû à un manque de données. Une des sources primaire d'ingestion de cuivre est l'eau potable dû à la plomberie en cuivre, bien qu'il est plus souvent considéré comme paramètre influant le goût et la couleur de l'eau et non un problème de santé. Plusieurs pays, le Canada inclus, n'ont pas encore établi des normes pour le cuivre dans l'eau potable.

Actuellement, le niveau recommandé par l'organisation mondiale de la santé (OMS) est le plus référencé des recommandations basées sur la santé à 2 mg/L. Toutefois, ces recommandations sont contestables dû aux manque de données et leur interprétation. Les études sur le niveau de consommation de cuivre n'incluent pas les taux provenant de l'eau potable bu au travail ou à l'école. Ceci peut résulter en une sous-estimation de la risques de problèmes de santé associé à la consommation de cuivre.

Premièrement, la fiabilité de l'évidence et la science utilise pour établir les recommandations des niveaux permissibles dans l'eau potable sont passer en revue et critiquer. Les recommandations, établi pour la toxicité aiguë, prends place rarement due au bas seuil de gout pour le cuivre. Il y a des irrégularités dans les niveaux rapporte pour les niveaux de cuivre causant des effets aigus et la calculations de niveau recommandes ne sont pas conservatives. Ils devront être conservatives dû au manque d'évidence de sécurité et à l'évidence d'effets nuisibles des cas en particulier. Deuxièmement, les niveaux de cuivre dans l'eau potable des grands bâtiments institutionnelles ont été mesures pour évaluer la quantité infestée. Les résultats indiquent que l'eau potable des grands bâtiments peut entrainer une contribution à l'ingestion de cuivre quotidienne de 50 à 100 pourcent du niveau quotidien recommandé de 0.7 à 0.8 mg Cu/jour propose par l'OMS. Les résultats ont

aussi indiqué que le rinçage d'une minute pour réduire les niveaux de cuivre par 40%. Dernièrement, les résultats confirment des niveau plus hautes dans les bâtiments neuves ou récemment renouvelés, probablement dû au manque de temps pour développer un dépôt d'oxydations sur les tuyaux réduisant solubilité.

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LIST OF ABBREVIATION

AI	Adequate Intake
ATP	Adenosine triphosphate
BR	Basal Requirement
CNS	Central Nervous System
ECC	Early Childhood Cirrhosis
GI	Gastrointestinal
ICC	Indian Childhood Cirrhosis
ICP-OES	Inductively Coupled Plasma-Optical Emission Spectrometry
LOAEL	Lowest Observed Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
NR	Normal Requirement
RDA (or RDI)	Recommended Dietary Allowance (or Recommended Dietary Intake)
ROS	Reactive Oxygen Species
RSC	Relative Source Contribution
TDI	Tolerable Daily Intake
UF	Uncertainty Factor
UL	Upper Limit

1 INTRODUCTION

1.1 Background

Copper (Cu) is one of the humankinds oldest metals and it has been used in a wide variety of applications in the postglacial epoch (since 5000 B.C.) (Mason, 1979). It is a transition metal, occurring in three oxidation state: Cu (solid metal), Cu^{1+} (cuprous ion), and Cu^{2+} (cupric ion) with Cu^{2+} being the main valence state in the environment (Flemming & Trevors, 1989). Copper in its metallic state is malleable and ductile, and a good conductor of electricity and heat. These characteristics led to its early use in many industrial applications including the manufacture of textiles, electrical conductors, plumbing fixtures and pipes, coins, and cooking utensils.

Copper, as a transition metal, can adopt distinct redox states, the reduced state as Cu^{1+} or the oxidized state as Cu^{2+}. This capacity allows copper to function as a catalytic cofactor in many enzymatic reactions in cells, which is required for the survival of all living organisms ranging from bacteria to mammals (Massaro, 2002). Therefore, copper compounds have been used as micronutrients in agriculture and as mineral nutritional supplements for humans. Although copper is a required nutritional element, slightly elevated levels of copper can be toxic. This explains why copper compounds have been used as an active ingredient in pesticides and fungicides (e.g. in anti-fouling paint).

The toxic effect of copper on microorganisms was recognized as useful leading to its use in appliances for cooking and storage, since it reduced the risk of bacterial contamination. Between the 16th and the early 19th centuries, bacterial diseases were the leading cause of morbidity and mortality. For example, in 18th century Sweden every third child died, and in 19th century Germany every second child died (Roser, 2018). In the latter part of the 19th century and into the 20th century, efforts were made to improve hygiene and sanitation, and produce safer food and water in many regions of the developed world (Cohen, 1998; NRC, 2004). One innovation was the increased use of copper in drinking water supply, and food and beverage preparation owing to its cytotoxic and antibacterial effects (Grimsdottir & Hensten-Pettersen, 1993). Over the course of modernization and improvements in hygiene, food safety and potable water quality, the mortality of children below 5 years of age has declined rapidly from 18.2% in 1960 to 6.3% in 2005 (Roser, 2018). Therefore, it can be postulated that using copper pipes and vessels contributed to increasing life expectancy by reducing child mortality (Sudha et al., 2012; Sudha et al., 2009).

However, there is a dilemma with using copper pipes and vessels because exposure even to relatively low levels of copper can cause acute gastrointestinal effects and severe chronic illness in certain populations. First reported in India in 1887, Indian Childhood Cirrhosis (ICC) (Bhave, Pandit, & Tanner, 1987; Tanner & Portmann, 1981) is a form of liver cirrhosis occurring in early childhood with a high case fatality. It results from early nourishment with milk and water heated in copper or brass vessels becoming contaminated with high levels of copper (Tanner, 1998). ICC cases have become rare in India since the late 1980's after education programs informed parents to eliminate the use of copper vessels in the preparation of food and drink for infants. However, ICC-like diseases were subsequently found in Australia, Europe and the US (Adamson et al., 1992; Klass, Kelly, & Warnes, 1980; Price et al., 1996).

Once copper was recognized as a public health concern, especially for infants, the public health authorities have referred to studies evaluating the toxic effect of a range of levels of copper exposure in order to establish guideline values. The most frequently referenced guideline value for copper in drinking water is that of the World Health Organization (WHO) of 2 mg Cu/L. However, this guideline value is only based on acute gastrointestinal (GI) effects. Thus, chronic exposure to copper and its adverse health effects have been completely omitted from the risk assessment. In Canada, copper in drinking water is not considered as a health threat but is only treated as an aesthetic objective.

1.2 Objectives

The WHO water quality guideline has been referenced to set the copper levels in drinking water regulations or guidelines across the world. However, the scientific evidence on which levels were established is poor and has not been updated recently.

Copper levels in drinking water leaving the treatment plant are usually much lower than the guideline values (often < 0.1 mg/L). However, the water passing through or left standing in the distribution system of a building for a length of time significantly increases its copper content due to leaching from the copper plumbing. Public health authorities have advised that exposure to copper-contaminated drinking water can be reduced by flushing, that is running the tap for a minute or two before collecting drinking water. However, the effectiveness of this process is unsure in large buildings such as multi-unit residential buildings, schools, etc. due to the volume of water stored in the long lengths of piping in the building water distribution system (requiring, for example, flushing of more than 30 minutes).

In North America 80 to 90% of houses have copper plumbing as do larger residential buildings and public institutions such as schools, hospitals, libraries and universities. All these building can therefore have higher levels of copper in the drinking water. Flushing the taps before consumption is less effective in larger buildings, resulting in higher potential exposure to copper ingestion.

The objectives of this study are i) to review the scientific basis for the development of guidelines or regulations for copper levels in drinking water and ii) to measure copper levels in drinking water in large institutional buildings. As defined by the WHO guidelines for drinking water quality, safe drinking water should not represent any significant risk to health over a lifetime of consumption considering the different sensitivities that may occur between life stages.

To meet the first objective, the supporting evidence for the current copper guideline values will be investigated to assess whether they meet the primary purpose of the guidelines. To meet the second objective, copper levels will be measured in buildings under different conditions: after weekend stagnation, weeknight stagnation, one-minute flushing and typical daytime use. The water quality parameters and effectiveness of one-minute flushing under these different conditions will be compared and discussed with reference to recommended daily copper intake values presented in the literature and recalculated drinking water guideline levels for copper.

1.3 Organisation of the thesis

The remainder of this thesis is organized in four chapters. Chapter 2 presents a literature review on copper as both a micronutrient and toxic substance causing health impacts, and on the chemistry of copper in drinking water. Chapter 2 also reviews copper levels measured in drinking water in previous studies. Chapter 3 provides the framework used for the critical assessment of the development of guideline values for copper in drinking water. Following this, the sampling locations, sampling methods and analytical methods used in the field study are described. Chapter 4 presents the assessment of the scientific rigour of the supporting evidence for copper guideline values and the recalculation of guideline values based on the evidence. The copper concentrations measured in institutional buildings are presented and correlated with water quality parameters (pH and temperature) and building characteristics. The effectiveness of one-minute flushing as well as the potential of adverse health impacts at the measured copper levels is also discussed. Finally, in Chapter 5, the conclusions drawn from the analysis of the drinking water samples are presented and recommendations for future work are provided.

2 LITERATURE REVIEW

2.1 Copper as a micronutrient and a toxic substance

Copper was found in plants and animal tissue in 1816, however, it was only in the 1920’s that it was found to be an essential trace element for the human body (Mann & David, 1938). Copper is required mainly due to its fundamental role as a transition metal in electron transport for respiration. The following sections present details about the role of copper in the human body, the maintenance of homeostasis in the body and the adverse health effects on the body due to its toxicity.

2.1.1 Functions of copper in human body

Copper is necessary for a wide range of metabolic processes in the human body due to the role of copper-dependent enzymes. Copper serves as an electron donor/recipient in numerous enzymatic activities owing to its ability to change oxidation states, cycling between Cu^{1+} and Cu^{2+}. The role of copper is as a catalytic cofactor in these critical enzyme reactions, as an allosteric enzyme component, or as a potent antioxidant in the oxidant defense system (Stern, 2010). As an allosteric enzyme component, copper is required for enzymes involved in aerobic metabolism. For example, cytochrome-c oxidase is the terminal enzyme for mitochondrial respiration in most cells, which is fundamental for the production of usable energy in the form of ATP. Copper plays a critical role in a process of electron transfer through this enzyme for the reduction of oxygen to water (Massaro, 2002). Copper also protects against free-radical damage to proteins, membrane lipids, and nucleic acids in cells and organs as a potent antioxidant for Cu/Zn superoxide dismutase. Some of the well-known copper-dependent enzymes in human body are summarized in Table 2.1. (Linder, 2013; Massaro, 2002; Stern, 2010).

Table 2.1 Copper-dependent enzymes

Enzyme	Function
Metallothionein	Storage of excess Cu and other transition metal ions
Cu/Zn superoxide dismutase	Antioxidant defense in cytoplasm
Ceruloplasmin	Source of Cu for tissues Iron flow from liver to blood Free-radical scavenger
Protein-lysine-6-oxidase	Crosslinking of collagen and elastin fibers
Tyrosinase	Formation of melanin and other pigments
Hephaestin	Iron absorption
Dopamine β-hydroxylase	Catecholamine production (nerve and metabolic function)

In addition to these enzymes, copper-containing non-enzymatic proteins also exist such as copper associated with amino acids, small peptides, and other metabolites (Linder, 2013). These proteins transport copper to different organs and tissues playing a critical role in the regulation of copper metabolism. However, there are still unidentified copper-binding components in living systems, which means that we do not yet understand the full importance of copper. For example, the functions of copper in the brain, the immune system and other tissues have not yet been well understood.

2.1.2 Copper homeostasis

Nearly all the copper found in mammals is taken in through oral ingestion of food or water, and absorbed from the gastrointestinal (GI) tract (Georgopoulos et al., 2001). In humans, copper is absorbed primarily by the small intestine and partially in the stomach. In the stomach, some of the bound copper ions are separated from digested food particles by the high acidity. In the intestinal tract, copper is complexed with amino acids, organic acids, or other chelators. Amino acids, particularly histidine, methionine, and cysteine bind to the copper to allow for absorption through an amino acid transport system. Reduced glutathione and organic acids, such as citric, gluconic, lactic, and acetic acids form ligands with copper, which makes copper more soluble and absorbable (Jacob et al., 1987; Turnlund, 1998). Copper absorbed in the GI tract then enters the cells of the intestinal mucosa and the blood. In the blood plasma, copper binds to the copper transport proteins, albumin and transcuprein. After binding, these proteins carry copper to the liver, where the copper is first deposited, and the kidney via the blood. Most of the copper carried to the liver is subsequently incorporated into ceruloplasmin for resecretion into the blood. Some of the copper carried to the liver is stored within hepatocytes to be used for production of internally required liver proteins (Bertinato & L'Abbé, 2004). Small quantities of copper are lost in the urine, feces, and sweat, and a large amount is excreted with the bile.

The gene responsible for the incorporation of copper into ceruloplasmin and the excretion of copper into the bile is ATP7B on chromosome 13, which provides instructions for making a transmembrane protein ATPase (Hoogenraad, 2006). In normal human bodies, copper-binding ceruloplasmin is the main source of copper for the other tissues. The ATP7A gene functions as a regulator of copper levels in the body and supplies copper to particular enzymes, described in the previous section. If copper levels in the cell are increased, the ATP7A protein eliminates the excess copper from the cell through the biliary excretory pathway (Lönnerdal, 2008). The homeostatic regulation of copper responds to copper intake by adjusting the rate of copper absorption and excretion, particularly at extreme levels (Massaro, 2002). However, homeostatic regulation of copper absorption in infants is uncertain raising concerns in the case of infants fed by formula containing copper salts and/or prepared with water containing a high concentration of copper (Salmenperä et al., 1989).

