MULTI-ROUTE EXPOSURE ASSESSMENT OF MAJOR DISINFECTION BYPRODUCTS AND ESTIMATION OF THEIR ALLOCATION TO DRINKING WATER

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Dedication

To my parents
Jun and Qian

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Chapter 1

Introduction

1.1 Background

1.1.1 Chlorination of Drinking Water and Disinfection Byproducts (DBPs)

To supply comfortable and safe drinking water is a very important public health issue. Chlorine is effective for inactivating pathogens in drinking water. Chlorination has been a key unit process in drinking water treatment in the 20th century. However, it also oxidizes organic matters, bromide, and iodide present in source waters (rivers, lakes, and many groundwaters), and consequently disinfection byproducts (DBPs) are formed (Krasner *et al*., 1989; Stevens *et al*., 1989; Peters *et al*., 1991; Symons, 1999). Some of them were already proved to be toxic to human (e.g., carcinogenicity and other reproductive and developmental effects) (Boorman *et al*., 1999; Zaveleta *et al*., 1999; Nieuwenhuijsen *et al*., 2000). In 1974, Rook found chloroform and the other trihalomethanes (THMs) in chlorinated drinking water (Rook, 1974). In 1976, the U.S. Environmental Protection Agency (EPA) reported that chloroform and the other THMs were ubiquitous in chlorinated drinking water based on a nationwide survey (Kopfler, 1976). In the same year, the National Cancer Institute first reported the link between chloroform and cancer production in laboratory animals (National Cancer Institute, 1976). After THMs became an important public health issue, extensive efforts have been made in detecting and identifying other DBPs. This is because that THMs were found to be only a small part (20% - 30%) of the total organic halides (TOX) in chlorinated water. So far, 600 – 700 DBPs have been identified. However, they only accounts for approximately 50% of the TOX (Richardson, 1998; Woo *et al.*, 2002; Zhang and Minear, 2002; Krasner *et al.*, 2006). Since toxicological information on a great part of them is still unknown, great efforts have also been made to evaluate their toxicities and find an appropriate way to regulate them. However, it should be noted that because waterborne pathogens brings much

worse public health risk than DBPs due to infection transmittion, chlorination is still one of the best choices for drinking water disinfection (Itoh and Echigo, 2008). In this research, trihalomethanes (THMs), haloacetic acids (HAAs) and haloacetonitriles (HANs), the major three DBPs were addressed.

1.1.2 Regulatory Frameworks for Drinking Water Quality in World Health Organization (WHO) and Japan

The World Health Organization (WHO) is the leader of the safeguard of the human health in the world. From 1983 to 2008, WHO published three editions of the Guidelines for Drinking-water Quality to globally ensure the safety of drinking water in both microbial and chemical aspects. The latest edition (the third edition) was incorporated in its first and second addenda (WHO, 2008). In the chemical aspect, WHO collected numerous information and scientific evidence of potential harmful chemical compounds including epidemiological information, toxicological data, their distributions, and fates in major environmental media (such as drinking water, food, and air). It also gave professional judgment on their regulations. Certainly many DBPs are included. The criteria were defined by WHO as the relationship between exposure to a pollutant or other factor and the risk or magnitude of undesirable effects (WHO, 1972). In other words, the process of setting the guideline values consists of two parts: (a) investigation on the relationship between dose and effect and (b) human exposure assessment.

Most developed and developing countries have created their national standards based on the WHO guidelines. Decisions on how to incorporate the WHO guidelines into domestic situation are very important and necessary because different countries have different regulatory capacities, investigations, discussions, and opinions on it. WHO recommends that it is necessary to take account of a variety of environmental, social, cultural, economic, and other conditions affecting potential exposure in establishing their national standards of drinking-water quality. This may lead to national standards that differ appreciably from the WHO guidelines.

The drinking-water quality regulation system in Japan was greatly revised from its previous version in May 2003, and implemented in May 2004 (the Ministry of Health,

Labor and Welfare, Japan, 2003). It was revised in December 2008 again, and implemented in April 2009 (the Ministry of Health, Labor and Welfare, Japan, 2008). In the first revision, the lists of regulated chemicals had been updated with much more items. As mentioned above, the regulation basically had referred to the concurrent WHO revision, but independent decisions were also made based on different scientific knowledge to accommodate domestic conditions. There are three categories of classification in the regulation system: the standard group, the management target group, and the under-consideration group. Items with relatively sufficient information were decided to be regulated in the standard group. The items with insufficient toxicological information, but are frequently used or detected in the environment are classified into the management target group. Those with poor knowledge on both toxicity and occurrences in the environment are classified into the under-consideration group. The purpose of this classification is to maintain the possibility of upgrading them into higher regulatory level with further information.

1.1.3 Guideline and Standard Value Derivation Approaches for Potentially Hazardous Chemicals

In this section, the derivation approaches of guideline and standard value are introduced. These approaches are applied to all the regulated chemicals which include the target DBPs of this research.

To estimate an acceptable exposure amount of a genotoxical chemical, it is generally considered that it initiates its carcinogenesis with the induction of mutation in the genetic material (DNA) of somatic cells (WHO, 2008). In this aspect, there is theoretical risk at any level of exposure to this chemical (so-called non-threshold chemicals). On the other aspect, there is carcinogen that produces tumors in animals or humans without exerting a genotoxical activity, but through an indirect mechanism. It is generally accepted that a threshold dose exists for that non-genotoxical carcinogens (so-called threshold chemicals). In addition, noncarcinogens are also considered as threshold chemicals. Both WHO guidelines and standard values of Japan for non-threshold and threshold chemicals have been derived from different approaches.

Non-threshold approach

In case of chemicals considered to be genotoxical carcinogens, guidelines or standard values are normally determined using several models (WHO, 2008). Among them, the linearized multistage model is generally adopted. It assumes the validity of a linear extrapolation from very high dose exposures in test animals to very low dose exposures in humans. Commonly, the model computes the lifetime cancer risk of 10^{-5} associated with a particular level of exposure called virtually safe dose (VSD). Guidelines and standard values are conservatively presented as the concentrations in drinking water corresponding with VSDs of various genotoxical carcinogens.

The derivation approach of guideline (standard value) is summarized in the following equation:

$$\text{Guideline (standard value)} = \text{VSD} \times \text{bw} / \text{C} \quad (1.1)$$

VSD = virtually safe dose (μg/(kg·day))
bw = body weight (kg)
C = daily drinking-water consumption (L/day)

Threshold approach

In case of chemicals considered to be non-genotoxical carcinogens or noncarcinogens, it is generally accepted that no adverse effect will occur below a certain dose (WHO, 2008). Instead of VSD, a tolerable daily intake (TDI) for human is applied with the most sensitive end-point in relevant studies which usually involves the administration in drinking water. TDI is derived from the no-observed-adverse-effect level (NOAEL), as the amount of a chemical in food and drinking water that can be ingested over a lifetime without appreciable health risk. NOAEL is defined as the highest dose or concentration of a chemical that causes no detectable adverse health effect. If a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) may be used. It is the lowest

observed dose or concentration of a chemical at which point there is a detectable adverse health effect. The NOAEL for the critical effect in animals is normally divided by an uncertainty factor of 100. This factor comprises two 10-fold factors. One is for interspecies differences, and the other is for inter-individual variability in humans. Extra uncertainty factors may be incorporated to allow database deficiencies and the severity and irreversibility of effects.

The derivation approach of TDI is summarized in the following equation:

$$TDI = (NOAEL \text{ or } LOAEL) / UF \quad (1.2)$$

TDI = tolerable daily intake (μg/(kg·day))
NOAEL = no-observed-adverse-effect level (mg/(kg·day))
LOAEL = lowest-observed-adverse-effect level (mg/(kg·day))
UF = uncertainty factor (-)

Guidelines or standard values are presented as the concentrations in drinking water corresponding with TDIs of various non-genotoxical carcinogens and non-carcinogens. The derivation includes the same factors as equation 1.1 except the allocation of TDI to drinking water. The concept of allocation is introduced in detail in 1.2.3.

The derivation approach of guideline (standard value) is summarized in the following equation:

$$\text{Guideline (standard value)} = (TDI \times bw \times P) / C \quad (1.3)$$

TDI = tolerable daily intake (μg/(kg·day))
bw = body weight (kg)
P = allocation of TDI to drinking water (-)
C = daily drinking-water consumption (L/day)

Additionally, in TDI approach, because NOAEL (LOAEL) is the only necessary factor, the dose-response relationship beyond it is not considered. Recently, a new approach called benchmark dose (BMD) method has been widely applied to correct this shortage. The BMD is the lower confidence limit of the dose that produces a small increase in the level of adverse effects (e.g., 5% or 10%). The BMD is derived on the basis of data from the entire dose-response curve for the critical effect rather than from the single dose group at the NOAEL (LOAEL). Thus, more biological information is incorporated. Also, since the dose corresponding with certain observed detrimental effect could be derived directly through this method, it could be applicable to the estimation for genotoxical carcinogens too (Itoh and Echigo, 2008).

1.1.4 Major Factors Applied to the Derivation Approaches of Guideline and Standard Value

Daily per Capita Water Consumption

In developing the guideline (standard) values for chemicals, a daily per capita consumption of 2 L by a person weighing 60 kg is generally assumed by WHO (2008). There is variation in both the volume of water consumption and the body weight of consumers. It is recognized that water intake can vary significantly in different parts of the world. WHO explained that using a default consumption of 2 L was not to underestimate the consumption in hot climates. Two-liter daily water consumption is also applied in Japan but with an average person weight of 50 kg (the Ministry of Health, Labor and Welfare, Japan, 2003). Kaneko (1996) specifically defined the composition of daily per capita water consumption as three major parts: drinking water and beverage consumption (1 L), fluid of foods (0.7 L) and metabolic water (0.3 L) which is produced in the human body through the oxidation of nutrition.

Allocation of TDI to Drinking Water

Drinking water is not usually the only media that human are exposed to chemicals. In many cases, the intake of chemical contaminants from drinking water is lower than that from other sources, like food and air (WHO, 2008). Consideration on the proportion of TDI attributable to different sources is therefore needed in establishing guidelines and risk management strategies. This approach ensures that total daily intake from all sources does not exceed the TDI of each chemical. WHO specifically explains that it is important to quantify the exposure from food and water since generally they are the primary sources of exposure to chemicals (WHO, 2008). It is also desirable to collect information in each country (domestic data). Furthermore, allocation factors could be applied to incorporate the likely contribution of water to total daily intake where appropriate information on exposure from food and water is not available. For most chemicals, the allocation factor of the TDI to drinking water is commonly set as 0.2 for such situation in guideline of WHO. This reflects a reasonable level of exposure based on broad experience. Additionally, in circumstances that exposure from food is very low, the allocation may set to be as high as 0.8. This still allows exposure from other sources (WHO, 2008). WHO recommends that detailed explanation behind the choice of allocation factor is very important, and the appropriate decisions should take into account the local circumstances when establishing national standards (WHO, 2008). Most importantly, it is also clearly notified that where a high proportion of the TDI has been allocated to drinking water but concentrations in water are generally well below the guideline value, it is not appropriate to allow contamination to increase up to the guideline value. Also, in certain circumstances such as volatile chemicals, additional routes of intake such as inhalation and dermal exposure should be taken into account in the adaptation of guidelines to local conditions.