2.2 Adverse health effects of copper

As a trace mineral nutrient, both too high and too low copper intake can cause adverse health effects. Humans obtain copper mostly through food, potable water, and supplements. Foods containing higher copper levels include shellfish, beef, organ meet, mushrooms, potatoes, legumes and raisins (Stern et al., 2007). Due to the extensive use of copper piping in plumbing systems, copper has been detected in most drinking water supplies at levels ranging from a few μg/L to 18 mg/L or even higher (Pal, Jayamani, & Prasad, 2014; USEPA, 1991). Lastly, most multivitamin supplements currently on the market contain 2 mg of copper per pill. The scientific committee of the scientific evaluation of dietary reference intakes, composed of U.S. Food and Nutrition Board, Institute of Medicine and National Academies, stated that current daily copper intake may be even less than that currently recommended by the National Research Council, 1.5 mg/day (Trumbo et al., 2001). As copper is a relatively easily obtainable mineral nutrient, copper deficiency does not occur to a significant extent in human populations. In fact, it was reported that most Americans and Europeans easily meet the current recommended range of copper intake (Brewer, 2010; Massaro, 2002; WHO, 2011). Previous research has indicated that copper toxicity is becoming a threat to the public health (Brewer, 2011; Harvey, Handley, & Taylor, 2016; Pal et al., 2014; Sidhu, Nash, & McBride, 1995). Therefore, adverse health effects of excess copper intake is considered.

2.2.1 Mechanism of copper toxicity

Although copper is subject to effective homeostatic control, excess copper intake can still be toxic and become harmful. Mechanisms by which copper becomes toxic include interactions of copper with proteins, enzymes, nucleic acids, and metabolites at cell surfaces. Copper acts to prevent cell division or growth at cell surfaces, which results in cell necrosis (Domek et al., 1984; Lamb & Tollefson, 1973). Copper is an essential mineral due to its redox properties, however, when levels are too high in the cells, it becomes highly cytotoxic. Copper interacts with oxygen to generate the highly reactive oxygen species (ROS), which are extremely damaging to proteins, lipids, membranes, and nucleic acids. Under conditions of copper overload, redox cycling can lead to the generation of unbound ionic copper, which yields hydroxyl radicals and produces oxidative damage or displaces other essential metal cofactors from metalloenzymes (Bertinato & L'Abbé, 2004; Letelier et al., 2005). Although the human body has its own scavenging systems for ROS, some ROS still escape especially when the copper load is excessive and the number of ROS becomes too high for the system to control. The high flux of ROS can be very dangerous to the central nervous system (CNS) as the CNS is composed mainly of polyunsaturated lipids and these lipids are particularly susceptible to oxidative stress and cellular damage (Cherny et al., 1999).

One of the key indicators of the development of copper toxicity is the accumulation of copper in the liver, as the liver plays a central role in the metabolism of copper. Another key feature is GI symptoms. Cytotoxic and antibacterial effects of copper can damage the intestinal bacterial flora causing various GI problems (Rosborg, 2016). GI symptoms are considered to be an acute-phase syndrome as compared to copper-induced liver symptoms. Cases of copper toxicity can be categorized into acute and chronic toxicity.

2.2.2 Acute copper toxicity

Acute copper toxicity was initially recognized due to occasional reports of suicidal copper poisoning. Accidental consumption of copper-contaminated beverages or food has been also reported. Reported cases for acute copper poisoning are summarized in Table 2.2.

Table 2.2 Cases of acute copper toxicity

References	Country	Exposed population (age)	Exposed Cu levels	Appearance of symptoms	Cause of high Cu exposure	Observed symptoms
Chuttani (1965)	India	53 (14-60 yr)	NA	From the point of the ingestion to 5 days	Suicidal ingestion	Metallic taste, burning sensation in the epigastrium, eructation, vomiting, severe diarrhoea, shock, smoky urine, oliguria, anuria, uraemia, enlarged tender liver, jaundice, coma, death
Chugh (1977)	India	29 (18-28 yr)	1-50 g (not reliable data)	From the point of the ingestion to 8 days	Suicidal ingestion	Acute renal failure, hepatic failure, methaemoglobinaemia, death
Gulliver (1991)	UK	1 (11 yr)	29 mg/L (total ingestion: 226 mg)	A few hours	Accidental ingestion from a jam jar containing a solution of copper sulfate	Severe stomachs pains, vomiting, cardiac arrest, death
Motlhatlhedi (2014)	Botswana	1 (29 yr)	NA	2-22 hours	Vaginal insertion of copper sulfate to terminate an unwanted pregnancy	Excessive vomiting, jaundiced, methaemoglobinaemia, death
Franchitto (2008)	NA	1 (29 yr)	NA	From the point of ingestion to 3 days	Suicidal ingestion	Vomiting, diarrhoea, fever, epigastric tenderness, aspiration pneumonitis, macroscopic haematuria, oliguria, tachycardia

As shown in Table 2.2, acute toxicity is commonly characterised by a metallic taste, nausea, diarrhea, and jaundice as initial symptoms, and then, fatal symptoms such as hepatic and renal failure appear at later stage of acute poisoning. In most accidental cases of acute copper poisoning, the exposure levels of copper were either unavailable or unreliable. Based on the cases with known exposure levels, an ingestion of 15-20 mg of copper sulfate or higher was reported to cause acute symptoms, and ingestion of higher than 1000 mg of copper sulfate can be lethal (Franchitto et al., 2008; Motlhatlhedi et al., 2014). However, this range of acute toxicity is not fixed as susceptibility to acute toxicity may depend on many factors, including age, diet, and other health conditions.

The average taste threshold for copper sulfate ranges between 2.5 and 3.5 mg/L (Stern et al., 2007), which is below the concentration required for acute effects. Therefore, accidental ingestion of high copper is very rare. Despite the infrequency of acute copper poisoning, cases with the less severe symptoms of acute toxicity have been more frequently reported.

In the late 1990s in Europe, there were increased reports of gastrointestinal symptoms especially in infants and small children (Dieter et al., 1999; Eife et al., 1999; Stenhammar, 1999). In these cases, most of the houses had copper plumbing installed, and elevated copper levels were detected in their drinking water. According to Dieter's study (1999), copper levels in infant formula prepared with the tap water were between 9 and 26.4 mg/L, which is slightly lower than the established range of acute copper toxicity, whereas in Eife's study (1999) the exposure level was lower, ranging from 0.1 to 16.9 mg/L. Studies on adults have been used to establish copper levels causing acute toxicity (Araya et al., 2003; Franchitto et al., 2008), while acute affects, attributed to copper contaminated drinking water, were found at lower levels for children (Eife et al., 1999). These investigations suggest that copper-contaminated drinking water may be a common cause of nausea, diarrhea, abdominal cramps, and headaches.

2.2.3 Chronic copper toxicity

The liver plays a central role in the metabolism of copper in human body so chronic copper exposure results in a gradual hepatic accumulation of copper, causing liver cirrhosis, and in extreme cases, in death (Bremner, 1987). Wilson's disease, a disease of copper overload, is an autosomal recessive disorder caused by defective ATP7B function resulting in the failure of biliary copper excretion and a failure to incorporate copper into the ceruloplasmin. One of the symptoms of Wilson’s disease is increased hepatic copper levels, which if untreated, leads to hepatic failure (Hoogenraad, 2010).

Adverse health effects of chronic exposure to copper were first recognized by an epidemic of Indian Childhood Cirrhosis in the late 1800s India. It was caused by the use of copper vessels to heat the milk fed to infants. In 1973, similar symptoms were observed with a 15-month-old boy in Australia (Walker-Smith & Blomfield, 1973). The boy’s drinking water was supplied from a bore hole via new copper pipes, which led to chronic copper poisoning. Indian Childhood Cirrhosis-like illness was increasingly observed in developed countries, including U.S., Australia, and countries in Europe, where copper was extensively used for plumbing. A summary of Indian Childhood Cirrhosis-like cases is presented in Table 2.3.

All Indian Childhood Cirrhosis-like cases in Table 2.3 present with similar symptoms, but were subject to different exposure levels. This may indicate that susceptibility to chronic copper poisoning varies, which may be due to a difference between individuals in the efficiency of the homeostatic control mechanisms. Most of the cases presented in Table 2.3 were fatal, indicating that formula-fed infants and small children are more susceptible to copper toxicity than adults. Infants and small children probably have a high efficiency in their copper absorption and an immaturity in the biliary excretory mechanisms (Bremner, 1998; Müller-Höcker et al., 1987).

Table 2.3 Indian Childhood Cirrhosis-like Cases

References	**Location**	**Cu exposure level (mg/L)**	**Exposure period**	**Subject**	**Symptoms**
Salmon (1971)	UK	0.3 – 0.8	3 months	15 months boy	Cirrhosis
Walker-Smith (1973)	Australia	0.3 – 9.7	14 months	15 months boy	Abdominal swelling, ascites, small cirrhotic liver, severe micronodular cirrhosis, high free Cu in plasma, high Cu level in liver, jaundice, death
Muller (1987)	Germany	0.4	7 months	7 months boy	Severe liver cell necrosis, excessive mallory body formation, liver failure, death
Schramel (1988)	Germany	3.4	4 - 8 months	3 infants (5 - 9 months)	High Cu in liver, kidneys, and other organs; micronodular cirrhosis, liver failure, death
Eife (1991)	Germany	1.3	5 months	6 months boy	Muscular hypotonia, micronodular cirrhosis, medium Cu in liver
Adamson (1992)	USA	NA	2 years	2 years boy	Hepatic dysfunction, micronodular cirrhosis, GI bleeding, death
Fischer (1994)	Germany	12.1 – 26.4	11 months	12 months girl	Acute GI bleeding, high liver Cu, complete cirrhosis, death
Bent (1995)	Germany	9.0 – 12.0	8 months	9 months boy	Micronodular cirrhosis, high Cu in liver
Baker (1995)	UK	2.3 – 8.0	NA	3 infants (10 - 19 months)	Pyrexia, severe liver cell necrosis, micronodular cirrhosis, Mallory bodies, liver failure, death
Trollmann (1998)	Germany	8.6	1 year	3 years girl	Elevated urinary Cu, micronodular cirrhosis, extremely high liver Cu, liver failure, death
Dieter (1999)	Germany	2.9	12 months	12 months boy	Micronodular cirrhosis

Although adverse health effects of chronic exposure to copper have been observed in many parts of the developed world (Bent & Böhm, 1995; Dieter et al., 1999; Eife et al., 1999; Müller-Höcker et al., 1996; Pettersson & Rasmussen, 1999; Price et al., 1996), the exposure levels causing chronic poisoning have not been investigated. In fact, copper has often been excluded from heavy metal exposure studies simply because it is a micronutrient (Erdman, MacDonald, & Zeisel, 2012; FAO/WHO, 2004). Chronic copper toxicity is of greater concern than the acute toxicity, as the taste of copper reduces the likelihood of ingestion of high levels, while large sections of the population have been subject to low exposure levels over long periods of time through drinking water.

2.3 Regulations

As a part of human nutrition and health studies of trace elements, the public health authorities are required to investigate (1) the trace-element content of all possible sources; (2) the requirements of daily intake; and (3) the safe levels of intake (WHO, 1996a). For copper, investigation began in 1970s, and the recommendations and regulations were initially set in 1990s. However, there is still a high level of uncertainty due to a lack of data, high uncertainty from animal-model studies, and use of old analytical methods. Moreover, only foods and milk were considered as the sources of copper in human nutrition although drinking water may contain from a few µg/L to several mg/L of copper. Many formulated foods and multi-vitamins are also enriched with essential trace elements including copper, yet current health studies do not include the added copper content in formulated foods, especially infant foods. Furthermore, the emphasis of the health assessment for copper has been on deficiency while new findings have proven that copper deficiency only occurs under a condition of severe malnutrition or rare genetic disorder called Menkes disease.

2.3.1 Recommended daily requirements

The definition of a requirement in human nutrition is the lowest continuing intake level of a nutrient that can maintain a defined level of nutrition in an individual (IOM, 2001). The recommended intake levels for copper from different public health organizations are listed in Table 2.4. However, the numbers presented in Table 2.4 are for slightly different requirement as indicated by the definition of the terms used, such as the Basal Requirement (BR), Normal Requirement (NR), safe and Adequate Intake (AI) and Recommended Dietary Allowance (RDA). Basal Requirement means the level of intake needed to prevent pathologically relevant and clinically detectable signs of a dietary inadequacy; whereas the terms, Normal Requirement (NR), safe and Adequate Intake (AI) and Recommended Dietary Allowance (RDA) represent the level of intake sufficient to maintain a desirable body store or reserve (WHO, 2002). In this case, the NR value was obtained by adding 15% to the average basal requirement to allow for some degree of copper storage (Turnlund, 1994).

Table 2.4 Recommended daily intakes of copper

References	**Year**	**Term**	**Copper intake (mg/day)**			
			Women	**Men**	**Infants**	**Children**
WHO	1996	Basal Requirement	0.6	0.7	NA	0.34
		Normal Requirement	0.7	0.8	0.3	0.38
National Research Council	1989	Adequate Intake	1.5 - 3.0		0.4	1.0 - 2.0
U.S. Institute of Medicine	2001	Recommended Dietary Allowance	0.9		NA	
Australian National Health & New Zealand Ministry of Health	2005	Recommended Dietary Allowance	1.2	1.7	0.2	1.2

As the criterion of nutritional adequacy may differ for individuals at different life stages, it is important to review the reference values at each different life stage (i.e. infant, adolescent, adult). For adults, the recommended copper intake levels range from 0.7 to 3.0 mg/day, and for infants and young children, the values vary between 0.3 and 2.0 mg/day. Regardless, the cumulative amount from drinking water or most of the infant foods may contain higher copper levels than the recommended daily intake.

The recommended intake values were developed based on the few studies listed in Table 2.5 and on unpublished national nutrition survey results. Some of the studies suggest even lower intake levels than the recommendations. For example, the study conducted by Shike (2009) stated that 0.3 mg/day is sufficient to maintain copper balance in a stable 70kg adult. However, the WHO added 40% to that based on the absorption efficiency in the intestine (40-60%) (WHO, 1996a).

Table 2.5 Studies of copper requirement values

References	Year	Term	Copper intake (mg/day)			
			Women	**Men**	**Infants**	**Children**
Mason	1979	Recommended Dietary Allowance	1.0 - 1.5		0.12 - 0.25	1.0 - 2.0
Turnlund	1994	Recommended Dietary Allowance	1.5 - 3.0		0.4 - 0.6	1.0 - 2.0
Trumbo	2001	Recommended Dietary Allowance	0.9		0.2	0.44
Shike	1981	Copper requirements	0.3		0.4 - 0.5	
Shike	2009	Copper requirements	0.3		0.1	0.4

The public health authorities listed recognized the problem of insufficient data, however, the numbers reported are still based on relatively old studies. There was a publication in 2004, the guidelines on mineral requirements in human nutrition by the WHO (WHO, 2004b), but it did not include copper. Since then, these same old studies have been repeatedly referenced.