However, Japan is significantly different from WHO on this point. In the current regulation system of Japan, it is considered appropriate to use different allocation factors for DBPs and other chemicals. The default allocation factors are set to be 0.2 for all DBPs, and 0.1 for other chemicals. This is because DBPs are generally considered to be much more ingested from drinking water than others (Ministry of Health, Labor and

Welfare, Japan, 2003). From the concept of the allocation itself, it should be noticed that to precisely decide the allocation factor of DBPs in establishing the national standard (instead of the defaults), it is important to estimate the total human exposure amount to them under domestic environment at first. Therefore, conducting their multi-route exposure assessment is necessary.

1.2 Purpose of This Research

(a) To survey the THM, HAA and HAN concentrations in various domestic environmental media (tap water, food and air).
(b) To estimate their exposure amounts via each exposure route (ingestion, inhalation and transdermal).
(c) To estimate their allocations to drinking water in total exposure.
(d) To suggest how to establish (revise) their standard values based on the obtained knowledge.

1.3 Structure of This Thesis

This study consists of four parts. The first part is to review the details of the regulation frameworks of THMs, HAAs, and HANs (Chapter 2). This chapter also aims to summarize the available information on them from the previous researches, and present the necessary works to achieve the objectives mentioned in 1.2. The second part (Chapter 3) aims to survey THM concentrations in tap water, food and air first, and estimate the total exposure to them, and discuss how to establish the allocation factors and standard values of them. In parallel, the third and forth parts (Chapters 4 and 5) aim to survey HAA and HAN concentrations in tap water, food (HAAs only) and air, and estimate the total human exposure to them, and discuss how to establish the allocation factors and standard values for them. Chapter 6 summarizes the major findings of this study, and Chapter 7 addresses future research topics derived from this study.

Chapter 2

Background

This chapter aims to summarize the available information on the details of the current regulatory frameworks of THMs, HAAs, and HANs in WHO and Japan. Also, the information on their concentrations in each environmental media and multi-route exposure are summarized from the previous researches. Additionally, the challenges and position of this research are presented.

2.1 Guidelines and Regulations of Major Disinfection Byproducts

As a disinfectant for drinking water, the added chlorine exists as hypochlorous acid and hypochlorite ion in water. It reacts with such natural organic matter such as humic and fulvic acids, to form a wide range of halogenated organic compounds (Itoh and Echigo, 2008). As was mentioned in 1.2, the DBPs have been regulated because of their potential harmfulness and frequent detection from drinking water. This research focuses on the major three potentially harmful groups (trihalomethanes, haloacetic acids, and haloacetonitriles). The current WHO guidelines, regulations in Japan, and relevant knowledge on them are summarized below, and the existing challenges are also specified.

2.1.1 Trihalomethanes (THMs)

The most frequently detected or well-known THMs in drinking water are chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM), and bromoform (TBM). Guidelines and standard values were set for the four species in WHO and many countries including Japan.

Derivation of guidelines and standard values

According to WHO, the ingestion exposure to TCM has induced liver tumors in mice and renal tumors in mice and rats. However, it is presumed that cytotoxicity with a period of sustained cell proliferation likely represents a secondary mechanism for the induction of tumors following exposure (WHO, 2005). Therefore, TCM was not proved to be genetically toxic via ingestion exposure. Hence, the guideline was derived following the TDI approach (Table 2.1). Similarly in Japan, the standard value of TCM was derived based on the same LOAEL of 15 mg/(kg·day) with different UF and body weight. For BDCM, WHO set the guideline using a linearized multistage model for the observed increased kidney tumors in male mice in an NTP bioassay. However, in Japan, it is considered appropriate to retain the LOAEL (6.1 mg/(kg·day)) reported by Aida *et al*. (1992) because BDCM gave both positive and negative results in a variety of *in vitro* and *in vivo* genotoxicity assays (Ministry of Health, Labor and Welfare, Japan, 2003). The standard value is derived by following TDI approach. Both WHO and Japan consider that the available data on the genotoxicity of DBCM are inconclusive. It is considered appropriate to retain the NOAEL (30 mg/(kg·day)) reported by National Toxicology Program (NTP) (1985). Therefore the guideline and standard value are derived following the TDI approach. Same as DBCM, TBM was also considered that the available data on genotoxicity are inconclusive. It is considered appropriate to retain the NOAEL (25 mg/(kg·day)) reported by NTP (1989). The guideline and standard value are also derived following the TDI approach.

However, Yamamoto *et al.* (2002) found an inhalation exposure to higher than 25 mg/m^3 of TCM induced kidney tumors in male mice. Consequently, the estimated lowest tolerable daily intake via inhalation for human is 5.4 μg/(kg·day), which is approximately half of the TDI than derived from the ingestion exposure (12.9 μg/(kg·day)) in Table 2.1. Additionally, Gordon *et al*. (2006) measured the TCM concentrations in human exhaled breath and blood samples after drinking 0.5 L cold tap water and 14-min bath separately, and found that inhalation and transdermal exposure leads to significant higher TCM concentration in both breath and blood samples than that in

ingestion. Other researches also implied that inhalation exposure to TCM causes higher health risk than ingestion exposure (Weisel *et al.*, 1998; Nazir and Khan, 2005).

Table 2.1 Regulatory frameworks of major disinfection byproducts in WHO and Japan (to be continued to the next page)

WHO [a]						
Non-threshold approach		Threshold approach				
		LOAEL (NOAEL) (mg/(kg·day))	TDI (μg/(kg·day))	Allocation factor	Body weight (kg)	Guideline value (mg/L)
TCM	Linearized multistage model	LOAEL 15	15	75%	60	0.3
BDCM					60	0.06
DBCM		NOAEL 30	21.4	20%	60	0.1
TBM		NOAEL 25	17.9	20%	60	0.1
MCA	Benchmark model	LOAEL 3.5	3.5	20%	60	0.02
DCA					60	0.04
TCA		NOAEL 32.5	32.5	20%	60	0.2 (rounded)
DCAN		NOAEL 8	2.7	20%	60	0.02
DBAN		NOAEL 11.3	11	20%	60	0.07

[a] WHO (2008)

Table 2.1 Regulatory frameworks of major disinfection byproducts in WHO and Japan (continues from the previous page)

	Japan [b]						
	Non-threshold approach	Threshold approach					
	VSD (μg/(kg·day))	LOAEL (NOAEL) (mg/(kg·day))	TDI (μg/(kg·day))	Allocation factor	Body weight (kg)	Standard value (mg/L)	Target value (mg/L)
TCM		LOAEL 15	12.9	20%	50	0.06	
BDCM		LOAEL 6.1	6.1	20%	50	0.03	
DBCM		NOAEL 30	21	20%	50	0.1	
TBM		NOAEL 25	17.9	20%	50	0.09	
MCA		LOAEL 3.5	3.5	20%	50	0.02 (rounded)	
DCA	1.43				50	0.04 (rounded)	
TCA		NOAEL 32.5	32.5	20%	50	0.2 (rounded)	
DCAN		LOAEL 8	8	20%	50		0.01P[c]
DBAN		NOAEL 11.3	11.3	20%	50		0.06 (rounded)

[b] Ministry of Health, Labor and Welfare, Japan (2009)

[c] Provisional value

Multi-route exposure

Beside the different consideration on toxicology of BDCM between WHO and Japan, allocation factors for THMs are another important issue worth studying. To determine the allocation of TDI to drinking water, knowledge on the concentrations of the target compounds in various environmental media needs to be obtained first. There are numerous studies devoted to measuring TCM and BDCM concentration in tap water, and indoor and outdoor airs. Decades ago, it was discovered that human has been exposes to TCM mostly during bathing via inhalation and transdermal, because tap water is the main emission source in bathroom (Krishnan, 2003). Therefore, WHO attributed the inhalation and dermal exposure to drinking water by applying the ingestion-equivalents (Ieq) of TCM and BDCM (WHO, 2008). The Ieq values were calculated through a physiologically based pharmacokinetic (PBPK) model-generated data on the absorbed fraction. The estimated highest total exposure values for drinking water were for adults in 30-min bath scenario: 4.61 Ieq/day (2 liters ingestion, 1.7 liters inhalation, and 0.91 liter transdermal) for TCM and 4.05 Ieq/day (approximately equal contributions from drinking water, food ingestion, and inhalation from common indoor environment and bathroom) for BDCM. For TCM, WHO has also pointed out that ingestion exposure via dietary is approximately equal to other three exposure routes, based on the results of the surveys for TCM concentration in foods in USA and Canada. The guideline value for TCM was therefore based on an allocation factor of 0.75, and there is not allocation value estimated for BDCM because the guideline is derived from non-threshold approach. The guideline value of TCM derived from this allocation (0.75) was 0.3 mg/L. In the second edition of the guideline (WHO, 1993) the guideline value was 0.2 mg/L based on an allocation factor of 0.5. The reason for this adjustment was because it was considered that much less TCM is used and produced than in the past. This adjustment directly led to a 1.5 times higher guideline value. As was mentioned in 2.2.3, WHO recommends that appropriate decisions should take into account the local circumstances when incorporating guidelines into national standards, and the allocation factor could be raised up to 0.8 if exposure from food is considered or proved being very low. However, there was a considerable difference between WHO and Japan on

this point. Since the domestic information on inhalation, transdermal and ingestion (food) exposure to THMs in Japan is not sufficient enough for estimating the total exposure amount, the allocation value of 0.2 is uniformly applied as a default to all four species of THMs in Japan.

Although, efforts have been made on estimating human exposure to THMs via various routes for more than 30 years in Japan (Tamakawa *et al*., 1987; Sato *et al*., 1993; Yamada *et al*., 1994). From 1988 to 2001, the Ministry of the Environment had annually monitored the TCM concentration in air (indoor and outdoor) (Ministry of the Environment, Japan, 2003). The results showed that inhalation exposure remained annually constant. But the survey did not investigate airborne TCM concentration in bathroom. According to WHO, obviously bathroom is a potentially high-exposure environment. Although shower is rather widely used in Japan, the traditional bathing style dose not involve shower system. Instead, people ladle water throughout the body. Also sometimes, to serve the whole family, bathtub is always filled with a large volume of hot water in the same room during each single shower behavior of every family member. The simultaneous larger amount of water-use possibly emits more THMs compared with the situation WHO described. Therefore, inhalation exposure to THMs under this unique daily activity needs to be investigated independently. Furthermore, most of the studies were designed to investigate airborne TCM as one of the volatile organic compounds (VOCs), and information of the entire four species of THM is rather limited.