2.3.2 Levels causing adverse health effects

The safe levels of intake are different from the recommended daily intakes. The terms, Tolerable Upper Intake Level, Upper Limit (UL) and No-Observed-Adverse-Effect Level (NOAEL), are commonly used to indicate the safe level of daily nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population (Trumbo et al., 2001).

In line with the recommended daily intakes, it is important to separately review the safe intake levels for newborn, young children, and adults, since newborn and young children are more sensitive to excess copper than normal adults due to their incomplete copper metabolism. Moreover, the liver of the newborn infant contains over 90% of the body burden, with much higher levels than in adults (WHO, 2004a). As previously mentioned, Indian Childhood Cirrhosis is one of the examples of such a susceptibility due to age. However, except for the WHO document published in 1996, all the other references in Table 2.6 were not able to determine safe levels for infants or young children due to insufficient data, which does not, however, mean that there is no potential for adverse effects.

Table 2.6 Upper safe levels of copper

References	**Year**	**Term**	**Copper mg/day**			
			Women	**Men**	**Infants**	**Children**
Joint Food and Agriculture Organization/WHO	1988	Tolerable Upper Intake Level	30		NA	
National Research Council	1989	Tolerable Upper Intake Level	10		NA	
European Commission	1993	Tolerable Upper Intake Level	10		NA	
WHO	1996	Upper limits of the safe range	12		1.5	3.0
Trumbo	2001	Tolerable Upper Intake Level	10		NA	3.0
Araya	2001	Acute No-Observed-Adverse-Effect Level	0.8		NA	
		Lowest-Observed-Adverse-Effect Level	1.2		NA	
Australian National Health & New Zealand Ministry of Health	2005	Upper limits of the safe range	10		NA	3.0 - 5.0

The safe levels of intake for adults in Table 2.6 vary widely ranging from 0.8 to 30 mg/day. The study by Araya (2001) proposes the NOAEL at 0.8 mg/day, which is more than 10 times less than the one suggested by the WHO. This can be explained by the different source for copper used in the assessment. All the references listed in Table 2.6 used the dietary sources for copper, whereas in Araya's assessment, drinking water was used as the source of copper. The WHO stated that inorganic copper ingested in water or as a supplement should be distinguished from organic copper in foods, because a few milligrams of ingested inorganic copper salts can provide stronger adverse health effects than much higher quantities of organic copper (WHO, 1996a). Later, several authors investigated the difference between the ingestion of inorganic and organic copper (Brewer, 2008; Pal et al., 2014; Rosborg, 2016; Salmenperä et al., 1989; Sparks et al., 2006). It was concluded that the safe levels of copper in drinking water has to be set differently from the dietary intake levels and with more caution.

2.3.3 Guidelines for copper in drinking water

As food and water are the primary sources of copper exposure in places where copper is used as a plumbing material, the public health organizations have set the limits to permissible copper concentrations in drinking water supplies. Table 2.7 shows drinking water guideline values for copper from different organizations or countries. The acceptable copper levels vary from country to country ranging widely from 0.1 to 10 mg/L (Förstner & Wittmann, 2012). The guideline values are categorized into health-based and aesthetics-based. The aesthetic objective for copper is staining acceptability, and Health Canada has only considered the aesthetic objective value for copper in drinking water unlike other health authorities. The WHO guideline value for copper was considered provisional until the 3rd edition of drinking water guidelines (2003) by the Expert Consultation requiring additional evidence. The Consultation stated that intake as low as 2 mg/day from water (about 1 mg/L) could produce an adverse reaction (WHO, 1996b).

Table 2.7 Drinking water guidelines for copper

References	Year	Copper level (mg/L)
Health-based guideline		
US Public Health Service	1962	1.0
Japan	1968	10
Russia	1970	0.1
WHO	1970	0.1
US National Academy of Sciences	1972	1.0
US EPA	1991	1.3
California EPA	1995	1.3
European Commission	-1997	3.0
European Commission	1998	2.0
Australia	1973	10
Australia	Current	2.0
WHO[a]	1993	2.0
WHO[b]	2004	2.0
Aesthetics-based guideline		
US EPA	1991	1.0
California	1995	1.0
Health Canada	1992	1.0
Australia	NA	1.0
WHO	1993	1.0

a. In view of the remaining uncertainties regarding copper toxicity in humans, this guideline value is considered provisional, based on an old unpublished study in dogs

b. Not provisional, based on tolerable upper intake level (UL) of 10 mg/day

The values in drinking water guidelines for copper do not consider the differences in copper metabolism in the neonate or young children, although there has been some concern regarding the involvement of copper from drinking water in early childhood liver cirrhosis in bottle-fed infants since 1980s (Klass et al., 1980; Müller-Höcker et al., 1987; Spitalny et al., 1984). The WHO guideline published in 1993 also mentioned that long-term ingestion could give rise to liver cirrhosis. However, the current guideline values are mostly based on acute toxicity studies (GI symptoms).

Typically, copper intake through diet accounts for the majority of one's daily copper intake, but the inorganic form of copper from drinking water may have significant impacts on health at much lower quantities (Brewer, 2008; Rosborg, 2016; WHO, 1996a). With the remaining uncertainty regarding copper toxicity in humans, the current guideline values for copper raise some important questions: (1) RDI and UL studies emphasize the difference in susceptibility of infants and young children compared to adults, however drinking water guideline values do not take into account. For example, 2 mg/L is too high for infants and young children considering the RDI and UL values listed above between 0.2 and 0.4 mg/day, (2) The WHO as well as other studies stated the potential of high risk with inorganic copper from drinking water. However, most studies used by the WHO in the development of guidelines consider only dietary sources of copper and (3) it is unclear what the basis is for the much quoted guideline of 2 mg/L.

2.4 Copper in drinking water

Copper has been widely used for the distribution of potable water due to its corrosion resistance and cytotoxic effect on bacterial contamination (Feng et al., 1996). Natural copper concentrations in drinking-water sources are at the level of a few micrograms per litre (Reisman et al., 1987). However, copper levels in drinking water are much higher due to the use of copper pipes for plumbing, copper service lines and the copper in brass fittings in the distribution system. Despite its corrosion resistance, copper corrosion does occur under normal drinking water conditions. Corrosion control has been accomplished by adjusting the water quality parameters of finished water, in terms of pH and alkalinity. However, corrosion processes can become more complex depending on the condition of the distribution system (e.g. pipe material, pipe age). Infrastructure corrosion factors are very site-specific and are not consistent within the distribution system so it is very difficult to control for corrosion at the plant based on monitoring at the point of consumption, the tap.

2.4.1 Corrosion process

The process of metal corrosion is a reduction-oxidation reaction. Copper corrosion results in copper oxidization at the pipe surface. The oxidation product is either incorporated as a solid onto the pipe surface, forming a scale, or is released into solution as a corrosion by-product in an electrochemical process. Minor impurities and variations, occurring in all metal pipes, can cause one point on the pipe to act as an electrical anode with another point acting as an electrical cathode. At the anode, atoms of copper from the pipe ionize, going into solution in the water, and lose one or two electrons, which travel through the pipe to the cathode. Chemical reactions then occur in the water to balance the electrical and chemical reactions at the anode and cathode (AWWA, 2009). The water molecules (H_2O) will dissociate into H^+ ions and OH^- radicals. The copper atoms released at the anode will combine with OH^- radicals to form $Cu(OH)_2$. Two H^+ ions near the cathode will pick up the two electrons originally lost by the copper atom, and bond together as H_2, hydrogen gas. The formation of $Cu(OH)_2$ leaves an excess of H^+, and the formation of the H_2 leaves an excess of OH^- near the cathode. This change in the distribution of H^+ and OH^- increases the rate of corrosion causing pitting in the anode area (Revie & Uhlig, 2008).

2.4.2 Types of corrosion

Corrosion in water systems can be categorized into two groups: localized and uniform. The most common type of corrosion is localized corrosion, which attacks metal surfaces unevenly. It is a more serious problem as it can lead to a more rapid failure of the pipe (Lytle & Nadagouda, 2010). The two types of localized corrosion are galvanic corrosion and concentration cell corrosion. Galvanic corrosion is described in the section below. The concentration cell corrosion process involves an electrolyte. Where the parts of the metal surface are in contact with different concentrations of electrolyte, localized corrosion occurs. Dissolved oxygen plays a key role in this type of corrosion since corrosion is enabled when oxygen comes into contact with a wet metal surface (AWWA, 2009). Uniform corrosion occurs where the water has very low pH and low alkalinity, and it corrodes the metal surface evenly. The key factors leading to uniform copper corrosion and copper release are pH, alkalinity, and plumbing age.

2.4.3 Corrosion control in drinking water distribution systems

Many water systems are now required to provide corrosion control treatment under federal or provincial regulation (e.g. Lead and Copper Rule, US EPA) enacted to protect the public from the health dangers of trace metals (USEPA, 2007). Common practices for corrosion control are the adjustment of pH or alkalinity and dosing the water with corrosion inhibitors such as silicate or orthophosphate (Tam & Elefsiniotis, 2009). However, complicated interactions often occur due to the treatment process, because a simple change to improve one characteristic for controlling corrosion problems may have an adverse effect on some other water characteristic or treatment process (Ahmad, 2006). In addition, there are many site-specific conditions involved in the corrosion process, which make it even more complex. As a result, it is difficult to determine what combinations of water will or will not have corrosion problems.

The importance of corrosion control was recently seen in Flint water crisis (Pieper, Tang, & Edwards, 2017). In Flint, the water utility did not implement corrosion control when the source water was change to a more acidic source. Initially the changes in the water chemistry did not seem harmful, however, it caused a deterioration of the metal scale on the pipes resulting in a release of lead (and likely copper) into the water supply. Corrosion of the pipes is likely also the cause of high copper and lead levels found in Detroit schools in August 2018 (Linkins, 2018) and in private homes in B.C. in September 2018 (Cruickshank, 2018). Both field and bench-scale investigations quantified the corrosion potential to enable the water utilities to implement the necessary corrective strategies. This section presents an overview of important factors in the control of corrosion.

2.4.3.1 Alkalinity and pH

Alkalinity and pH are among the few water quality parameter that can be controlled during water treatment to reduce the impact of corrosion. The pH of the water alters the equilibrium potential of the oxygen reduction half-reaction by changing the form of copper. Generally, a lower pH is known to increase corrosion rates and, hence, copper release. Alkalinity measures the water's buffering capacity, which is its ability to maintain a stable pH. The lower the alkalinity, the more likely the water is to become corrosive as pH levels are easily changed. The highest copper solubility was observed at very low alkalinities (<25 mg CaCo3/L) (Shock, 1995).

However, high alkalinity waters can be also problematic, and become aggressive towards copper pipes (Schock & Sandvig, 2009). The type of scale formed on copper pipes can affect the alkalinity levels associated with copper release (Edwards, Hidmi, & Gladwell, 2002). The rate of copper corrosion at high alkalinity levels is complex being a function of several other factors and is not yet fully understood.

Water with a pH below 6.5 is generally considered corrosive, especially if alkalinity is also low. At a pH above 7.5, it can be corrosive if alkalinity is low (Merkel, 2004; Revie & Uhlig, 2008). Currently, the Canadian drinking water quality guideline has an aesthetic objective for pH of between 6.5 and 8.5. In fact, the range of pH for most potable water is between 7.0 and 8.5 (Edwards, Schock, & Meyer, 1996). However, for alkalinity, there is no guideline value, although US EPA stated that the ideal range for alkalinity is between 100 - 200 mg/L as $CaCO_3$ to prevent metal corrosion in water (USEPA, 2007). Therefore, it is important to investigate corrosion behaviour within these ranges of pH and alkalinity.

Based on bench-scale experiments, a linear relationship between copper release and alkalinity was shown over the pH range of 7.0 - 8.5 (most tap water) (Edwards et al., 1996). For example, copper release increased to a level higher than the EPA's action level (1.3 mg/L) as the alkalinity level increased up to 273 $CaCO_3$ mg/L within the pH range of normal tap water (Grace, Lytle, & Goltz, 2012). Several other studies also demonstrated increased copper corrosion at higher alkalinity at pH values between 7.0 - 8.0 (Broo, Berghult, & Hedberg, 1997; Edwards et al., 1996; Ferguson, 2017; Schock, Lytle, & Clement, 1995). This linear relationship was stronger in the water that does not form insoluble malachite scale (Arnold, Griffin, & Edwards, 2012). With an alkalinity ranging between 100 and 150 mg/L for $CaCO_3$, copper leaching was observed to increase as the pH decreases, and the rate of copper leaching reached the lowest value at pH 9.0 (Tam & Elefsiniotis, 2009). In the higher ranges of pH, the prediction of copper solubility had a weak dependency on alkalinity potentially due to an underestimation of copper carbonate complexes at higher pH. In virtually all drinking water, some dissolved inorganic carbonate is present because Cu^{2+} forms several very strong and some weaker aqueous complexes with carbonate species such as HCO^{3-}, CO_3^{2-}. These carbonate complexes becomes more important as the pH increases (Schock et al., 1995). This results in trends in corrosion rates not always being a linear function of alkalinity or pH. However, it is important to note that, over the typical pH range of tap water, the copper release increased consistently with higher alkalinity.

2.4.3.2 Adjustment of pH and alkalinity

A common practice for reducing corrosion is a moderate increase in pH and alkalinity levels. Increasing the pH can result in the formation of a protective film on the interior of copper pipes reducing copper release. The adjustment of the pH or alkalinity is usually determined based on both the chemical characteristics of the source water and the effects of other treatment processes being used (e.g. gaseous chlorine reduces pH levels) (AWWA, 2009). Lime is usually used to increase pH levels. In highly alkaline water, the corrosion inhibitor orthophosphate is added to remove bicarbonate (AWWA, 2009). When the formation of the less soluble scales such as malachite and tenorite is favoured, higher alkalinity can reduce the concentration of copper in the water (Schock et al., 1995). In this case, sodium carbonate or soda ash are added in addition to lime to insure the increase in alkalinity. However, the addition of lime to the water may cause severe scale problems. This is corrected through recarbonation, the addition of carbon dioxide or sulfuric acid, to lower the pH so that calcium carbonate will not precipitate (Revie & Uhlig, 2008). In summary, both pH and alkalinity must be adjusted together to control corrosion.

2.4.3.3 Temperature

Since chemical reactions occur more quickly at higher temperatures, it has been suggested that corrosion is more likely and more rapid at higher water temperatures (AWWA, 2009). In a survey of copper leaching in residential and high-rise plumbing, water from cold taps contained about one-third of the copper concentration measured in hot water taps (Singh & Mavinic, 1991). Likewise, reduced corrosion rates were observed in soft water at lower temperature in a survey of corrosion inhibitors (MacQuarrie, Mavinic, & Neden, 1997).

However, under specific combinations of water quality parameters, high temperatures have been observed to decrease copper corrosion (Boulay & Edwards, 2001; Edwards, Jacobs, & Taylor, 2000). This has occurred under conditions of blue water (Edwards et al., 2000) and under stagnant conditions with temperatures as high as 64℃ possibly due to the killing of microorganisms (Arens et al, 1995). In another case, the cold water plumbing had a pitted surface whereas the hot water one did not (Lytle & Nadagouda, 2010). It was postulated that water temperature may impact the rate of pipe aging, and in some cases, the scale forming in the hot water pipes may be the more stable and less soluble forms of copper (e.g. malachite at a low pH, tenorite at a high pH). In general, hot water is more likely to results in an increased release of copper corrosion by-product than cold water (Boulay & Edwards, 2001).

2.4.3.4 Corrosion inhibitors

Several types of phosphate corrosion inhibitors (e.g. orthophosphate, zinc orthophosphate, polyphosphates) are used to decrease copper release in copper pipes, the most common being orthophosphate and polyphosphate. Addition of orthophosphate results in the formation of a $Cu_3(PO_4)_2$ or similar scale on the surface of the copper pipe (Edwards et al., 2002). This scale has lower solubility than the fresh $Cu(OH)_2$ scale formed in relatively new copper plumbing. However, the effectiveness of using orthophosphate varies depending on the pH level, and its effectiveness is believed to be limited to $pH < 8.0$ (Tam & Elefsiniotis, 2009). It has also been argued it may not be of long term benefit (Schock & Sandvig, 2009; Tam & Elefsiniotis, 2009) as the minimum copper levels achievable may be substantially higher than what would have been achieved through natural aging of the copper pipes and formation of malachite or tenorite scales that have a lower theoretical copper solubility (Schock & Sandvig, 2009). There is still uncertainty about how orthophosphate acts as an inhibitor under all conditions.

There is still less knowledge about effects of polyphosphates on copper leaching and a concern due to its theoretical potential to increase the leaching of lead (Edwards et al., 2002). It is still unproven whether polyphosphate is a better or worse inhibitor than orthophosphate. Regardless of the types of inhibitor, the addition of a corrosion inhibitor can complicate the role of pH and alkalinity in copper release, thus, utilities need to take account all three factors (e.g. pH, alkalinity, corrosion inhibitor) in corrosion control.

2.4.3.5 Type of pipe material

Copper is one of the least corrosive metals used for pipes (AWWA, 2009). The water distribution system contains pipes made of different metals that are in electrical contact with each other. When dissimilar metals are electrically connected, the more corrosive metal will become the anode, the less corrosive metal will become the cathode and galvanic corrosion will occur (Oldfield, 1988). The rate of galvanic corrosion depends on the difference in the corrosiveness of the metals. The larger the difference the more rapid the corrosion of the anode. For example, when a brass alloy connects a copper service line to a cast-iron main, the copper will be protected at the expense of the brass and cast iron. (Lytle & Nadagouda, 2010).

2.4.3.6 Age of the piping

Copper dissolution depends greatly on the type of scale formed, which is a function of the age of the pipes. The more stable scales such as malachite and tenorite are more commonly found in older pipes. It has been observed that copper release decreases with increasing age of the piping (Edwards & McNeill, 2002; Lagos, Cuadrado, & Letelier, 2001), while the highest corrosion rates and solubility are most often associated with the newest piping. Therefore, plumbing age needs to be included in the consideration of the adjustment of water quality parameters for corrosion control (Schock et al., 1995).

Most of these studies reviewed above were bench-scale or pilot experiments using new pipes in short term experiments. The results are not applicable to aged pipes in the field (Lytle & Nadagouda, 2010). In addition, the use of phosphate inhibitors may prevent the formation of the stable scales in the long term causing old pipes to release high levels of copper into the water (Arnold et al., 2012; Edwards et al., 2002; Schock & Sandvig, 2009). The US EPA Lead and Copper Rule compliance is applied to older buildings, those built after 1982 and before 1988. Since older pipes are likely to have lower corrosion rate and solubility, the Lead and Copper Rule compliance may underestimate copper exposure (USEPA, 1991).

2.4.3.7 Stagnation time of the water

Copper release can be affected by different flow conditions, stagnant and flowing. In a bench scale study with water, at constant pH and alkalinity, flowing in new copper pipes copper release increased during the first 24 hr, after which it reached an equilibrium state (Tam & Elefsiniotis, 2009). Copper levels vary over time, depending on oxidant levels (Lytle & Schock, 2000). Copper levels increased with the stagnation time but only until dissolved oxygen fell below 1 mg/L, after which the concertation of copper dropped significantly. Maximum copper concentrations occur when the oxidant level is less than 1 mg/L (Sorg, Schock, & Lytle, 1999). The rate of decreases depends on the softness of the water. Therefore, copper concentration increases with stagnation time but it may vary with water quality and plumbing characteristics.

Flushing, letting the tap run at full flow, is often recommended by the public health authorities as a mitigation strategy to reduce copper concentrations in water. It is generally accepted that longer flushing times result in lower copper concentrations. However, flushing the cold water tap for a few minutes may not be sufficient to reduce the levels of copper depending on the quality of water, stagnation period and length of piping (Barn et al., 2014; Murphy, 1993). Therefore, periodic flushing throughout the day or extensive flushing following a long stagnation period may be recommended.

2.4.3.8 Flow rate

The velocity of water (flow rate) can affect the corrosion rate depending on the water characteristics. For example, if the water is acidic, higher flow rate can cause turbulent conditions that bring dissolved oxygen to the corroding surface more rapidly, which increases the corrosion rate (AWWA, 2009). The flow velocity is determined by the shape of fittings, the diameter of the lines, etc. However, copper release solely caused by flow velocity is not considered as a corrosion problem but as poor system design causing leaks.

2.5 Previous studies on copper levels in drinking water

There have been many reports on copper-induced disease, and in some of the cases, the patients were exposed to excess copper through drinking water contaminated with copper, see Table 2.3. The concentration of copper in theses cases varies widely ranging between 0.15 and 26.4 mg Cu/L. Considering the WHO's guideline value (2 mg/L) and US EPA's action limit (1.3 mg/L), the results presented in Table 2.3 are of great concern. It is important to note that the affected subjects were infants or young children showing gastrointestinal symptoms and hepatic problems. Note that there is difficulty in obtaining representative copper levels as they depend on time of sample collection, changes to water chemistry, and the types of pipes. Therefore, it is not easy to obtain representative copper exposure levels from sampling locations for corrosion monitoring systems (Arnold et al., 2012). It is likely that copper exposure is underestimated in the studies in Table 2.3.

Table 2.8 Surveys of copper levels in drinking water

References	Location	No. of sampling locations	Exposure level (mg Cu/L)
Kenneth (1984)	Vermont, USA	1	7.8
Knobeloch (1994)	Wisconsin, USA	NA	1.6 - 7.7
Buchanan (1994)	Nebraska, USA	148	1.3 - >3.0
Fewtrell (1996)	UK	14	3.1 - 26.0
Scheinberg (1996)	Messachusetts, USA	60	8.5 - 8.8
Stenhammar (1999)	Sweden	3	0.22 - 1.1
Dieter (1999)	Germany	103	9.0 - 26.4
Zietz (2003)	Lower Saxony, Germany	1674	0.18 - 6.4
Barn (2014)	British Colombia, Canada	48	0.4 - 10.7
Harvey (2016)	New South Wales, Australia	212	0.15 - 3.8

3 METHODOLOGY

The framework used for the critical assessment of the development of drinking water guidelines for copper is provided. The field study, used to obtain and analyze drinking water samples in institution buildings, is described in terms of the sampling locations, the sampling methods and the analytical methods used.

3.1 Review of the scientific basis for copper levels in the drinking water guidelines

First, the scientific basis used in the development of copper guideline values is reviewed. The drinking water standards set by the WHO and the US EPA are investigated as they are the most referenced authorities and were the first involved in the development of copper guidelines. In addition, the document *Public Health Goal for Copper in Drinking Water* by California Environmental Protection Agency (CEPA, 2008) is reviewed as it proposed the most stringent regulatory levels for copper and the document *Copper in Drinking Water* published by Health Canada (1992) is reviewed as it presents the justification for the guideline levels used in Canada. The reports used in the establishment of guideline values are critically evaluated based on the following three aspects:

1. The tolerable daily intake value (TDI: an estimated ingestion rate that is safe over a lifetime) and the uncertainty factor are the two main factors used to set the guideline levels. Therefore, the scientific basis used in the development of these factors is investigated.
2. Since dietary sources are generally considered to be the cause of acute effects of over exposure while drinking water sources are considered to be the cause of chronic effects, the end-points used in the reports are examined to determine if they are acute or chronic symptoms. If the end-points are acute-phase symptoms, the method used to produce chronic exposure guideline values from acute phase data will be investigated.
3. Infants and small children are much more susceptible to excess copper than healthy adults due to their high copper absorption rate and immature biliary excretion system. Therefore, it is important to investigate whether the differences in metabolic capacities at each life stage (e.g. infants, young children, pregnancy, adults) are considered in the development of the guidelines levels for copper.

3.2 Field survey

The review of the literature indicated that it is difficult to predict whether and to what extent copper is leached from the drinking water distribution system and difficult to design effective strategies to reduce or eliminate copper from drinking water. It is therefore necessary to measure in the field the copper levels in the drinking water at the point of consumption. The field survey, therefore, measured the concentration of copper in institutional buildings drinking water taps and fountains at different times during a typical school/work day. The collection of the samples took place from November 2nd to 16th, 2018.

3.2.1 Sampling sites

Water samples were collected from buildings in the downtown campus of McGill University located in the city of Montreal in Quebec, Canada, as listed in Table 3.1.

Table 3.1 Building information

Building name	**Year of construction (renovation)**	**Copper plumbing materials**
Arts Building	1843	Maybe
Macdonald Harrington	1896 (under renovation)	Not identifiable
Macdonald Engineering	1907 (1998)	Yes
Frank Dawson Adams Building	1951	Yes
McConnell	1958	Not identifiable
Macdonald/McConnell	1959 (2010)	Maybe
McLennan Library	1967	Not identifiable
Burnside Hall	1970	Yes
Wong Chemical	1996	Yes
Brown Building	1999	Maybe
Trottier Building	2004	Yes

The year of construction was obtained from the McGill University website. As several buildings have been renovated, the year of renovation was obtained from the staff at McGill (verbal communication). Macdonald Harrington building is currently being renovated.

3.2.2 Piping materials

The information on piping materials used in the buildings tested was not available. However, visual inspection allowed the piping material at some outlets tested to be identified (Table 3.1). Some of the pipes at the sampling locations were covered by a plastic or stainless steel sheath, and piping materials were not identifiable by visual inspection (listed as *Not Identifiable* in Table 3.1).

On the surface of some of the sheathed pipes, blue stain was observed, indicating the likelihood of copper plumbing materials (listed as *Maybe* in Table 3.1).

Figure 3.1 Visual inspection a) copper, b) maybe, c) not identifiable

In North America, the use of copper plumbing materials has been very common since the Second World War (1945) replacing lead lines, cast iron and galvanised steel pipes and copper is still being installed today. Plastics have also been used, as they are cheaper and easier to install (about 1/3 the price), since the 1950's for PVC and since the 1990 for PEX. Provincial building codes endorse the use of these materials providing regulations for the installation of copper, PVC and PEX plumbing ("The Ontario building code", 2017). The majority of the buildings tested in this study were built before the 1970s, and so are likely to have copper plumbing as that was the most commonly used plumbing material at the time, in addition copper plumbing is considered more durable. Copper tube and fittings have 50 - 70 years of life expectancies depending on the water chemistry. After its lifespan, the chance of pinhole leaks in the copper plumbing increases, and pitting corrosion is more likely to results in pinhole leaks. Therefore, buildings older than 70 years in Table 3.1 likely have old copper plumbing that has been oxidized and hence has a scale on the inside which reduces dissolution, but which may either flake off or corrode. Buildings that have been renovated have likely had their old copper plumbing removed (which likely also had lead solder) and new copper piping installed (using solder without lead).

3.2.3 Water outlets

As the aim was to sample at points of consumption of drinking water, samples were collected from kitchen taps, washroom taps, and water fountains in each building. There are two types of water fountain: regular water fountains without a filter, and new bottle-filling water fountains with filters. Figure 3.2 presents examples of water outlets from which water samples were collected.

Figure 3.2 Examples of water outlets from which water samples were collected. a) water fountain with filter, b) regular water fountain, c) newer sink, d) older sink

The water fountains selected for sampling were high-use fountains to improve the representation of typical exposure levels. The other water outlets (washroom taps, kitchen taps) were randomly selected and samples were taken from one cold water tap per sampling location. If a blue stain was observed in a sink, indicating of copper leaching (Figure 3.3), that tap was selected for sampling.

Figure 3.3 Blue stains in sinks due to leaching of copper

In the subsequent analysis, the water outlets were categorized into two groups: outlets with filters and outlets without filters.

Outlets with filters	Bottle-filling water fountains
Outlets without filters	Washroom taps, kitchen taps, regular water fountains

3.2.4 Sample types

The range of copper levels in the drinking water was observed by taking the samples at different time of the day and different days of the week. This tested the impact of stagnation time and flushing on the concentration of copper in the drinking water. Samples were collected as first draw samples and after one-minute flush after weekend stagnation and weeknight stagnation, and as mid-day samples (at lunchtime, approximately 3-5 hr after the first-draw samples). The types of samples are summarized in Table 3.2.