Compared with inhalation exposure, more researchers are working on ingestion exposure (e.g. THM concentrations in tap water, table-ready meal or specific types of food). However, very few of them covered the whole typical dietary items. Yanagibashi (2008) conducted an extensive literature survey on THM concentrations in foods and beverages, but its spatial and temporal variability led to quite wide ranges of exposure (TCM 2.56-173, BDCM 0.45-3.8, DBCM 0.15-1.7, TBM 0.16-0.27 mg/day).

Additionally, there are studies which discovered that TCM could be formed in food during contact with chlorine-contained water (Toyoda *et al.*, 1985). Oppositely, it is also found that TCM could be lost from tap water during 5-min boiling due to volatilization (Tamakawa *et al.*, 1987). Since the estimation of ingestion exposure is

usually based on tap-water-prepared food, it is also necessary to investigate the ingestion exposure from cooking tap water to precisely estimate the allocation factors. Furthermore, transdermal exposure to THMs was rarely touched compared to others. Various studies scattered in their own interests, and none of them were designed for the purpose of seeking for more rational allocation factors of THMs.

In Chapter 3 of this research, multi-route exposure to THMs is thoroughly estimated. Especially for inhalation exposure, it is designed to investigate in a wider scale compared with ingestion exposure because of its poorer domestic knowledge. In addition, the exposure amounts are estimated based on actual measured THM concentrations in indoor air (bathroom, kitchen and living room), outdoor air, and in whole typical dietary samples prepared with and without tap water to estimate the allocation factors of THMs.

2.1.2 Haloacetic Acids (HAAs)

The most well-known HAAs in drinking water or regulated are monochloroacetic acid (MCA), monobromoacetic acid (MBA), dichloroacetic acid (DCA), trichloroacetic acid (TCA), bromochloroacetic acid (BCA), bromodichloroacetic acid (BDCA), dibromoacetic acid (DBA) dibromochloroacetic acid (DBCA), and tribromoacetic acid (TBA). In WHO, guidelines of MCA, DCA and TCA were established, and the available data are considered inadequate for regulating MBA, DBA and BCA (WHO, 2008). In Japan, MCA, DCA, and TCA have been regulated since 2004 (Ministry of Health, Labor and Welfare, Japan, 2003), mainly because their toxicological information was considered to be sufficient. The other 6 species are regulated as under-consideration group with positive attitude on collecting the information on both toxicity and their environmental level.

Derivation of guidelines and standard values

Both WHO and Japan considered that it was appropriate to derive the guideline (standard value) of MCA in TDI approach (Ministry of Health, Labor and Welfare,

Japan, 2003; WHO, 2008). Therefore, a LOAEL (3.5 mg/(kg·day)) reported by De Angelo (1997) was applied. DCA was recently (IARC, 2002) reclassified as a possible carcinogenic to human, based on the absence of data on human carcinogenicity and sufficient evidence of its carcinogenicity in experimental animals. The tumor prevalence data from male mice reported by DeAngelo (1999) were used to quantify the cancer risk. Combined data for carcinomas and slope factor were obtained from a benchmark model and a linear multistage model. In Japan, DCA is regulated as genotoxic based primarily on findings of the induced liver tumors in rats and mice via ingestion exposure. Therefore, a VSD (1.43 μg/(kg·day)) reported by De Angelo (1999) is applied to the derivation of the standard value. TCA has been shown to induce tumors in liver, but it is not considered as genotoxic because the effect was only observed in mice. For this, a NOAEL (32.5 mg/(kg·day)) reported by De Angelo is applied. The guideline and standard value are therefore derived by TDI approach.

Multi-route exposure

Compared to THMs, the information on human exposure to HAAs is much limited, even it was found to to be nearly 12% of total organic halogens (TOX) in chlorinated tap water. According to WHO, although the available data for MCA and TCA are sufficient to demonstrate that food and air are relevant exposure sources in addition to drinking water, the data are not adequate to quantify the contribution of each source to an overall assessment of exposure. For DCA, the available data are sufficient to demonstrate that food and water are relevant sources for exposure to DCA, but also not adequate to quantify the contributions of each source to an overall assessment of exposure. Available information on MBA, DBA, and BCA is still limited to only their concentrations in drinking-water.

The information on multi-route exposure to them under domestic environment is even poorer than their unclear toxicity. Although HAAs have rather greater Henry's law constants compared to THMs, studies showed that naturally formed airborne HAAs could partition into droplets clouds and be removed by rainfall. Airborne HAAs are much easier to move into liquid phase than the opposite way. It has also been found that

shower spraying produces a large number of large water droplets and small aerosols in a shower stall (Xu and Weisel, 2003). In addition, the condensation of the water vapor in shower air also forms small liquid aerosols. Xu (2003) investigated that major aerosols in shower stall ranged from 0.1 to 0.3 mm. The inhalation exposure to aerosolized DBPs, particularly non-volatile species, is controlled by the amount of aerosols that could be inhaled. The nasal passages protect the lungs against large particle (with a diameter greater than 10 mm) by trapping the particles with the hairs and liming of the nose. Small aerosols (less than 10 mm) may travel though the upper airways, reach the deep lungs, and be deposited. Aerosols between 0.003 and 5 mm can be efficiently deposited in the alveolar region, in a broad sense, exposed (Xu, 2003). Therefore, similarly to THMs, during bathing or other water-use behavior, inhalation exposure possibly occurs through small water aerosols containing HAAs.

More importantly, since HAAs are not emitted from aqueous phase into gas phase, they could be physically much more stable in food. Evidence showed that TCA may be assimilated by plants via their roots or by leaves via uptake from the air (Schroll, 1994; Sutinen *et al.*, 1995). Reimann *et al.* (1996) detected MCA and TCA in a very limited number of dietary samples. Studies also showed that HAAs have been used as preservatives for beverages because of their exquisite fungicidal and bactericidal properties. As chlorine is used in food production and processing, HAAs are also likely to be found as byproducts in food products (USEPA, 1994). Therefore, collecting information about HAAs in common domestic food is essential. In the second position, as discussed in 2.4.1 (b), preparation with tap water may influence HAA concentrations in food.

In Chapter 4 of this study, multi-route exposure to HAAs is thoroughly estimated with an emphasis on ingestion exposure via dietary which was expected to be the major exposure route to human. HAA concentrations in dietary are widely measured through a National Total Diet Study, and the ingestion exposure is estimated consequently. Also, the inhalation exposure amount are estimated based on HAA concentrations in indoor (bathroom, living room) and outdoor air in common domestic environment. From the obtained information, preliminary estimation of the allocation factors of HAAs is conducted.

2.1.3 Haloacetonitriles (HANs)

HANs are produced during water chlorination or chloramination from naturally occurring substances, including algae, fulvic acids and proteinaceous material. The most common HANs in drinking water are dichloroacetonitrile (DCAN), dibromoacetonitrile (DBAN), bromochloroacetonitrile (BCAN), and trichloroacetonitrile (TCAN). Since available information are very limited to serve as the basis for setting guidelines or provisional standard values for TCAN, only DCAN, BCAN, and DBAN were discussed in this study.

Derivation of guidelines and standard values

Both WHO and Japan considered that it is appropriate to derive the guideline (provisional standard value) of DCAN in TDI approach (Ministry of Health, Labor and Welfare, Japan, 2003; WHO, 2008). But there is a difference in their evaluations. According to WHO, a TDI of 2.7 μg/kg of body weight was calculated based on a LOAEL of 8 mg/(kg·day) for increased relative liver weight in male and female rats in a 90-day study (Hayes *et al*., 1986). A composite uncertainty factor of 3000 was used, based on a factor of 10 each for intra- and interspecies variation, a factor of 3 for the short duration of the study, a factor of 3 for the use of a minimal LOAEL, and a factor of 10 for database deficiencies. Due to the overlap of uncertainty factors, the product of three factors of 10 and two partial factors of 3 (actually the square root of 10) is 3000. In the current Japanese drinking-water quality regulation system, DCAN was classified into the management target group, and its provisional target value was derived from a NOAEL of 8 mg/(kg·day) based on the same study. A composite uncertainty factor of 1000 (10 each for intra- and interspecies variation, a factor of 10 for the short duration of the study) was used. Furthermore, DCAN was recently reevaluated based on a different viewpoint to the same toxicological knowledge (Ministry of Health, Labor and Welfare, Japan, 2009). Since it is considered to be appropriate to apply a LOAEL instead of NOAEL, an uncertainty factor of 3000 was used. And the provisional target value was revised from the current 0.04 mg/L to 0.01 mg/L consequently. DBAN was

also considered appropriate to derive the guideline (provisional standard value) in TDI approach, WHO and Japan used the same NOAEL of 11.3 mg/(kg·day).

Multi-route exposure

WHO has not provided information on environmental level or human exposure to HANs via media other than drinking water. Domestic or abroad information on HANs in water, air and food are very limited or none. Generally, halogenated acetonitriles could be decomposed through hydrolysis, which occurs at a faster rate in alkaline water and in the presence of chlorine (WHO, 2008). Since the boiling points of HANs (67-130°C) are closer to THMs (61.2-149.4 °C) than HAAs (189-245 °C), it is possible that HANs emitted from tap water during bathing with hot water, similarly with other chlorination byproducts. Studies showed that the change of pH (6-8) would lead to considerable loss of dichloroacetonitrile (DCAN) (60%) and dibromoacetonitrile (DBAN) (20%) in water. HANs are also sensitive to temperature. DCAN and bromochloroacetonitrile (BCAN) concentrations were found to dramatically decrease upon 5-minute boiling of chlroraminated (96%, 100% respectively) and chlorinated water (98%, 100%). Weisel (1994) heated HAN contained tap water to 65 °C which represents the typical temperature of bathing hot water without diluted with cold water for 30, 60, and 480 minutes. The concentration of trichloroacetonitrile (TCAN) was below detection limit in all samples. The concentration of BCAN remained low and constant even after 480 minutes while that of the DCAN remained more than 33% after one-hour heating. These facts show that when considering the exposure scenario in real-life situation, water temperature and time are important factors. In real life, boiling food in hot water at 100 °C longer than 5 minutes is rather common, so is taking a bath with hot water lower than 65 degrees by 30 minutes. Additionally, in a background material (Raymer, 2001) of a recent research, the chlorination byproduct contamination during food preparation was specifically investigated. It included rinsing, soaking and boiling various food with water spiked with HANs. The results showed that exposure to HANs via foods prepared with drinking water that are boiled during preparation are likely to be minimal. Therefore, when collecting information on multi-route exposure to

HANs, air concentration and inhalation exposure should be the first attempt. Chapter 5 of this research is designed to survey the airborne HAN concentrations in bathroom and drinking-water in common residences. Ingestion, inhalation exposure are also estimated for the purpose of estimating the allocation factors.