Table 3.2 Sample types

Type of sample	**Description**
Weekend stagnation	First draw sample on Monday morning after weekend stagnation
Weekend stagnation flushing	1-min flush immediately after collection of weekend stagnated sample
Weeknight stagnation	First draw sample in the morning between Tuesday and Friday
Weeknight stagnation flushing	1-min flush immediately after collection of weeknight stagnated sample
Mid-day	Typical daytime samples around lunchtime

3.2.5 Sample collection, preservation, and analysis

Samples were collected in 125ml wide-mouth glass bottles. Temperature and pH were measured at the time of sampling using a pH 6+ meter kit (Cole Parmer Oakton). Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES) was used for the determination of copper concentrations following the drinking water quality analysis protocols established by the US EPA (USEPA, 2002, 2005). Immediately after the sample was collected, it was preserved by adding 3.5 mL of 5% nitric acid solution to reduce the sample pH to less than 2 to ensure metal dissolution. Following acidification, each sample was mixed, held for at least 24 hours, and then verified to ascertain that the pH was less than 2 prior to analysis for copper. The ICP-OES (Agilent Technologies, 5100) at the Centre de recherche NanoQAM in the Chemistry Department at I'Université du Quebec à Montréal is used for copper analysis. To avoid interference from iron in water, wavelengths of 327.395nm, 324.754nm, 213.598nm, and 223.009nm were selected. The ICP-OES was calibrated using one blank and six copper standard solutions at different concentrations (0.1ppm, 0.2ppm, 0.5ppm, 1ppm, 2ppm, 5ppm). A volume of 3.5 ml of 5% nitric acid solution was added to the blank and to each of the standard solutions. Triplicates for each sample are analysed for quality assurance. Blind split samples were sent to the Eurofins Scientific laboratory (commercial certified laboratory) to check accuracy of the analysis.

4 RESULTS AND DISCUSSION

4.1 Review of drinking water guidelines for copper

Copper is a metal that is toxic at relatively low levels. Drinking water can be a major source of copper exposure depending on the plumbing material used and the characteristics of the water (water quality parameters). Guidelines for copper concentrations permissible in drinking water were originally set on an aesthetic basis (taste, colour, discoloring of laundry), and there are still countries, in which copper is only an aesthetic concern (e.g. Canada). The development of the drinking water quality guideline values for copper set by the WHO and the US EPA were investigated as the WHO and US EPA are the principal health authorities referenced by other countries. The guideline value for copper levels in Canada is also briefly reviewed. The technical support document from the California Environmental Protection Agency (CEPA) is reviewed, as it is a comprehensive document, and set the most stringent guidelines for copper in drinking water for the state of California. This review assesses both the quality of the data used to set permissible levels and the methodology used to determine permissible levels in drinking water for humans.

4.1.1 WHO

The oldest available WHO's drinking water guideline for copper dates from 1993. A concentration of 2 mg/L of copper was proposed as a provisional health-based guideline value in drinking water. This provisional value was derived as follows:

$$\begin{aligned}&Guideline\ value\\&=\frac{maximum\ tolerable\ daily\ intake \times \%\ daily\ intake\ from\ drinking\ water \times body\ weight}{adult\ daily\ water\ consumption}\\&=\frac{0.5\ mg\cdot kg^{-1}\cdot d^{-1}\times 10\% \times 60\ kg}{2\ L/d}=1.5\ mg/L\ \approx 2\ mg/L\ (rounded\ up)\end{aligned}$$

The WHO used default values of 60 kg and 2L for average adult body weight and daily water consumption. They also allocated 10% of the maximum tolerable daily intake to drinking water (WHO, 1993). However, the portion of daily intake originating from drinking water can vary widely between individuals depending on their diet and health condition. Rounding up from 1.5 mg/L to 2 mg/L may seem minor yet represents an increase of 33%, which may be significant considering the narrow safety margin between sufficient copper and copper overload.

The provisional maximum tolerable daily intake value (TDI) of 0.5 mg/kg of body weight is interpreted as an estimate of the amount of copper that can be ingested daily over a lifetime without any considerable health risk. The TDI value was based on the lowest-observed-adverse-effect-level (LOAEL) obtained from a small-scale unpublished study on 12 Beagle dogs (Shanaman, Wazeter, & Goldenthal, 1972). Only a short poorly reported summary of this study is available. According to this summary, chronic symptoms were the endpoint of the dogs study. However, toxicity testing on dogs is not acceptable because dogs have a different form of albumin, which is one of the major copper transporter proteins of the blood, to that of rats and humans. Moreover, dog albumins have a low number of affinity sites for copper, and dogs have unusually high levels of copper in the liver compared to humans. Therefore, dogs are not a good animal model risk assessment of copper for humans. In this study, copper gluconate was dosed at three different concentrations; 3, 15, and 60 mg copper gluconate/kg body weight/day for 6 to 12 months. After one year, minimal liver function changes were reported from only one of the dogs exposed to the highest tested dose (60 mg copper gluconate/kg bw/day). As a result, the second highest dose of 15 mg/kg bw/day of copper gluconate was proposed as the no-observed-adverse-effect-level (NOAEL). However, in the summary of the study and as reported by WHO, 5mg copper/kg body weight was stated as both NOAEL and LOAEL (WHO 1982). After communicating directly with Shanaman, Fitzgerald (1995) identified a transcription error in the summary of the study, the dosage had been recorded as copper and not as copper gluconate. Therefore, the copper-equivalent doses calculated based on the actual doses of copper gluconate (of 3, 15 and 60 mg/kg bw/day) are 0.42, 2.1, and 8.4 mg copper/kg bw/day (see the example calculation below).

$Molecular\ weight$:

$C_{12}H_{22}CuO_{14}\ (copper\ gluconate) = 453.84\ g/mol\,, Cu = 63.55\ g/mol$

$Copper - equivalent\ doses$:

$$\frac{63.55\ g\ Cu/mol}{453.84\ g\,\frac{C_{12}H_{22}CuO_{14}}{mol}} \times 60\ mg\ copper\ gluconate/kg\ bw/day$$

$$= 8.40\ mg\ Cu/kg\ bw/day$$

Based on the corrected doses, the NOAEL should be 2.1 mg Cu/kg bw/day. Unaware of these errors, WHO has used 5 mg Cu/kg bw/day for the calculation of copper guideline level.

With a 10-fold reduction for inter-species variation, 0.5 mg Cu/kg bw/day was obtained for humans. The 10-fold uncertainty factor was used as a "margin of safety". However, using a 100-fold factor is the standard practice for extrapolating from short duration animal toxicity data to safe levels for life-time human exposure (Dankovic et al., 2015; Lehman & Fitzhugh, 1954). The WHO also listed several circumstances in which uncertainty factors need to be used: when the data are not sufficient to fully account for variability of populations; when the data are obtained in studies of insufficient duration to assure chronic safety, etc (WHO, 2002). An uncertainty factor of 10 is applied in each circumstance. In this study on dogs, at least two of these criteria are met resulting in an uncertainty factor of 100. Although applying a 100-fold uncertainty factor is still an empirical rule-of-thumb, when the standard uncertainty factor is not used, the authorities should at least be required to provide a scientific explanation or justification for the modification. Using the correct NOAEL value and a 10-fold reduction gives a lower TDI value of 0.21 mg Cu/kg bw/day, and the guideline level becomes 0.6 mg Cu/L.

$$\boxed{Revised\ guideline\ value = \frac{0.21\ mg \cdot kg^{-1} \cdot d^{-1} \times 10\% \times 60\ kg}{2\ L/day} = 0.6\ mg/L}$$

If a 100-fold reduction is used, the TDI is 0.021 mg Cu/kg bw/day and the guideline level is 0.06 mg Cu/L.

$$\boxed{Revised\ guideline\ value = \frac{0.021\ mg \cdot kg^{-1} \cdot d^{-1} \times 10\% \times 60\ kg}{2\ L/day} = 0.06\ mg/L}$$

The WHO guideline document emphasizes that acute copper toxicity caused by drinking water results in gastrointestinal symptoms. However, the acute toxicity data was not used in the development of a copper guideline by the WHO in 1993. The WHO document also briefly discusses the possibility of long-term ingestion of copper from drinking water causing early childhood liver cirrhosis and adult hepatic problems. Again, this was not taken into account in the development of the guideline values.

In 1996, the WHO included two additional long-term exposure animal studies in the discussion for the development of the guideline copper levels. The end-points tested in these animal-model experiments were liver function changes. The first study, conducted on rats for 2 years, resulted in a TDI of 160 mg/kg of body weight per day, and the second study, a 16-month rabbit study, resulted in a TDI value of 12 mg/kg of body weight per day as reported in (FAO/WHO, 1988). A comparison of the TDI values of rats and rabbits clearly indicates that there is an interspecies difference in tolerance to copper loads. There is currently no evidence to indicate how human tolerance to copper compares to that of rats, rabbits or dogs. Therefore, it is unclear how these values should be adjusted to be relevant to humans. If these TDI values are reduced using an uncertainty factor of 100 (to be applied to humans), it would result in calculated guideline values of 4.8 mg/L (rats are known to have a high tolerance of toxic substances) and 0.36 mg/L, respectively. Although these studies were discussed, the WHO document (1996) did not use them to modify the previous guideline value, based on the study of 12 beagle dogs (and the transcription error in the data), so the recommended value of 2 mg/L was kept.

In 1996, the WHO also established a maximum safe level of ingestion of copper for adults of 12 mg/day. The upper safe level of 12 mg/day is a 1700% increase of the basal requirement of 0.7 mg/day. The basal requirement of copper was obtained from the copper-responsive clinical and biochemical changes that occur when copper intake was low (WHO, 1996a). It was also stated that the upper safe level was based on only dietary copper, although it was stated that the upper safe level of inorganic copper (e.g. drinking water) might be less than that in food. If one used the correct NOAEL from the beagle dog study to estimate a TDI value for humans, it would give a maximum daily intake of 12.6 mg for adults (= 2.1mg/kg x 60 kg/10). Using this upper limit value for copper, the guideline value becomes:

$$Revised\ guideline\ value = \frac{12\,mg/day \times 10\%}{2\ L/day} = 0.6\ mg/L$$

It was remarked that the guideline value of 0.6 mg/L was provisional in view of the remaining uncertainties, and therefore the previously established guideline value of 2 mg/L was retained as a provisional value until 2004.

In 2004, the WHO finally decided that the study on 12 beagle dogs could not be considered an appropriate model for humans, but was only helpful to establish a mode of action for the response as the dog showing hepatic symptoms was treated (WHO, 2004a). Instead, the WHO adopted the conclusions published by the International Programme on Chemical Safety (IPCS, 1998). IPCS concluded that the upper limit of the acceptable range in adults is uncertain but is most likely above

2 or 3 mg/day. This conclusion was based solely on studies of acute gastrointestinal symptoms due to copper-contaminated drinking water. Using these, the WHO concluded that the provisional guideline value of 2 mg/L should be protective against the adverse effects of copper (considering acute symptoms) and would provide an adequate margin of safety for those who are more susceptible to copper toxicity (e.g. infants, young children). The studies, which IPCS used to establish the upper limit of 2-3 mg/L, are listed in Table 4.1.

As shown in Table 4.1, the majority of the studies were conducted by the same research group at the University of Chile, and the design of the experiments were similar with the similar results and conclusions. Moreover, these studies focused only on acute symptoms in the form of gastrointestinal effects, although the previous guideline had pointed out the need to include chronic symptoms (e.g. hepatic problems). Two of these studies considered total serum copper levels which is not an indicator of chronic copper toxicity, as it is the non-ceruloplasm bound copper that is the toxic form and the indicator required (Hoogenraad, 2006; McMillin, Travis, & Hunt, 2009; Squitti et al., 2005).

The experimental studies conducted by the University of Chile can lead to misinterpretation because the daily copper intake (mg Cu/day) is not provided explicitly. This information can be calculated from the concentration of the copper in the water (mg Cu/L) and the quantity of water consumed (200 ml). For example, in Araya's study (2001), gastrointestinal effects were observed with 200 ml of 6 and 8 mg Cu/L, given once per week for 5 weeks. An acute NOAEL and LOAEL of 4 and 6 mg Cu/L were incorrectly declared, as although the concentration of the copper dosed water was 4 and 6 mg/L only 200 ml were consumed resulting in a total copper ingestion of 0.8 mg Cu/day and 1.2 mg Cu/day. Note that 1.2 mg/day is 1.5 times greater than the basal requirement, thus a relatively small increase caused by the very narrow range between a sufficiency and an excess of copper. Given the default volume of water consumption for adults of 2L, if Araya's NOAEL is used, the guideline value is calculated as,

If only 10% of copper is assumed to come from drinking water as WHO set 10% as the default value for allocation of TDI from water,

$$\boxed{Revised\ guideline\ value = \frac{1.2\, mg/day \times 10\%}{2\ L/day} = 0.06\ mg/L}$$

If 100% of copper is assumed to come from drinking water since the LOAEL was obtained from an exposure study where copper was dosed through drinking water,

$$\boxed{Revised\ guideline\ value = \frac{1.2\, mg/day \times 100\%}{2\ L/day} = 0.60\ \ mg/L}$$

Furthermore, the 2004 WHO guideline value did not take into account the differences in copper metabolism between the neonates and adults. It stated, without any supporting evidence, that a concentration of 2 mg/L should provide a sufficient margin of safety for formula-fed infants because their copper intake from other sources is usually low. However, it should be also noted that on a body weight basis, infants drink considerably more water than adults, especially formula-fed infants. This does not consider the additional copper that is added to infant formula (e.g. Similac with 0.6mg/L copper). The fourth, and newest, edition of the WHO guideline for drinking water quality was published in 2011, but the material for copper has not been updated since the 2004 publication (WHO, 2011).

Table 4.1 Studies used for IPCS's copper research

References	Institution	Type of study	Exposed group (age)	Population	Exposure level (Cu)	Duration	Symptoms	Results	Problems
Olivares (1998)	University of Chile	Experimental	Infants (3-12 months)	128	<0.1 mg/L 2 mg/L (varies between 0.1 and 2.4 mg/day)	1 year	Total serum copper analysis, Gastrointestinal symptoms	Reported as no adverse effect at 2mg/L. Total daily copper intake not provided as quantity of water consumed not given.	-Daily water consumption was not identified and hence daily copper load was not reported -Claims only to be verifying the tolerance of infants to the WHO guideline of 2mg/L for drinking water applied to infants. However, this is meaningless as the total daily intake of copper is what is important and it is not specified -It is hard to diagnose GI symptoms for infants -Total serum copper is not a good indicator for chronic toxicity -The high copper exposure groups had higher drop-out rates than the low copper groups (not specified in the study)
Olivares (2001)	University of Chile	Experimental	Adults	61	200 ml of 0, 2, 4, 6, 8, 10, and 12 mg/L (0, 0.4, 0.8, 1.2, 1.6, 2.0, and 2.4mg/day)	once a week exposure for 3 weeks	Nausea, vomiting	Nausia at (200ml of) 2mg/L (NOAEL), vomiting at (200ml of) 4 mg/L (LOAEL)	-Actual NOAEL and LOAEL are 0.4 mg/day and 0.8 mg/day, when taken 1/week -The correlation between GI symptoms and weekly copper exposure is not justified
Pizarro (1999)	University of Chile	Review					Gastrointestinal symptoms	No adverse effect reported at 2mg/L, but total daily copper intake not provided	-No information provided on total daily copper intake. Only providing the concentration of copper in water is insufficient data for assessment -No information on acute toxicity symptoms.
Pizarro (2001)	University of Chile	Experimental	Women (18-55 yrs)	45	5 mg/L of Cu containing different ratios of soluble and insoluble Cu	9 weeks	Gastrointestinal symptoms	40 subjects reported GI symptoms	-Daily consumption of 5 mg/L Cu water not specified, hence copper exposure not provided. -This study claimed to be reporting on whether total copper or soluble copper was the cause of GI symptoms. Important result was that 40 of 45 subjects experienced GI symptoms.

References	Institution	Type of study	Exposed group (age)	Population	Exposure level (Cu)	Duration	Symptoms	Results	Problems
Araya (2001)	University of Chile	Experimental	Adults	179	200 ml of 0, 2, 4, 6, and 8mg/L (0, 0.4, 0.8, 1.2, and 1.6 mg) once a week	5 weeks	Gastrointestinal symptoms	GI effects occurred at (200ml/week) at 6mg/L for NOAEL and at (200ml/week) at 8mg/L for an LOAEL	-Almost same experimental design as Olivares (2001) but the results differ -The actual copper intake is 0, 0.4, 0.8, 1.2, and 1.6 mg Cu per week, therefore the actual NOAEL and LOAEL are 0.8 mg/day and 1.2 mg/day of copper, when taken
Araya (2003)	University of Chile	Experimental	Adults	1,365	<0.01, 2, 4, or 6 mg/L water Individual mean daily consumption of 1.5L	2 months	Gastrointestinal symptoms	GI symptoms increased significantly in response to 6 mg/L	-Mean intake is 3, 6 and 9 mg/day. It is not stated at what intake there are no GI symptoms
Zeitz (2003)	University of Gottingen	Epidemiological	Infants	2,944	Mean Cu levels 0.50mg/L	Up to age 18 months	Total serum copper, liver parameters	No dose relation with total serum copper. No fatal liver disease within 18 months	-Sole use of total serum copper analysis is not a good indicator for copper status -Exposure levels are not clear -Study aimed to investigate chronic effects of copper exposure, however exposure period was too short for damage to liver to become apparent

4.1.2 US EPA

The US EPA has a maximum contaminant level goal (MCLG) of 1.3 mg/L. This is an action level, which triggers a treatment process if more than 10% of tap water samples exceed 1.3 mg/L (USEPA, 1991, 2007). The MCLG value is based on a case study of gastrointestinal symptoms in 10 of 15 nurses after consumption of a whisky cocktail contaminated with copper from the cocktail shaker, which occurred in 1957 (Wyllie, 1957). The occurrence was an accidental ingestion, and the cocktail consumption rate was remembered after the event, hence having a level of uncertainty. The time for the appearance of symptoms was not noted nor how many of the nurses consumed the contaminated beverage. A low estimate of the amount of copper in the drinks was 5.3 mg copper in a half a glass of cocktail, presumably a volume of 21 ml (Fewtrell, Kay, & MacGill, 2001). In spite of the uncertainty in the data, the value of 5.3 mg became a NOAEL. However, this value has been variously referenced by other authors as 5.3 mg/L or 5.3 mg/day (Fitzgerald, 1996).

The MCLG was derived in a following manner:

$$MCLG = \frac{NOAEL}{uncertainty\ factor \times daily\ water\ consumption}$$

$$= \frac{5.3\ mg\ Cu}{2 \times 2\ L} = 1.325\ \ mg\ Cu/L \approx 1.3 mg/L$$

If the uncertainty factor is increased to 5 (up from 2)

$$MCLG = \frac{NOAEL}{uncertainty\ factor \times daily\ water\ consumption}$$

$$= \frac{5.3\ mg\ Cu}{5 \times 2\ L} = 0.53\ \ mg\ Cu/L \approx 0.50\ mg/L$$

For the derivation, an uncertainty factor of 2 was used, but without explanation. Overall, the US EPA standard was based on an uncertain data from a case study of an accidental acute copper toxicity.

4.1.3 Health Canada

Currently, Canada has set an aesthetic objective for copper in drinking water at 1.0 mg/L. The aesthetic objective was established to minimize staining of laundry and plumbing fixtures. Health

Canada stated that the levels at which adverse health effects occur are much higher than the aesthetic objective, therefore, a health-based guideline is not necessary (Health Canada, 1992).

In the discussion of daily intake for copper, Health Canada references the WHO and US EPA values, but uses a daily water consumption of 1.5L and 70kg for average adult body weight instead of the default figures suggested by the WHO (2L, 60kg). Moreover, it states that copper is generally non-toxic, but may become toxic above 15 mg/day or more without providing any reference.

4.1.4 California EPA (CEPA)

A Public Health Goal for copper in drinking water for CEPA in 2008 was to investigate the estimation of the safe level of copper in drinking water and this was published in a document (CEPA, 2008). Its aim was not to establish a regulatory standard or guideline but to provide an information document. The CEPA assessed the sub-group most vulnerable to copper overload - infants and young children. They stated that relatively low levels of copper in drinking water, between 0.2 to 1.0 mg/L, could still have adverse effects on infants, causing symptoms such as diarrhea and weight loss (CEPA, 2008). Unlike other drinking water guidelines, CEPA developed a safe level for copper targeting infants. The estimation of the safe level was obtained using the following equation:

$$Safe\ level = \frac{NOAEL \times RSC}{UF \times L/kg \cdot day}$$

Where, RSC = relative source contribution (usually 20 to 80%)

UF = uncertainty factor

L/kg/day = daily water consumption

The NOAEL of 426 µg/kg/day was derived from Olivares (1998) (possibly from an average weight of infant aged 2 to 9 months of 6 kg drinking 1.28 L of 2 mg/L water = 1.28 L x 2 mg/L /6 kg = 426 µg/kg/day). Note the problem of Olivares study is that the daily amount of copper ingested was not reported (see Table 4.1). An RSC of 50% (or 0.5) was estimated for non-breastfed infants. An upper 95th percentile of water intake for non-breastfed infants less than six months was used for daily water consumption, which was 0.221 L/kg/day. The document did not specify why an uncertainty factor of 3 was adopted. The resultant calculation is as follows:

$$Safe\ level = \frac{426\ \mu g/kg \cdot day \times 0.5}{3 \times 0.221\ L/kg \cdot day} = 321\ \mu g/L = 0.3\ mg/L\ \ (rounded)$$

This safe level of 0.3 mg/L is supposed to be protective of the sensitive subpopulation of infants, young children, pregnant women and their fetuses, the elderly, and other subgroups. Although this figure is not a regulatory guideline value, this study laid out very important groundwork for the future direction for establishing drinking water guideline levels.

A summary of the recalculated guideline values is presented in Table 4.2 below.

Table 4.2 Summary of recalculated drinking water guideline values for copper

References	**Recalculated drinking water guideline values**
WHO 1993 (beagle dogs, NOAEL)	0.16 mg/L
WHO 1996 (beagle dogs, TDI)	0.60 mg/L
WHO 2004 (human acute effect studies)	0.06 mg/L (or 0.6 mg/L[a])
US EPA 1991 & 2007 (acute human effect case)	0.53 mg/L[b]
CEPA 2008 (acute human baby study)	0.30 mg/L[c]

a. If all copper is assumed to come from water
b. UF = 5 is used
c. As calculated in CEPA study

4.2 Assessment of copper levels in drinking water

The results of the field survey of copper concentrations measured in institutional buildings are presented. In total 237 water samples were collected from 11 buildings. The copper levels measured are analyzed by type: sampling time, stagnation or flushed, type of water outlet, building age. Possible correlations between copper levels and sample characteristics (stagnation, flushed, time of day, water quality parameters of pH and temperature, building age) are presented and assessed.

Blind split samples were analyzed by a commercial certified laboratory (Eurofins), and the results are presented in Table 4.3. Two samples were taken sequentially from the same outlet, and the ones for the verification were taken right after our own sample collection. That may be why most of the measured concentrations in Table 4.3 are slightly higher than the results from Eurofins.

Table 4.3 Data validation

Lable	Date of collection	Eurofins	Measured	% difference
MH-5-5-W-M	2018-11-05	0.48	0.55	12%
MD-4-3-S-S	2018-11-06	0.53	0.54	2%
MD-4-4-W-S	2018-11-06	0.42	0.45	8%
TB-B-1-W-S	2018-11-02	0.66	0.61	-9%
WC-7-3-S-S	2018-11-14	0.51	0.59	14%
MH-B-1-B-S	2018-11-14	0.50	0.65	23%
BH-12-4-W-5F	2018-11-14	0.12	0.14	14%

Two-sample t-test assuming unequal variances is applied to test if the difference between the concentrations measured by ICP-OES (M=0.50, SD=0.17, n=7) and the concentrations obtained from Eurofins (M=0.46, SD=0.17, n=7) is significant. The result from t-test confirms that the difference is not significant, t(12)=2.18, p=0.63 (2 tail). The results are illustrated in Figure 4.1.

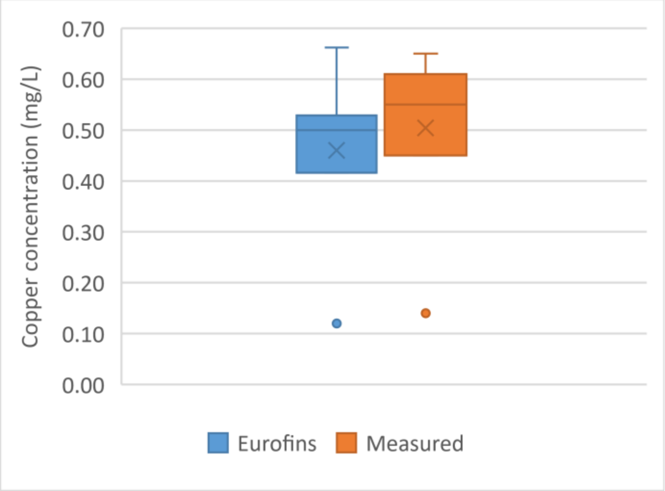


Figure 4.1 Box plots of copper concentrations measured for data validation

4.2.1 pH and temperature

The range of measured pH values (Table 4.4) is well within the range of pH 6.5 - 8.5 set by Health Canada (1992). However, temperature, measured between Nov 6th and 16th, varies widely ranging from 4.3 to 47 °C. The highest temperature was observed from a washroom tap after one-minute flushing.

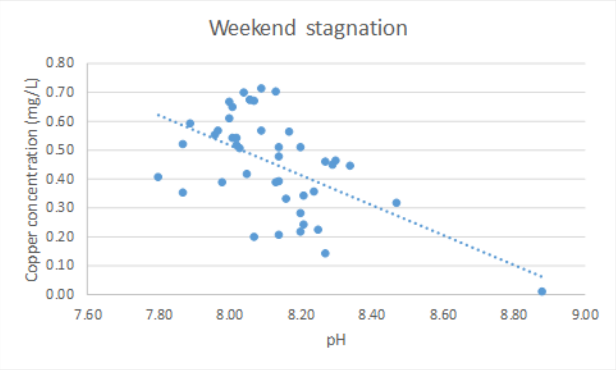
Table 4.4 Overall results of Cu level, pH, and temperature

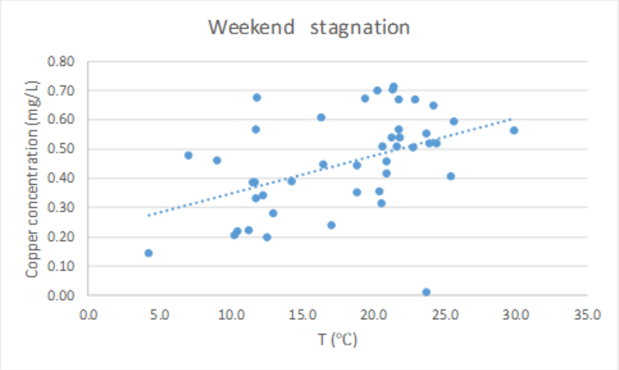
	Cu level (mg/L)	pH	T (℃)
Minimum	0.01	7.61	4.3
1st quartile	0.17	7.98	13.6
Median	0.31	8.08	19.2
3rd quartile	0.46	8.17	21.6
Maximum	0.77	8.88	47.0

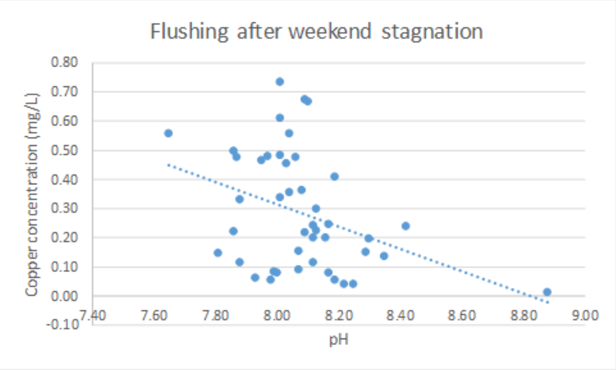
Measured temperature and pH values are grouped by sample type (e.g. weekend stagnation, flushing, etc.), and plotted against copper concentrations in Table 4.2. In all sample type groups, a negative correlation between pH and copper concentrations and positive correlation between temperature and copper concentrations are observed, as demonstrated in other corrosion studies (Boulay & Edwards, 2001; Edwards et al., 1996; Feng et al., 1996). However, the strength of these correlations between pH or temperature and copper levels is not strong and the strength varies somewhat between sample types. This is very likely due to the presence of other corrosion factors affecting copper release as was also concluded from previous field surveys (Tam & Elefsiniotis, 2009).