2.2 Summary

Chapter 2 reviewed the current regulatory framworks of major three classes of DBPs (THMs, HAAs and HANs) in drinking water of WHO and Japan. The obtained knowledge, existent challenges, and the position of this study are summarized below.

(a) When setting the national standards for target chemicals in drinking water, independent considerations on variety of domestic environmental, social, and cultural conditions affecting their potential exposure should be taken into account.
(b) To estimate the allocation factors of drinking water for THMs, HAAs and HANs, it is necessary to investigate their total exposure first by conducting multi-route exposure assessment. However, the information of those target chemicals in various domestic environmental media is rather limited.
(c) This study is designed to conduct the unprecedented multi-route exposure assessments to THMs, HAAs and HANs under domestic environment, and to provide the necessary information and discussion on how the allocation factors and standard values of THMs, HAAs, and HANs should be determined.

Chapter 3

Multi-route Exposure Assessment and the Allocation to Drinking Water of Trihalomethanes

This chapter aims to survey the THM concentrations in tap water, food and air. THM concentrations in indoor air were intensively investigated because it is very likely to be the major exposure route. The THM multi-route exposure amounts were estimated consequently. Their allocation factors were calculated and recommended based on the obtained knowledge.

3.1 Introduction

Human exposure to trihalomethanes (THMs) has attracted extensive concerns of researchers for more than one decade (Toyoda *et al*., 1985; Tamakawa *et al*., 1987; Weisel and Chen, 1994). Besides, the traditional thought and studies of ingestion exposure have already showed that inhalation and transdermal exposure also greatly contribute to the total exposure (Gordon *et al*., 2006). WHO has taken this consideration into setting the guidelines of TCM and BDCM. It also recommended that appropriate decisions should take into account the local circumstances when incorporating guidelines into national standards and the allocation factor could be raised up to 80% if exposure from food is considered or proved being very low (WHO, 2005). Therefore, a rational allocation factor complied with domestic environment is necessary. Since the information on various domestic environmental media or multi-route exposure is considered insufficient to estimate allocation factors, the default 20% was chosen to apply to the derivation of the standard values to all DBPs.

Because the importance of inhalation exposure to THMs has already been well known abroad, the airborne THM concentrations are designed to investigate in a wider scale in this research. Additionally, besides bathroom, other indoor environments are also included. For ingestion exposure via dietary, one of the emphases is to cover the

whole typical dietary items, and the other one is to investigate the exposure via cooking water by finding the ingestion exposure difference between tap-water and reagent-water prepared dietary.

The objectives of this chapter are summarized as follows: (a) to survey THM concentrations in common indoor (bathroom, kitchen and living room), and outdoor airs and tap water, (b) to survey THM concentrations in diets of the whole typical items, (c) to estimate the inhalation, transdermal, ingestion (drinking water and dietary) exposure, and (d) to discuss how the allocation factors of THMs should be established based on the obtained knowledge.

3.2 Materials and Methods

3.2.1 Reagents

Reagent water for all experiments was purified using a Millipore (Tokyo, Japan) Academic-A10 purification system. All the reagents shown below were purchased from Wako Pure Chemical Industries (Osaka, Japan). Water-analysis-grade *n*-hexane, standard of trihalomethane and *p*-bromofluorobezene were used for the generation of calibration curve and check of extraction recoveries. Residual pesticide analysis grade sodium sulfate and Japanese Industry Standard (JIS) reagent-grade phosphoric acid, sulfuric acid, sodium sulfite, sodium chloride, and silicone antifoam were used as the additives for the analysis of the dietary sample.

3.2.2 Survey Protocol

Air and tap water sampling

In total, 59 residences participated to the survey: 15 from November to December 2005, 15 were from August to December 2006, and 29 were from August to September 2009. Permissions of the survey and cooperations were received from the residents. The residences were geographically scattered in a watershed area. In this area, Region A is

located upstream of Region B. Basically, two types of drinking-water treatment are applied to this area. One was the traditional coagulation and rapid sand filtration (mainly applied to Region A), and the other one was with ozone-granular active carbon (GAC) (Region B). In some part of Region B, tap water is supplied with blended water purified through both treatments. For each process, chlorine was added as the final disinfectant. Among the 59 residences, there were 31 detached houses and 28 apartments. Each residence was occupied with a single family with one to six persons. Air samplings were conducted in bathrooms (during occupation) of all 59 residences. For kitchens (during occupation), living rooms and outdoors (from 6 p.m. to 10 a.m.), air samplings were only conducted in the first 30 residences. Ventilation was not controlled for all residences.

Airborne THMs were collected by passing the air through one (for kitchen, livingroom and outdoor) or two (for bathroom) Supelco (PA, USA) glass tubes containing Tenax-TA adsorbents using a GL Science (Tokyo, Japan) SP208-100 Dual air sampling pump (Figure 3.1). Two tubes set in line for bathroom sampling were to confirm whether air with high humidity break through the adsorbent. Air flow rates were set at either 20 mL/min (long-time bathing) or 40 mL/min (short-time bathing) for bathroom sampling, 30 mL/min for kitchen, and 5 mL/min for living room and outdoor sampling. The glass tubes were conditioned with helium (50 mL/min) at 100 °C for 30 minutes, and stored in a stainless container before sampling. During each visit, a recall questionnaire was also conducted on their lifestyles.

Concurrently, cold tap water samples were collected in glass vials with Teflon-lined enclosures. Prior to sampling, 50 mg sodium L-ascorbate was placed in the vials to quench residual chlorine. All samples were stored below 5 °C until THM extraction.

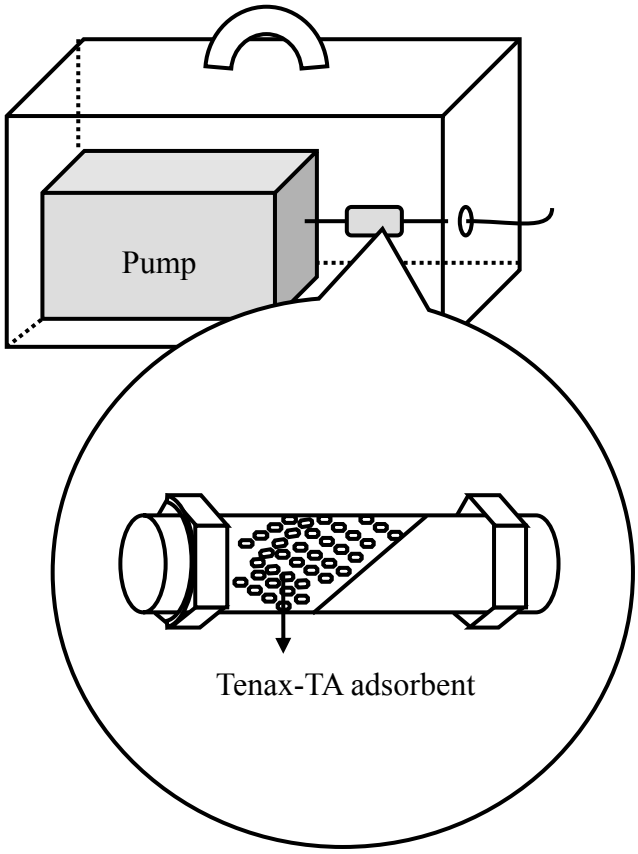

Figure 3.1 Air sampling equipment

Dietary sampling

A market-basket survey was conducted in Kyoto City in August 2009. Following the explanation of the National Nutrition Survey (National Institute of Health and Nutrition, 2006), 121 items of food were randomly purchased to represent the 17 groups of typical dietary classification (Table 3.1). All purchased food and beverages were stored at 5 °C and prepared within 24 hours. In the 17 groups of food samples, nine of them were prepared through boiling or dissolving (Table 3.1) with water as the cooking matrix. For these samples, tap water and reagent water samples were used in the same manner respectively. Immediately after preparation, food samples were homogenized with a food processor and blended according to their intake proportion in each group. Samples were stored at -20 °C and analyzed within 48 hours.

Table 3.1 Dietary classification and preparation

Group	Preparation
Grain	Boiling (30 min for rice and 10 min for others)
Potato	Boiling (10 min)
Sweetener	Dissolving in cold water
Bean	Boiling (10 min)
Nut	None
Vegetable	Boiling (5 min)
Fruit	None
Mushroom	Boiling (5 min)
Algae	Reconstituting in cold water (5 min)
Seafood	None
Meat	Fry (10 min)
Egg	None
dairy	None
Lipid	None
Snack	None
Beverage	Dissolving and extracting in hot water
Seasoning	Dissolving in cold water

3.2.3 Desorption and Analysis of THMs

Using a Shimadzu (Kyoto, Japan) TDTS-2010 thermal desorption unit with an auto-sampler and a purge-and-trap system, collected THMs were thermally desorbed from Supelco tubes, and the emitted THMs were cryofocused and concentrated in a cold trap with helium gas flow. After desorption from the adsorbent, it was heated and the THMs were desorbed again from the trap and injected into a Shimadzu (Kyoto, Japan) QP2010 gas chromatograph equipped with mass spectrometry system. The conditions are shown in Table 3.2.

Table 3.2 Analytical conditions of THMs

	GC-MS	GC-ECD
Preparation	Thermal desorption 280 ºC (10 min)	-
Column	Restek Rtx-1 (0.32 mm×60 m, film 1 μm)	Silicone GE SE-30 (2 m×2.6 mm) [a] J & W DB-624 (0.53 mm×30 m, film 3.0 mm)
Program of GC oven	40 ºC - 3 ºC /min - 100 ºC - 20 ºC /min - 250 ºC	30 ºC (4 min) - 5 ºC/min - 70 ºC (25 min) [a] 50 ºC (6 min) - 2 ºC/min - 78 ºC - 20 ºC/min - 220 ºC (15 min)
Injection	250 ºC, split (25:1)	150 ºC, splitless [a] 200 ºC, splitless
Detection	250 ºC	200 ºC [a] 280 ºC
Purge gas	-	Nitrogen (25 mL/min)
Carrier gas	Helium (2.35 mL/min)	Nitrogen (50 mL/min) [a] Helium (8 mL/min)

[a] Analytical conditions for the first 30 tap water samples

3.2.4 Extraction and Analysis of THMs in Tap Water Samples

(a) Add 1 mL of sulfuric acid (10%) aqueous solution to 40 mL of the water sample.
(b) Add 16 g sodium chloride and 4 mL of *p*-bromofluorobezene hexane solution.
(c) Shake for 15 minutes using a wrist action shaker and allow phases to separate.
(d) Transfer approximately 3 mL of hexane layer to a conical 15-mL centrifuge tube.
(e) Add approximately 2 g sodium sulfate to remove remained water.
(f) Transfer 2 mL of the upper phase to a sampler-vial and analyze it using a Shimadzu (Kyoto, Japan) GC-14B gas chromatograph equipped with electron-capture detector (^{63}Ni). The conditions are shown in Table 3.2.

3.2.5 Extraction and Analysis of THMs in Dietary Samples

The extraction procedure was developed based on literature method (Tamakawa et.a., 1987) as follow.

(a) Disperse 100-g dietary sample in 200 mL of reagent water containing several boiling stones and approximately 0.15 mL of silicone antifoam.
(b) Add 10 mL of phosphoric aqueous solution (10%), 10 mL of sodium sulfite aqueous solution (10%) and 10 mL of *n*-hexane.
(c) Extract THMs using a Dean-Stark distillatory apparatus. Cooling water was provided with a Yamato (Tokyo, Japan) CF-300 refulx condenser. The apparatus collects water and organic solvent that contains THMs from the mixture solution, and they separate into two phases.
(d) After 60-minute of distillation, take 4 mL of *n*-hexane layer out and allow it to cool for 5 minutes.
(e) Add 1 mL hexane with *p*-bromofluorobezene (10 mg/L) to the extract just prior to analysis.
(f) Transfer 2 mL of the sample to a sampler-vial and analyze it using the same GC-ECD equipment mentioned in 3.2.3.

3.2.6 Extraction Recovery Check and Quantifications

The extraction recoveries from dietary and water samples were investigated through the entire extraction procedure after introducing appropriate mass of analytes dissolved in 1 mL of hexane (Table 3.3) to 100 g dietary sample dispersed in 200 mL or 40 mL of water.

The THMs were quantified with *p*-bromofluorobezene (2 mg/L added to the extracts) as the internal standard. Method Quantification Limit (MQL) was defined as the THM concentrations (in hexane solution) that give the signal-to-noise ratios of 10 for THMs in both tap water and dietary. MQLs for airborne THMs were the minimum

absolute amounts (Table 3.4). Not-detected (ND) values were expressed and calculated as zero.

It is appropriate to consider that even for the same raw food, preparation with different water matrix may lead to different extraction performance. Therefore, recoveries for tap water and reagent water prepared samples were both investigated.

Table 3.3 THMs spiking concentrations (μg/L in hexane)

	Spike 1	Spike 2	Spike 3
TCM	100	500	1000
BDCM	25	125	250
DBCM	40	200	400
TBM	200	1000	2000

Table 3.4 MQLs of THMs

Water (μg/L)	MQL
TCM	0.26 [a], 0.5
BDCM	0.07 [a], 0.25
DBCM	0.11 [a], 0.2
TBM	0.5 [a], 0.2

Air (ng)	MQL
TCM	0.1
BDCM	0.1
DBCM	0.2
TBM	0.2

[a] MQLs of THMs for the first 30 tap water samples

3.2.7 Exposure Assessment

The exposure amounts via each route were calculated through the following equations.

Ingestion exposure via tap water (μg/day)
=Tap water concentration (μg/L) × Consumption (L /day) (3.1)

Ingestion exposure via dietary (μg/day)
= ∑ (Food and beverage concentration (μg/kg) × Intake (kg/day)) (3.2)

Inhalation exposure (μg/day)
= ∑ (Airborne concentration in either indoor or outdoor environment (μg/m^3) × Breathing Rate (m^3/day) × Occupation time in each indoor and outdoor environment (hour)/24(hour)) (3.3)

Transdermal exposure amount was calculated with the equations below.

$$D = 2 \times A \times K_p \times C \times \sqrt{\frac{6 \times \tau_{event} \times t_{event}}{\pi}} \quad (3.4)$$

D = transdermal exposure (μg/day);
A = body surface area (cm^2);
K_p = permeability coefficient (cm/hr);
C = aqueous concentration (μg/L);
τ_{event} = lag time (hr);
t_{event} = bathing duration (hr)

$$A = 71.82 \times H^{0.725} \times W^{0.425} \quad (3.5)$$

A = body surface area (cm^2)

H = height (cm)

W = weight (kg)

Daily per capita water consumption of 2 L was applied in the evaluation of ingestion exposure. Intake amounts of foods or beverages were based on the literature values (National Institute of Health and Nutrition, 2006). Occupation time in bathroom and kitchen were applied by the actual time recorded in air sampling pumps. For living room and outdoor, occupation times (948 and 72 min /day) were applied based on literal values (Ministry of Environment, Japan, 2003). The rest of the time was assumed to be in unpolluted environment. Breathing rate (15 m^3/day) was based on the literature value (Ministry of Environment, Japan, 2003). The inhalation exposures in kitchen, living room and outdoor of the latter 29 subjects were applied by the median values of the former 30 subjects. Transdermal exposure was estimated based on the formula introduced by EPA (USEPA, 2004). Body surface area was estimated based on the formula developed by Dubois (USEPA, 1997). The transdermal exposure during bathing time was estimated with a assumption of a 100% of body area contact with water in either case of bathing and shower. Parameters are shown in Table 3.5.

Table 3.5 Parameters of transdermal exposure assessment

	Permeability coefficient (cm/hr)	Lag time (hr)
TCM	0.16	0.27
BDCM	0.18	0.15
DBCM	0.2	0.22
TBM	0.21	0.33

3.3 Results and Discussion

3.3.1 THM Concentrations in Tap Water

From all of the 59 tap water samples of the visited residences, BDCM and DBCM were detected. TCM was detected from 56 samples, and TBM from 29 of them. The widest range of concentration was observed for TCM (0 – 13.1 μg/L) with a highest median value (4.14 μg/L), followed by BDCM (0.15 – 11.3 μg/L, median 4.09 μg/L), DBCM (0.23 – 4.17 μg/L, median 1.71μg/L), and TBM (0 – 3.83 μg/L, median 0 μg/L) (Table 3.6 and Figure 3.2). The large max/min ratios shown in Table 3.6 imply that the THM concentrations in tap water had a regional difference. The min values were calculated with the minimum quantified concentration in tap water.

Table 3.6 THM concentrations in tap water samples (μg/L)

	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
TCM	4.85	4.14	13.10	0.00	52	56
BDCM	4.18	4.09	11.30	0.15	75	59
DBCM	1.73	1.71	4.17	0.23	18	59
TBM	0.48	0.00	3.83	0.00	96	29

[a] Calculated with the minimum and max quantified values

[b] The number of quantified samples in 59

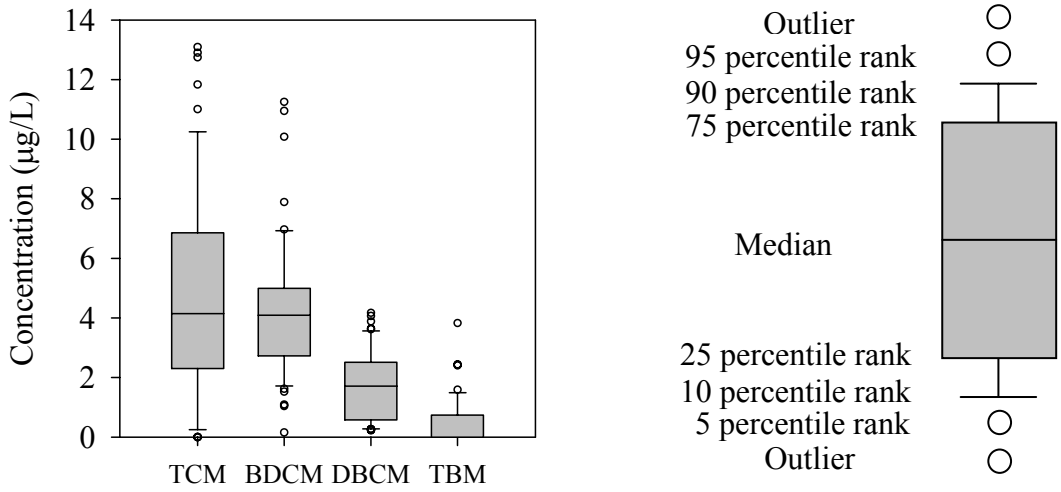

Figure 3.2 THM concentrations in tap water

The statistical differences between the THM concentrations tap waters of the Regions A and B were tested in nonparametric Mann-Whitney test since they did not pass the normality test ($p \leq 0.05$). All statistical analyses were performed with a Sigmaplot (CA, USA) software (Version 10.0). As is shown in Figure 3.3, TCM concentration in Region A (median 5.38 μg/L) is statistically higher than that in B (median 2.44 μg/L). But TBM concentration (median 0 μg/L) is statistically lower than that in B (median 0.78 μg/L). No statistical difference was found for BDCM and DBCM concentrations. Advanced drinking-water treatment system with ozonation and GAC treatment is well-known to be effective to reduce the total THMs in tap water (Glaze and Wenber, 1993; Richardson *et al*., 1999). However, since there is possibly higher concentration of bromide ion in downstream than upstream (Tagami and Uchida, 2006), the concentrations of brominated THMs in the tap water of Region B could be comparable to that in Region A.