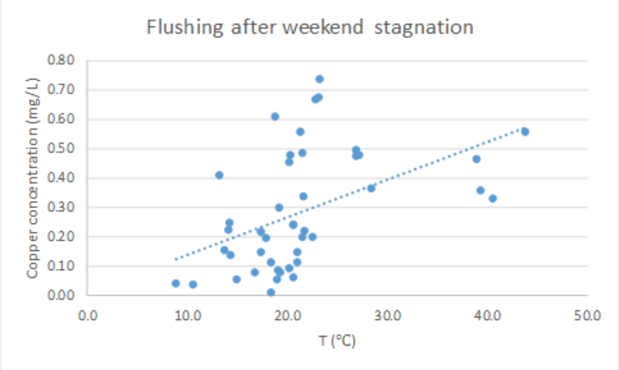
Copper concentrations across pH

Copper concentrations across temperature









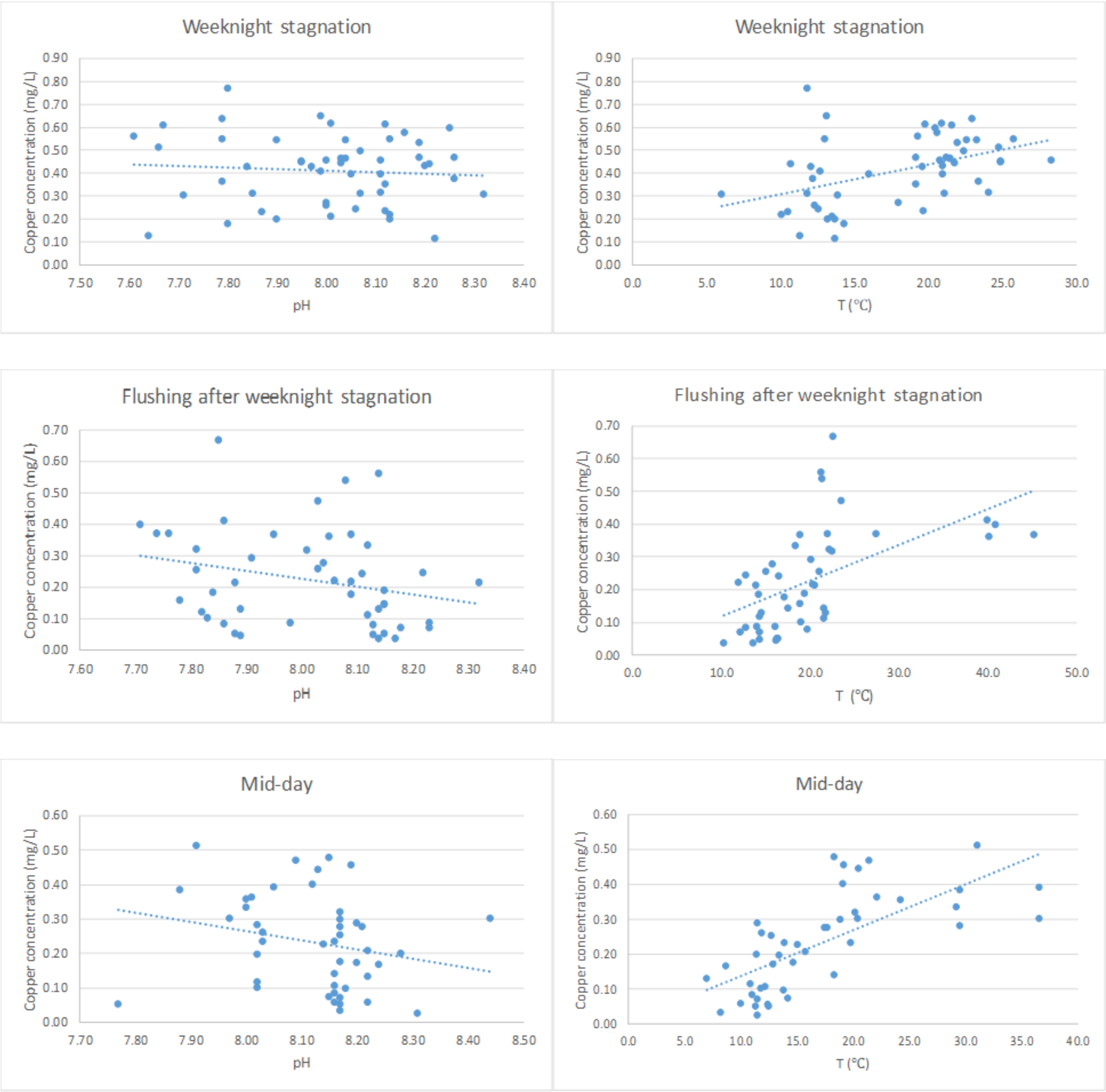


Figure 4.2 pH and temperature versus copper concentrations measured in each sample type

4.2.2 Effectiveness of one-minute flushing

4.2.2.1 Type of sample

The distribution of the data according to the time the samples were taken, time of day and day of the week, is shown in Figure 4.3. The highest overall copper levels are in first-draw samples after weekend stagnation. The medians from weekend stagnation and weeknight stagnation samples are similar (0.48 mg/L compared to 0.42 mg/L), but the median from mid-day samples are significantly lower (0.23 mg/L).

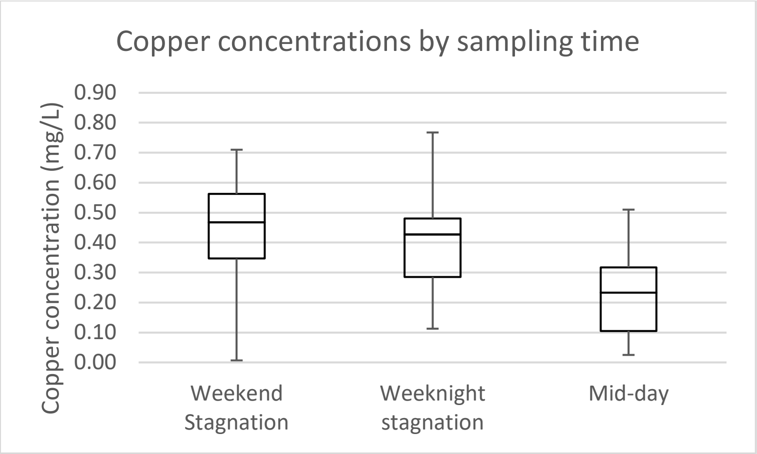


Figure 4.3 Copper concentrations by sampling time (25th, median and 75th percentile)

Copper concentrations after one-minute of flushing are compared to the first-draw samples in Table 4.5, presenting also the mean rate of copper reduction. The results show that one-minute flushing is effective at reducing the copper levels by approximately 40% for both weekend stagnation and weeknight stagnation samples. One-minute flushing lowers the concentration of copper down to close to the levels measured for typical daytime use (mean of 0.23 mg/L).

Table 4.5 Copper concentrations and mean copper reduction rates by type of sample

Type of sample	No. of samples	Copper concentration (mg/L)				Mean Cu Reduction %
		Mean	Median	Lowest	Highest	
Weekend stagnation	44	0.453	0.468	0.007	0.710	
Weekend 1min flushing	44	0.285	0.230	0.010	0.733	37%
Weekday stagnation	47	0.397	0.428	0.113	0.768	
Weekday 1min flushing	47	0.224	0.213	0.035	0.665	42%
Mid-day	45	0.231	0.233	0.025	0.510	

However, high copper concentrations after flushing were observed in many of the samples taken after both weekend and weeknight stagnation. In order to further investigate, the effectiveness of one-minute flushing, the data is broken down by type of water outlet and building.

4.2.2.2 Type of water outlet

The data from each sampling type are divided into two groups: outlets without filters (washroom taps, kitchen taps, and non-filtered fountains) and outlets with filters (filtered fountains).

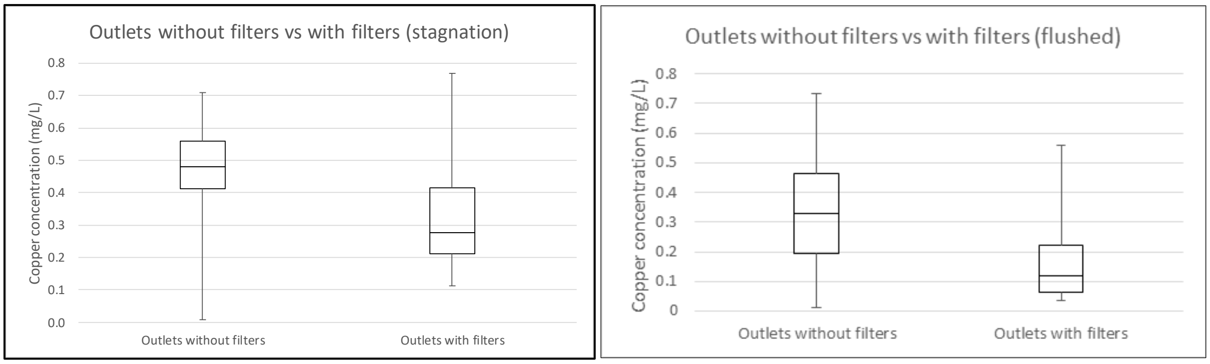


Figure 4.4 Copper concentrations by type of water outlet

Figure 4.4 compares copper levels between these two groups, showing that copper concentrations are higher in the samples collected from the outlets without filters. This pattern is consistent in both the stagnation (means of 0.48 mg/L versus 0.28 mg/L) and the one-minute flushing samples (means of 0.33 mg/L versus 0.12 mg/L).

Figure 4.5 presents the rates of copper reduction due to the one-minute flushing from each outlet type. The samples collected from the outlets with filters have higher copper reduction rates (mean of 0.28 mg/L to 0.12 mg/L) than the samples from the outlets without filters (means of 0.48 mg/L to 0.33 mg/L). It is also observed that the difference in flushing effectiveness between the types of outlet is more obvious after weekend stagnation (outlets without filters, means from 0.52 mg/L to 0.38 mg/L: outlets with filters, mean from 0.34 mg/L to 0.13 mg/L) than weeknight stagnation (outlets without filters, means from 0.45 mg/L to 0.27 mg/L: outlets with filters, mean from 0.32 mg/L to 0.16 mg/L) (Table 4.6).

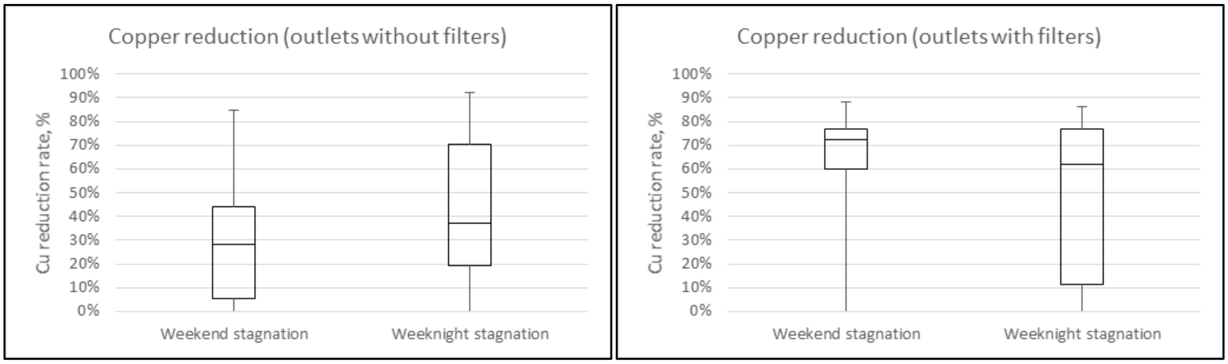


Figure 4.5 Copper reduction rates by type of water outlet

Table 4.6 Copper concentrations and mean copper reduction rates by type of water outlet

Type of sample	**Type of water outlet**	**Pre-flushing**	**Post-flushing**	**Mean copper reduction %**
		Mean copper concentration (mg/L)		
Weekend stagnation	Washroom tap, sink tap, no filtered fountains	0.53	0.38	26%
	Bottle-filling fountains	0.33	0.10	56%
Weeknight stagnation	Washroom tap, sink tap, no filtered fountains	0.45	0.27	43%
	Bottle-filling fountains	0.26	0.13	40%

Adequate flushing is ascertained by a drop in temperature of the water. A drop in temperature indicates that the water in the pipes has not been stagnant inside the building and therefore flushing is expected to result in a decrease in temperature. However, in 68% of the samples the temperature of the sample had increased after one-minute of flushing and only in 32% of the samples had the temperature either dropped or stayed the same. The lack of drop in temperature indicated that the pipes within the building had not been fully flushed of the water that had been stagnating in them for long enough for them to increase in temperature. However, the copper concentrations were reduced by the one-minute flushing. This might indicate that the major source of copper leaching is from the components of the branch supply lines, which have a smaller diameter. The water stagnating in the larger diameter distribution lines will have a lower ratio of leachable surface area to water volume, resulting in lower copper concentrations. Note that regular water taps sampled had an average flow rate of 3.8L/min hence. At this flow rate, in detached houses, where the length of copper piping within the house is relatively short, flushing is effective as 30m of a ½ inch (most commonly used size of individual components in houses) pipe can be flushed in one minute and this is longer than the typical distance from the mains connection to the water outlet. In larger buildings, a much greater volume is required to completely flush out the pipes that are within the building, particularly as large buildings also have larger diameter distribution lines (e.g. only 7m of a 1inch pipe or 5m of a 1 ¼ inch pipe can be flushed in one minute).