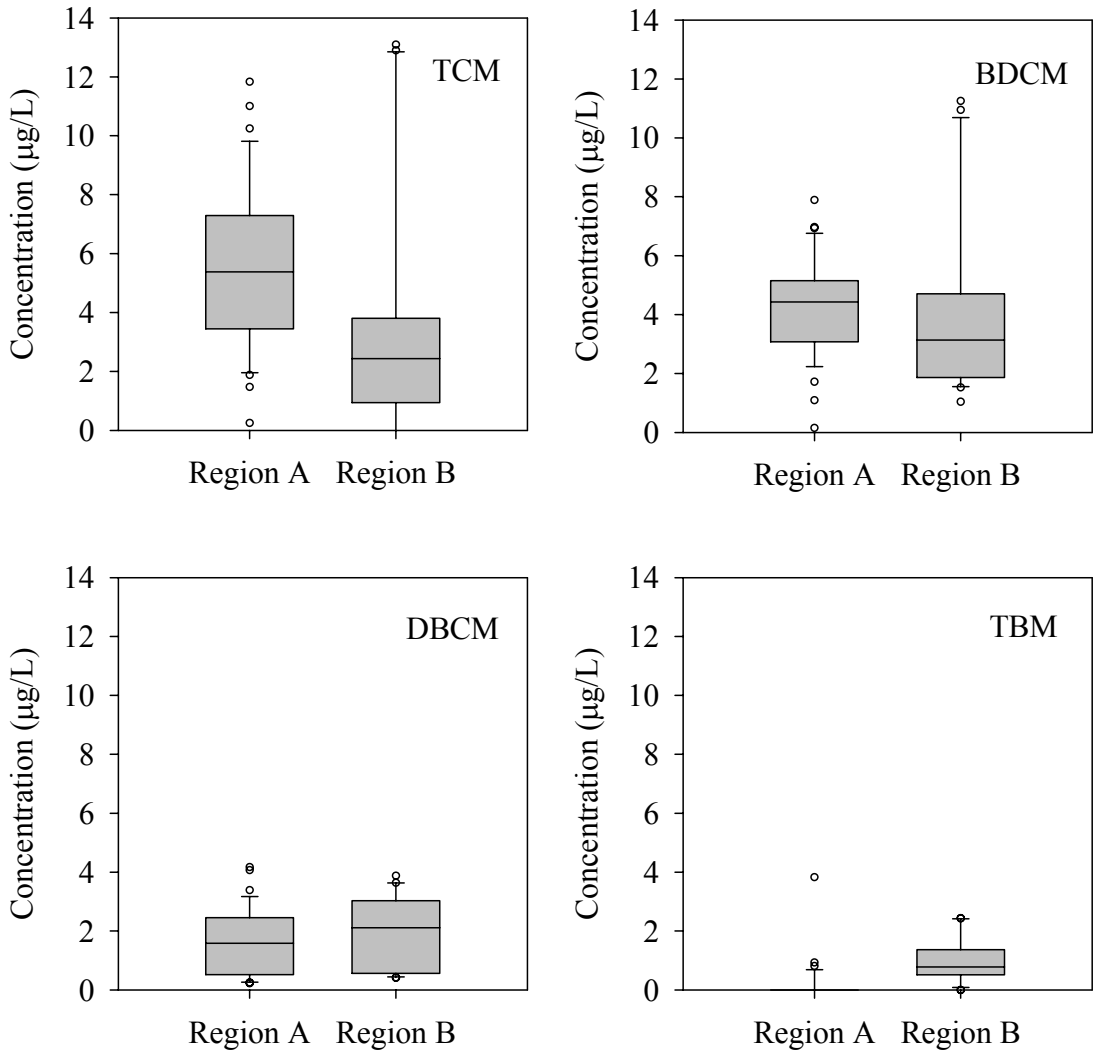

Figure 3.3 THM concentrations in tap water of Regions A and B

3.3.2 THM Concentrations in Indoor and Outdoor Airs

THMs in bathroom air

TCM was detected from all the samples taken in bathroom air. BDCM, DBCM and TBM were also found from 58, 57 and 44 of the total. TCM was found in a wider range (0.89 – 178 μg/m^3, median 14 μg/m^3) than BDCM (0 – 104 μg/m^3, median 14.5 μg/m^3), DBCM (0 – 44 μg/m^3, median 9.57 μg/m^3), and TBM (0 – 7.63 μg/m^3, median 1.27 μg/m^3) (Table 3.7 and Figure 3.4). The max/min values shown in Table 3.7 imply that

the THM concentrations in bathroom air varied greatly. As was mentioned in chapter 2, THMs could be emitted from tap water into air during bathing. Therefore, the great max/min ratios were probably because of the different life-styles (e.g. short or long bathing duration) and regional difference of their concentrations in the tap water.

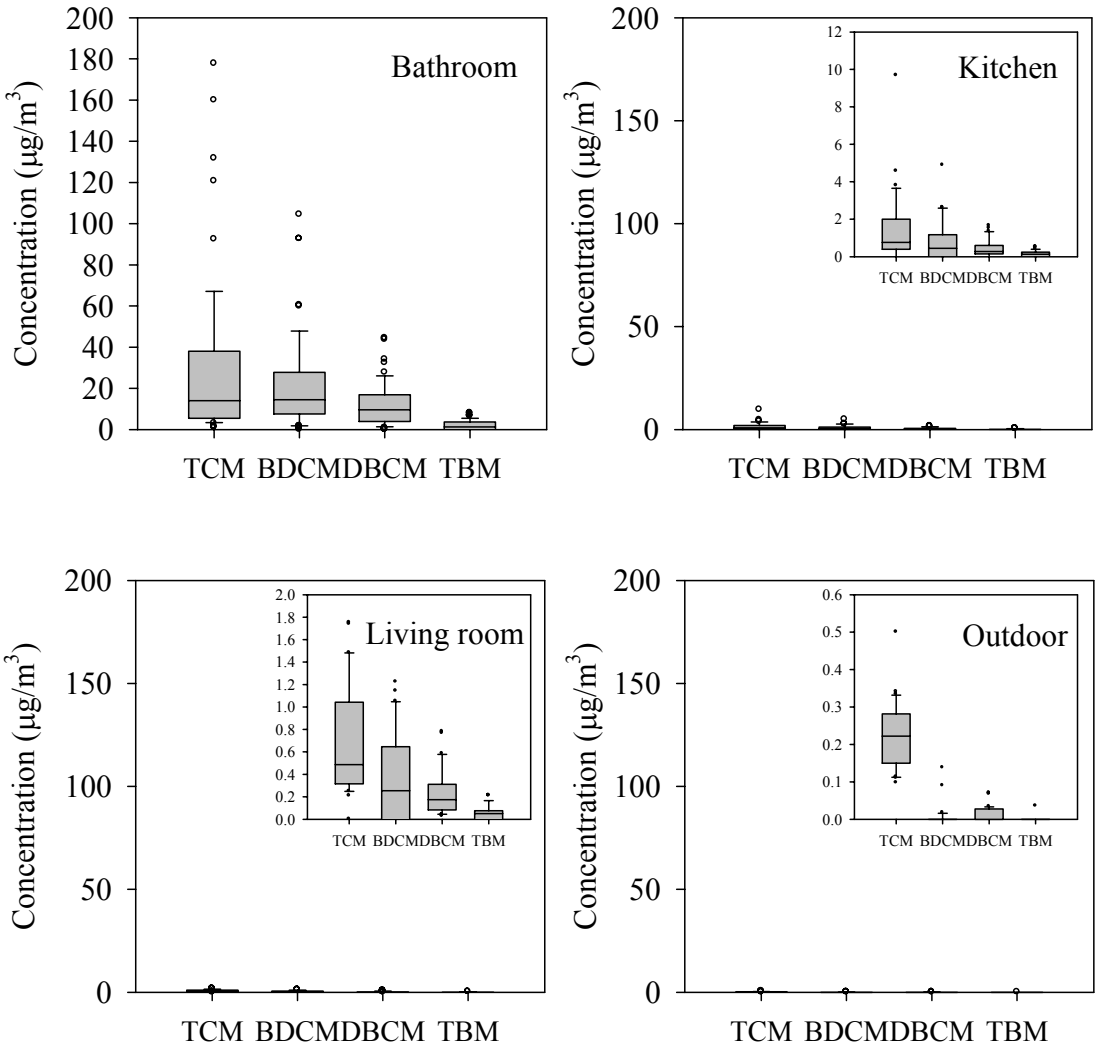

Figure 3.4 THM concentrations in air of each environment

Table 3.7 THM concentrations in air of each environment (μg/m^3)

Bathroom	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
TCM	30.10	14.00	178.00	0.89	200	59
BDCM	21.40	14.50	104.00	0.00	141	58
DBCM	11.70	9.57	44.00	0.00	100	57
TBM	2.05	1.27	7.63	0.00	21	44
Kitchen	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
TCM	1.43	0.76	9.68	0.00	31	26
BDCM	0.86	0.44	4.89	0.00	22	22
DBCM	0.46	0.27	1.65	0.00	21	26
TBM	0.15	0.13	0.53	0.00	7	19
Living room	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
TCM	0.68	0.49	1.75	0.00	8	29
BDCM	0.39	0.26	1.22	0.00	8	20
DBCM	0.24	0.18	0.78	0.03	26	30
TBM	0.06	0.05	0.21	0.00	5	17
Outdoor	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
TCM	0.22	0.22	0.50	0.10	5	30
BDCM	0.01	0.09	0.14	0.00	7	3
DBCM	0.01	0.03	0.07	0.00	4	11
TBM	0.00	0.00	0.04	0.00	1	1

[a] Calculated with the minimum and max quantified values

[b] The number of quantified samples in 59

The statistical differences between the THM concentrations in bathroom air of Regions A and B were also tested in the Mann-Whitney test ($p \leq 0.05$). Comparison results of THM concentrations in bathroom air between Regions A and B were very similar to those of the tap water (Figure 3.5) except that DBCM concentration in Region A was statistically lower than that in Region B.

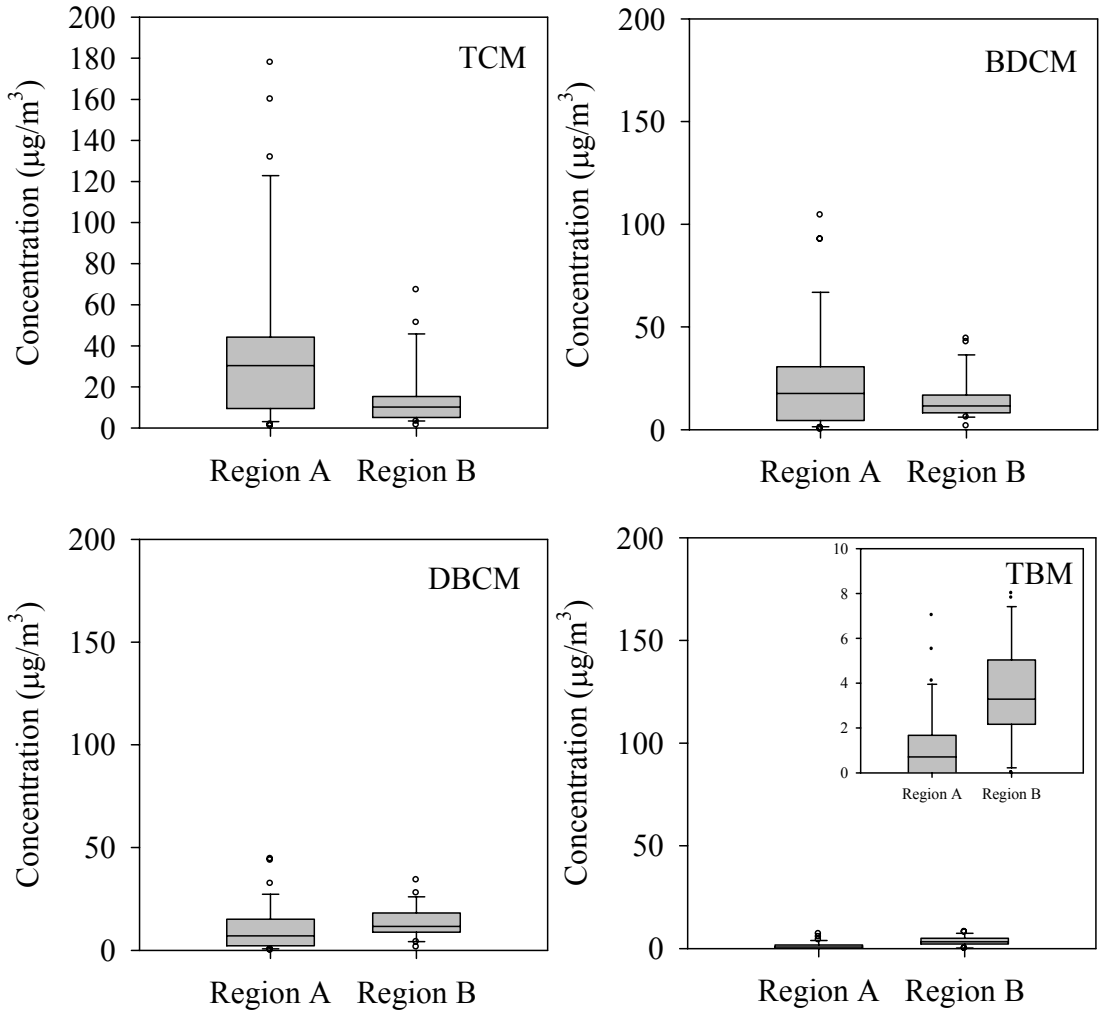

Figure 3.5 THM concentrations in bathroom air of region A and B

To compare this research with abroad ones, the ratios of the bathroom air THM concentrations to that of the local tap water were calculated (Figure 3.6). The median values of TCM, BDCM, DBCM and TBM were 5.51, 4.03, 5.78 and 2.81 respectively. These values are slightly higher than the ratios reported by Nuckols *et al*. (TCM, 3.1; BDCM, 3.3 and DBCM, 3.9), who studied airborne THM in a shower stall. As was mentioned in 2.3.1, in Japan, besides shower, the bathtub is usually filled with a great volume of water to serve the whole family. Therefore, more THMs are likely to be emitted in this situation because of its larger amount of water use.