4.2.2.3 Buildings

Newer copper pipes are likely to have higher copper solubility as a result of the presence of less stable scales, cupric hydroxide or other metastable scales (Edwards et al., 1996; Schock et al., 1995). Therefore, higher copper concentrations may be associated with newer or recently renovated buildings. The median copper concentrations and the rates of copper reduction after one minute flushing are presented in Table 4.7 by building with building age noted.

Table 4.7 Summary of results by building

Building name	Year of construction (renovation)	Copper plumbing[a]	Copper concentration (mg/L)						
			Stagnation		1min flushing		Weekday		Cu reduction %
			Mean	Range	Mean	Range	Mean	Range	
Frank Dawson Adams	1951	C	0.36	0.20-0.50	0.07	0.04-0.11	0.11	0.03-0.29	79%
Macdonald Engineering	1907 (1998)	C	0.46	0.18-0.67	0.39	0.11-0.73	0.29	0.05-0.51	18%
Macdonald/ McConnell	1959 (2010)	C	0.50	0.30-0.67	0.37	0.21-0.56	0.35	0.25-0.40	27%
McConnell	1958	C	0.32	0.12-0.56	0.13	0.04-0.24	0.12	0.03-0.30	56%
Macdonald Harrington	1896 (under renovation)	C	0.52	0.33-0.77	0.26	0.09-0.48	0.19	0.10-0.33	49%
Trottier Building	2004	C	0.49	0.31-0.67	0.28	0.22-0.41	0.24	0.13-0.48	40%
Wong Chemical	1996	C	0.59	0.39-0.71	0.48	0.13-0.67	0.30	0.21-0.46	20%
Burnside Hall	1970	C	0.34	0.21-0.54	0.13	0.04-0.26	0.25	0.07-0.47	60%
Arts Building	1843	C	0.36	0.20-0.54	0.27	0.08-0.56	0.24	0.14-0.36	25%
McLennan Library	1967	C	0.22	0.01-0.52	0.25	0.01-0.46	0.24	0.05-0.39	3%
Brown Building	1999	C	0.44	0.31-0.56	0.12	0.07-0.20	0.31	0.20-0.44	69%

a. Whether copper pipes are used at each buildings were confirmed by either visual inspection or the results from copper analysis; *C: copper pipes are confirmed, N: not confirmed*

To determine the effect of the age of the pipes on copper concentrations, a two-sample t test is used. The data are divided into older buildings, those built before 1990, and newer buildings, those built or renovated after 1990. The year of renovation does not always imply the replacement of old pipes, but it is assumed that the year of renovation is most likely to be the age of the pipes. As expected, the result from two-sample t-test confirmed that the concentrations of copper are higher in the samples collected from newer or recently renovated buildings (illustrated in Figure 4.6 & Figure 4.7).

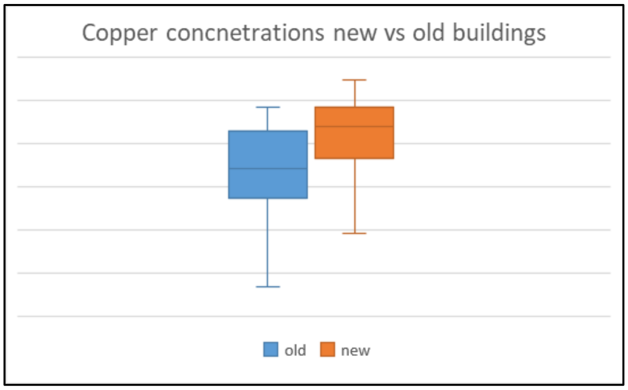


Figure 4.6 Box plots of copper concentrations by new and old buildings

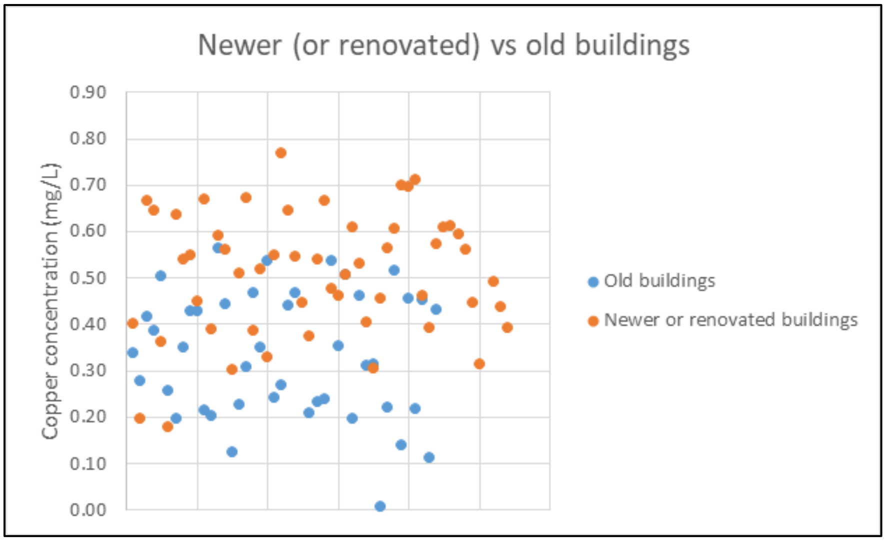


Figure 4.7 Distribution of copper concentrations between old and new buildings

Figure 4.8 compares effectiveness of one-minute flushing between old and newer or renovated buildings. The median copper reduction rate shows that flushing works more effectively in older buildings (mean: 0.34 mg/L to 0.14 mg/L) than newer or renovated buildings (mean: 0.51 mg/L to 0.31 mg/L) (Table 4.8).

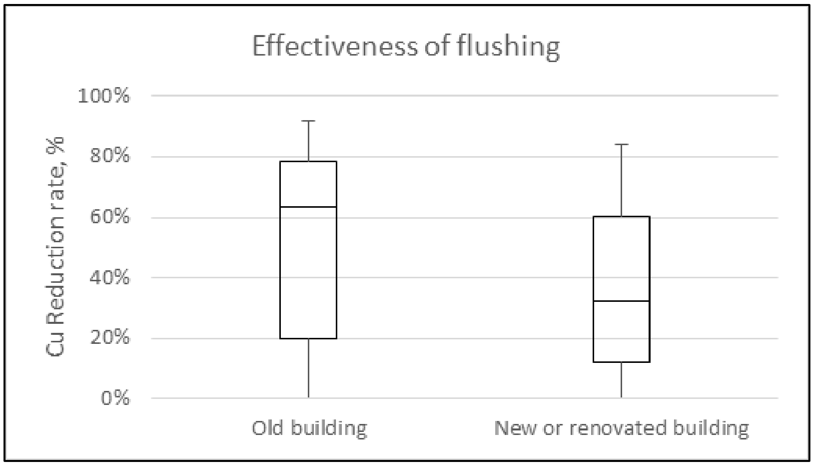


Figure 4.8 Effectiveness of one-minute flushing measured in old buildings versus newer or renovated buildings

Table 4.8 Copper concentrations of pre-flushing and post-flushing by old and newer or renovated buildings

	Pre-flushing	Post-flushing	Copper reduction %
	Mean copper concentration (mg/L)		
Old buildings	0.34	0.14	63%
Newer or renovated buildings	0.51	0.31	32%

4.2.3 Piping materials

Although piping materials at some of the sampling sites were identified by visual inspection, without a complete information of piping structure and the materials at each sampling site, it is not possible to statistically analyse the effect of piping materials on copper concentrations. Based on visual inspection, most of the buildings tested likely had copper plumbing.

4.2.4 Copper exposure levels

The levels of copper in all the collected samples are under the guideline values set by the WHO (2.0 mg/L) and US EPA (1.3 mg/L). However, as discussed in the preceding section, it is concluded that these values were neither based on chronic copper toxicity data nor developed on a firm scientific basis, and thus the guideline values are likely to cause adverse health effects from chronic exposure. Recalculated guideline values for copper in drinking water range between 0.06 mg/L and 0.60 mg/L (Table 4.2). According to Table 2.4, the range of daily reference intakes for copper is between 0.8 and 3.0 mg/day for adult men, and the WHO's default number for the percentage contribution to daily copper ingestion from drinking water is 10% (WHO, 1996b). Using the range of 0.8 - 3.0 mg Cu/day and 10% contribution from drinking water, a range of daily copper intake from drinking water can be obtained, which is between 0.08 and 0.30 mg Cu/day. Using the WHO rate of water consumption per day for an adult of 2 L, this results in a range of 0.04 to 0.15 mg/L. These two recalculated ranges of 0.06 - 0.60 mg/L for drinking water guideline values for copper and 0.04 - 0.15 mg/day for required dietary amounts are considered instead of the current guideline values to discuss the measured copper levels in drinking water in the institutional buildings. The ranges are indicated in Figure 4.9.

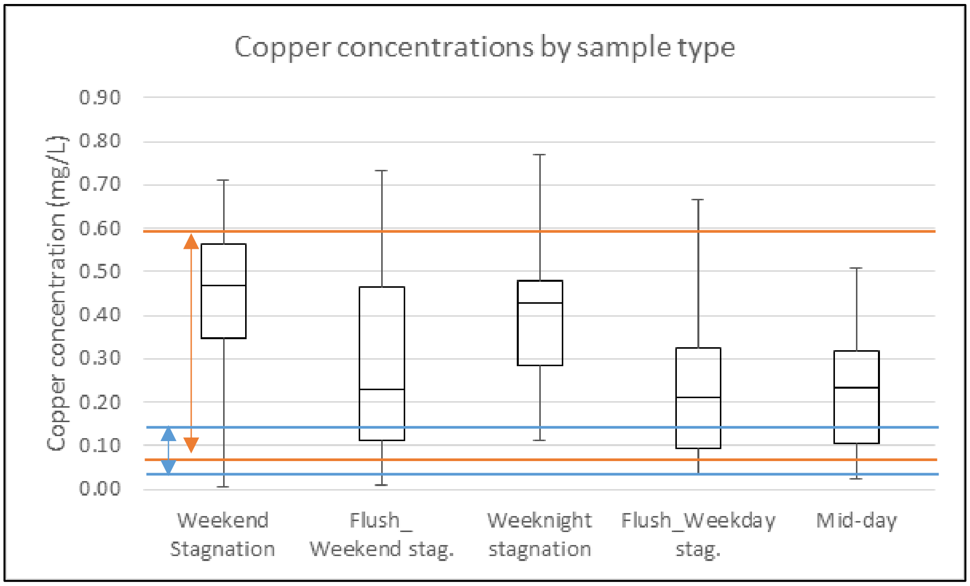


Figure 4.9 Copper concentrations by sample type

The orange lines indicate the range of recalculated drinking water guideline values, whereas the blue lines indicate the range of recommended daily copper intakes from drinking water (Figure 4.9). The median copper concentration for all sample types is above the lower range of the recalculated range for a guideline value, but less than the highest value. All mean values are above the largest value of the recommended daily intake from drinking water. 24% of samples from the stagnant samples are above the highest of the recalculated guidelines values for maximum copper concentration. All the samples of stagnant water are above the range of recommended daily copper intakes from drinking water. The results are also a concern to those only consuming 1 L of water per day in these types of building or those who are more susceptible to excess copper. In addition, the recalculated ranges are still based only on acute symptoms of copper ingestion and not for chronic symptoms. Exposure to copper at this level over the long term may still have potential health risks. Moreover, the ranges indicated in Figure 4.9 should be much lower if the exposed subjects are infants or young children.

5 CONCLUSIONS

Guideline values for copper in drinking water established by the WHO and US EPA were reviewed, and copper levels in drinking water in large institutional buildings were investigated. The results from the critical review showed that the scientific evidence used in the development process is of poor quality, has high uncertainty (as it is due to animal studies or acute effect studies) or is misrepresented. In addition, the health risks resulting from chronic exposure to copper are not at all understood. The guideline values for copper in drinking water proposed by WHO, US EPA, CEPA and Health Canada range from 0.3 mg/L to 2.0 mg/L. After a critical review this values were recalculated and range from 0.06 mg/L to 0.6 mg/L, as presented in Table 5.1.

Table 5.1 Summary of drinking water guidelines for copper and recalculated values

References	Drinking water guideline values for copper (mg Cu/L)	Recalculated guideline values (mg Cu/L)
WHO (1993)	2.0[a]	0.06
WHO (1996)	2.0[a]	0.60
WHO (2004)	2.0[b]	0.06 (or 0.6)
US EPA (1991, 2007)	1.3	0.53
Health Canada (1992)	1.0[c]	NA
CEPA (2000)	0.3	NA

a. Provisional value
b. Not provisional
c. Aesthetic objective

The field survey of copper levels in large institutional buildings, Table 4.4, resulted in a mean value of 0.31 mg/L and a range from 0.17 to 0.46 mg/L for the 25th to 75th percentile. 24% of the stagnation samples were above the highest of the recalculated guideline levels of 0.6 mg/L and 66% of the stagnation samples were above the lowest of the published guideline values, 0.30 mg/L by CEPA (2008). Given the uncertainty in the data, the uncertainty in the conversion of animal model studies to humans and the uncertainty in the conversion of acute risk to chronic risk, the public needs to be educated to reduce risk. Risk reduction can be accomplished by flushing the taps before consumption as on average this reduced the copper levels by 40%. However, the effectiveness of one-minute flushing may differ by building and may not significantly reduce copper concentrations. The public should also be advised not to consume water from the hot tap, and to install a filter if possible.

The variation of copper levels measured at different water outlets in the same building indicates that one sample per building can lead to misrepresentation of copper exposure levels. Moreover, the current corrosion monitoring system in North America does not require new buildings to be monitored due to the priority given to lead toxicity, which may lead to an inaccurate exposure assessment of copper (USEPA, 2007). Thus, separate sampling strategies for the health risk due to copper and for corrosion monitoring may be needed.

5.1 Future Work

- ☐ Review of more recent studies on chronic copper toxicity from a range of populations
- ☐ Additional sampling to examine if copper levels remain low after flushing throughout the day
- ☐ Additional sampling at different types of building and building uses (e.g. daycares, elementary schools, high-rise apartment buildings)
- ☐ Testing effectiveness of different filtering devices

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