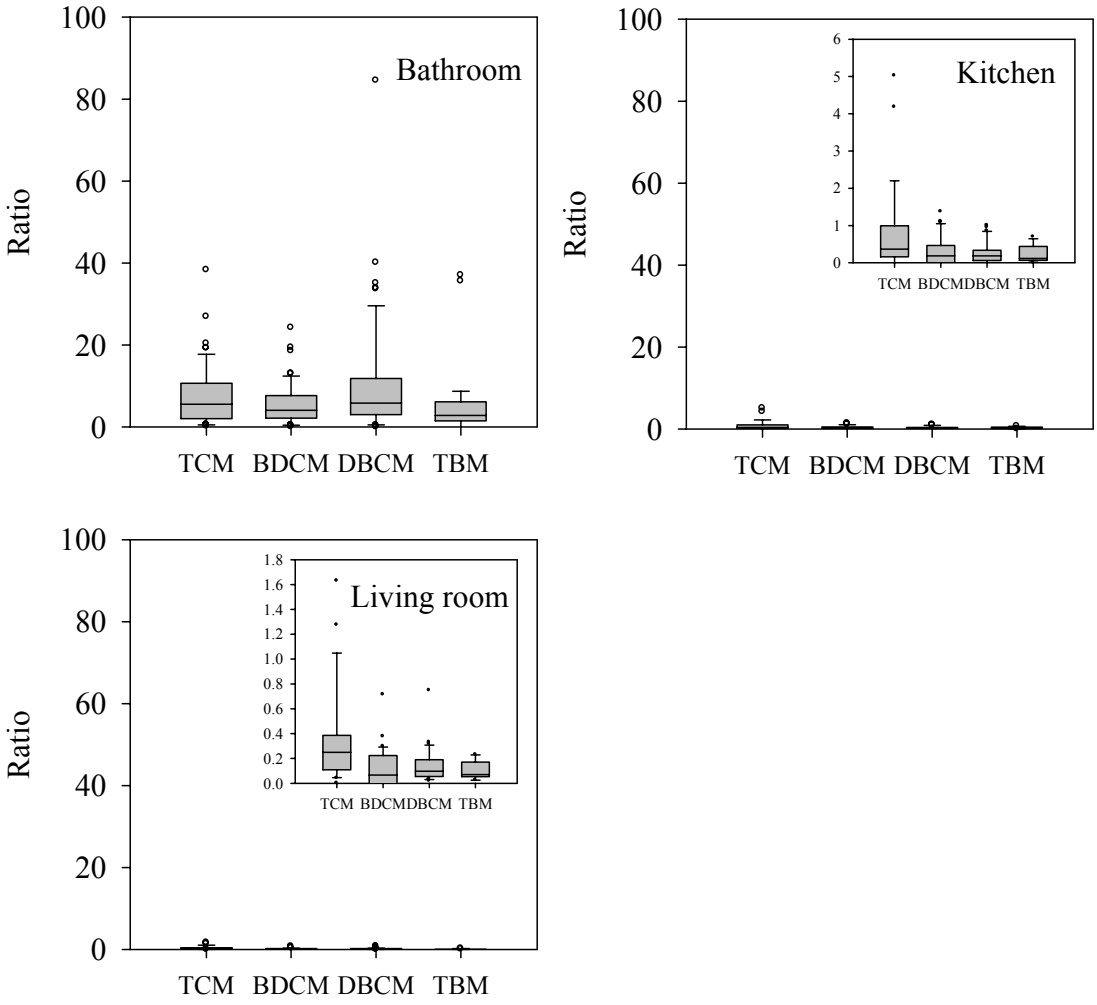

Figure 3.6 Ratios between THM concentrations in indoor air and local tap water

THMs in kitchen and living room airs

Airborne TCM and DBCM were found from 26 kitchens among 30 of them. BDCM and TBM were found from 22 and 19 of them. TCM was found in a wider and higher range (0 – 9.68 μg/m^3, median 0.76 μg/m^3) than BDCM (0 – 4.89 μg/m^3, median 0.44 μg/m^3), DBCM (0 – 1.65 μg/m^3, median 0.0.27 μg/m^3) and TBM (0 – 0.53 μg/m^3, median 0.13 μg/m^3) (Table 3.7 and Figure 3.4).

DBCM were detected from all 30 living rooms. TCM, BDCM and DBCM were from 29, 20 and 17 of them. TCM was also found in a wider and higher range (0 – 1.75 μg/m^3, median 0.49 μg/m^3) than BDCM (0 – 1.22 μg/m^3, median 0.26 μg/m^3), DBCM (0.03 – 0.78 μg/m^3, median 0.18 μg/m^3) and TBM (0 – 0.21 μg/m^3, median 0.05 μg/m^3) (Table 3.7 and Figure 3.4).

Studies (Sato *et al*., 1993; Gordon *et al*., 2006) showed that the emission source of THMs in kitchen and living room air is also probably tap water. Figure 3.6 shows the ratios of the THM concentrations in kitchen and living room airs to that of tap water in each residence. In kitchen and living room, the median values of TCM, BDCM, DBCM and TBM were 0.36, 0.18, 0.18 and 0.12, and 0.25, 0.07, 0.1, and 0.07, respectively. In case of kitchen, median value of TCM is much higher than the ratio (0.05) reported by Sato *et al* (1993). In living room, median values of TCM and BDCM are very close to those reported by Watanabe *et al*. (1990) (0.16 and 0.05). Furthermore, the order of max/min ratios of THM concentrations in living room air was not in agreement with bathroom and kitchen (Table 3.7). These facts imply that THM concentrations in kitchen air were more dependent to tap-water-use than living room.

THMs in outdoor air

Airborne TCM and DBCM were detected from 30, and 11 samples among 30 of them. BDCM and TBM were detected from only 3, and 1 out of them. They were detected from outdoor air in much lower concentrations than in other indoor environments (TCM, 0.1 – 0.5 μg/m^3; median 0.22 μg/m^3, BDCM, 0 – 0.14 μg/m^3; median 0.09 μg/m^3; DBCM 0 – 0.07 μg/m^3; median 0.03 μg/m^3; TBM0 – 0.04 μg/m^3; median 0 μg/m^3)

(Figure 3.4). As is shown in Table 3.7, the max/min ratios of TCM concentration in outdoor air were lower than in other environments. This implies that the TCM concentrations in outdoor air had almost no regional difference, and they were independent with tap-water-use.

3.3.3 THM Concentrations in Dietary Samples

Tables 3.8, 3.9, and 3.10 show that the average THM recoveries (TCM 54.6%, BDCM 68.3%, DBCM 72.4%, and TBM 72%) were lower than those reported in the previous research (Yamada *et al*., 1994) based on a one-week constant survey on table-ready meals of three subjects. The simpler composite of food and less complicated matrix of analysis samples in that research may explain its better recoveries. The recoveries also varied greatly in different dietary groups, but relative standard deviations were less than 30% in all samples. Therefore, the measured THM concentrations were corrected through the division of them with their recoveries.

Table 3.8 THM extraction recoveries of dietary samples without water preparation

Group	TCM		BDCM		DBCM		TBM	
	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
Nut	0.52	0.09	0.60	0.04	0.59	0.09	0.48	0.15
Fruit	0.69	0.26	0.53	0.16	0.89	0.03	0.66	0.20
Seafood	0.31	0.06	0.50	0.16	0.72	0.09	0.85	0.18
Meat	0.27	0.03	0.25	0.12	0.55	0.10	0.76	0.12
Egg	0.72	0.19	0.84	0.15	0.81	0.05	0.86	0.07
dairy	0.36	0.13	0.64	0.13	0.71	0.01	0.64	0.21
Lipid	0.64	0.25	0.74	0.20	0.71	0.06	0.67	0.01
Snack	0.37	0.13	0.49	0.29	0.62	0.18	0.46	0.20

Table 3.9 THM extraction recoveries of dietary samples prepared with tap water

Group	TCM		BDCM		DBCM		TBM	
	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
Grain	0.55	0.05	0.53	0.15	0.60	0.24	0.86	0.09
Potato	0.28	0.23	0.47	0.06	0.75	0.19	0.68	0.21
Sweetener	0.69	0.15	1.09	0.24	0.76	0.23	0.88	0.09
Bean	0.71	0.24	0.87	0.23	0.82	0.09	0.78	0.08
Vegetable	1.02	0.09	1.03	0.01	1.09	0.03	1.05	0.10
Mushroom	0.34	0.13	0.62	0.11	0.85	0.04	0.79	0.08
Algae	0.61	0.14	0.71	0.27	0.47	0.22	0.40	0.16
Beverage	0.32	0.22	0.52	0.19	0.79	0.06	0.61	0.18
Seasoning	0.47	0.03	0.77	0.23	0.67	0.17	0.71	0.08

Table 3.10 THM extraction recoveries of dietary samples prepared with reagent water

Group	TCM		BDCM		DBCM		TBM	
	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
Grain	0.62	0.05	0.81	0.17	0.80	0.19	0.66	0.20
Potato	0.44	0.05	0.49	0.04	0.75	0.19	0.68	0.21
Sweetener	0.40	0.11	0.64	0.04	0.62	0.21	0.86	0.09
Bean	0.41	0.24	0.89	0.17	0.59	0.23	0.78	0.08
Vegetable	1.10	0.08	1.17	0.21	1.00	0.17	0.99	0.01
Mushroom	0.40	0.20	0.59	0.12	0.70	0.03	0.60	0.26
Algae	1.12	0.18	0.76	0.06	0.68	0.07	0.54	0.21
Beverage	0.52	0.01	0.70	0.02	0.61	0.24	0.60	0.18
Seasoning	0.31	0.20	0.54	0.14	0.68	0.08	0.87	0.20

Tables 3.11 and 3.12 show that TCM was found from all the samples in a lower range (0.02-32 ng/g) than that reported by Yanagibashi (2008) (2-320 ng/g). The algae group had the highest concentration of TCM (32 ng/g), followed by the seasoning (18.9 ng/g), meat (12.8 ng/g) and sweetener groups (10.2 ng/g). Among these four groups, three of them were prepared with cold tap water. This is probably because the volatilization of TCM did not occur. BDCM (0 – 6.45 ng/g) and DBCM (0 – 3.39 ng/g) were detected from almost all the samples. There were not great difference between them and those reported by Yanagibashi (2008) (0.4 – 3.53 ng/g, 0.2 – 1.45 ng/g). TBM was not detected from all samples.

Table 3.11 THM concentrations in dietary samples without water preparation (ng/g)

Group	TCM		BDCM		DBCM		TBM	
	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)
Nut	0.18	0.34	0.01	0.02	0.03	0.05	0.00	0.00
Fruit	0.02	0.02	0.00	0.00	0.00	0.00	0.00	0.00
Seafood	2.77	8.80	0.57	1.15	0.24	0.33	0.00	0.00
Meat	3.43	12.81	1.62	6.54	0.72	1.31	0.00	0.00
Egg	0.22	0.30	0.05	0.06	0.06	0.07	0.00	0.00
dairy	2.70	7.58	0.39	0.60	0.20	0.29	0.00	0.00
Lipid	2.88	4.49	0.38	0.51	0.16	0.22	0.00	0.00
Snack	1.89	5.15	0.16	0.32	0.19	0.30	0.00	0.00

Table 3.12 THM concentrations in tap water prepared dietary samples (ng/g)

Group	TCM		BDCM		DBCM		TBM	
	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)
Potato	0.70	2.52	0.26	0.56	0.00	0.00	0.00	0.00
Vegetable	1.69	1.65	0.32	0.31	0.46	0.42	0.00	0.00
Mushroom	1.77	5.17	0.63	1.01	0.38	0.45	0.00	0.00
Bean	3.76	5.26	2.44	2.80	1.18	1.44	0.00	0.00
Seasoning	8.97	18.90	4.37	5.69	2.28	3.39	0.00	0.00
Tap water [a]	11.27	12.10	6.49	6.79	3.35	3.51	0.00	0.00
Beverage	3.21	9.92	0.78	1.49	0.45	0.56	0.00	0.00
Algae	19.39	32.0	0.48	0.67	0.49	1.05	0.00	0.00
Tap water [a]	9.94	10.30	5.76	5.70	2.91	3.03	0.09	0.1
Grain	0.05	0.10	0.19	0.36	0.10	0.17	0.00	0.00
Tap water [a]	9.04	9.49	4.90	5.33	2.92	2.85	0.00	0.00
Sweetener	7.03	10.17	3.57	3.27	1.80	2.36	0.00	0.00
Tap water [a]	2.67	2.72	1.56	1.64	0.85	0.87	0.00	0.00

[a] tap water as preparation base

3.3.4 Comparison of THM Concentrations between Tap-water and Reagent-water Prepared Dietary Samples

Table 3.13 shows that TCM, BDCM and DBCM were detected from the dietary prepared with reagent water in lower range (0 – 18.7, 0 – 6.45, 0 – 1.31 ng/g) compared to the samples prepared with tap water (0.1 – 32, 0.31 – 5.69, 0 – 3.39 ng/g) (Table 3.12), and that no TBM detected. TCM, BDCM, and DBCM concentrations were higher in every dietary group prepared with tap water than its corresponding sample prepared with reagent water. Food preparation with tap water did lead samples to higher concentrations of major THMs.

Table 3.13 THM concentrations in reagent water prepared dietary samples (ng/g)

Group	TCM		BDCM		DBCM		TBM	
	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)	Average measured concentration (n=2)	Average corrected concentration (n=2)
Grain	0.00	0.00	0.01	0.02	0.01	0.02	0.00	0.00
Potato	0.23	0.53	0.24	0.48	0.00	0.00	0.00	0.00
Sweetener	0.46	1.14	0.09	0.14	0.06	0.09	0.00	0.00
Bean	0.29	0.71	0.30	0.34	0.17	0.29	0.00	0.00
Vegetable	0.36	0.33	0.06	0.05	0.12	0.12	0.00	0.00
Mushroom	0.00	0.00	0.09	0.15	0.06	0.09	0.00	0.00
Algae	20.96	18.66	0.00	0.00	0.04	0.06	0.00	0.00
Beverage	0.34	0.66	0.05	0.07	0.18	0.30	0.00	0.00
Seasoning	1.59	5.19	0.17	0.31	0.14	0.20	0.00	0.00
Reagent water	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

3.3.5 Water Absorption of Food

The water absorption of food was also investigated. It was calculated through the subtraction of the weight of the food before preparation with water from that after preparation. As shown in Table 3.14, obviously each food absorbed water during preparation in different level. Especially for dried algae group, approximately 7-8 time weight increase was observed. Dried tea leaves and regular or instant coffee powder were prepared according to their package directions. In such cases, instead of water absorption, the amounts of the water used were recorded. Other beverages such as canned coffee or milk were excluded form the calculation. In this way, tap water was considered being indirectly ingested as cooking water via prepared foods. It was estimated to be 658 mL/day in this study. The concept of this indirect tap-water-intake is different with that described in 1.1.4. In the explanation of Kaneko (1996), the water consumed via beverages was separated from that of food. However, because we attempt to investigate the indirect tap-water-intake here, items which are irrelevant with tap water preparation (in this experiment) were exclusively considered. If we define the two-liter daily per capita water consumption as the summation of (a) daily direct tap water intake, (b) daily indirect tap water intake, and (c) daily water intake in other forms (e.g., milk, juice, fluid in food and metabolic water), Figure 3.7 could be created.

Table 3.14 Water absorption of food

Group	Weight of raw food (g)	Weight of prepared food (g)	Water absorption ratio	Dietary intake (g/day)	Indirect tap water intake (mL/day)
Grain	500	596	19%	449.5	72
Potato	500	514	3%	60.5	2
Sweetener [a]	500	1000	not calculated	7.1	0
Bean	500	605	21%	61.5	11
Vegetable	500	542	8%	253.9	20
Mushroom	500	600	20%	15	3
Algae	500	4375	775%	12.9	11
Beverage [a]	100	807	not calculated	616.4	540
Seasoning [a]	500	1000	not calculated	92	0
Sum					658

[a] Not calculated because sample was in solution form

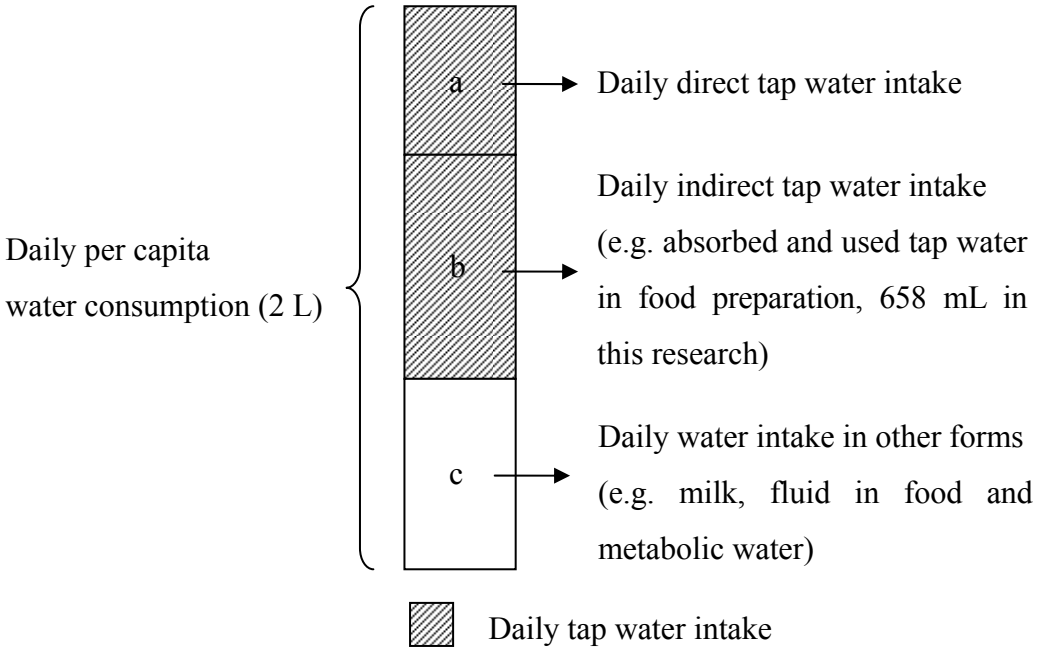

Figure 3.7 Conceptual illustration of the composition
of daily per capita water consumption

3.3.6 THM Ingestion Exposure via Tap Water

THM ingestion exposure amounts via tap water are shown in Table 3.15 and Figure 3.8. Subjects were exposed to TCM in high amounts (0 – 26.2 μg/day, median 8.28 μg/day), followed by BDCM (0.3 – 22.5 μg/day, median 8.19 μg/day), DBCM (0.45 – 8.34 μg/day, median 3.42 μg/day), and TBM (0 – 7.65 μg/day, median 0 μg/day).

Table 3.15 THM ingestion exposure (μg/day)

Ingestion	Arithmetic mean	Median	Max	Min
TCM	9.70	8.28	26.20	0.00
BDCA	8.35	8.19	22.50	0.30
DBCA	3.47	3.42	8.34	0.46
TBM	0.96	0.00	7.65	0.00

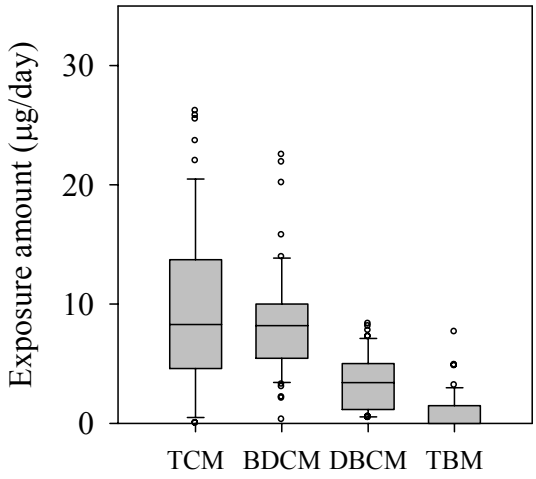

Figure 3.8 THM ingestion exposure

As is shown in Figure 3.9, TCM exposure amount was statistically higher in Region A (median 10.8 μg/day) than that in B (median 4.87 μg/day), but TBM was statistically lower (median 0 and 1.56 μg/day). There were not statistically differences of BDCM (median 8.86 and 6.27 μg/day) and DBCM (median 3.17 and 4.23 μg/day) exposure amounts between two regions.

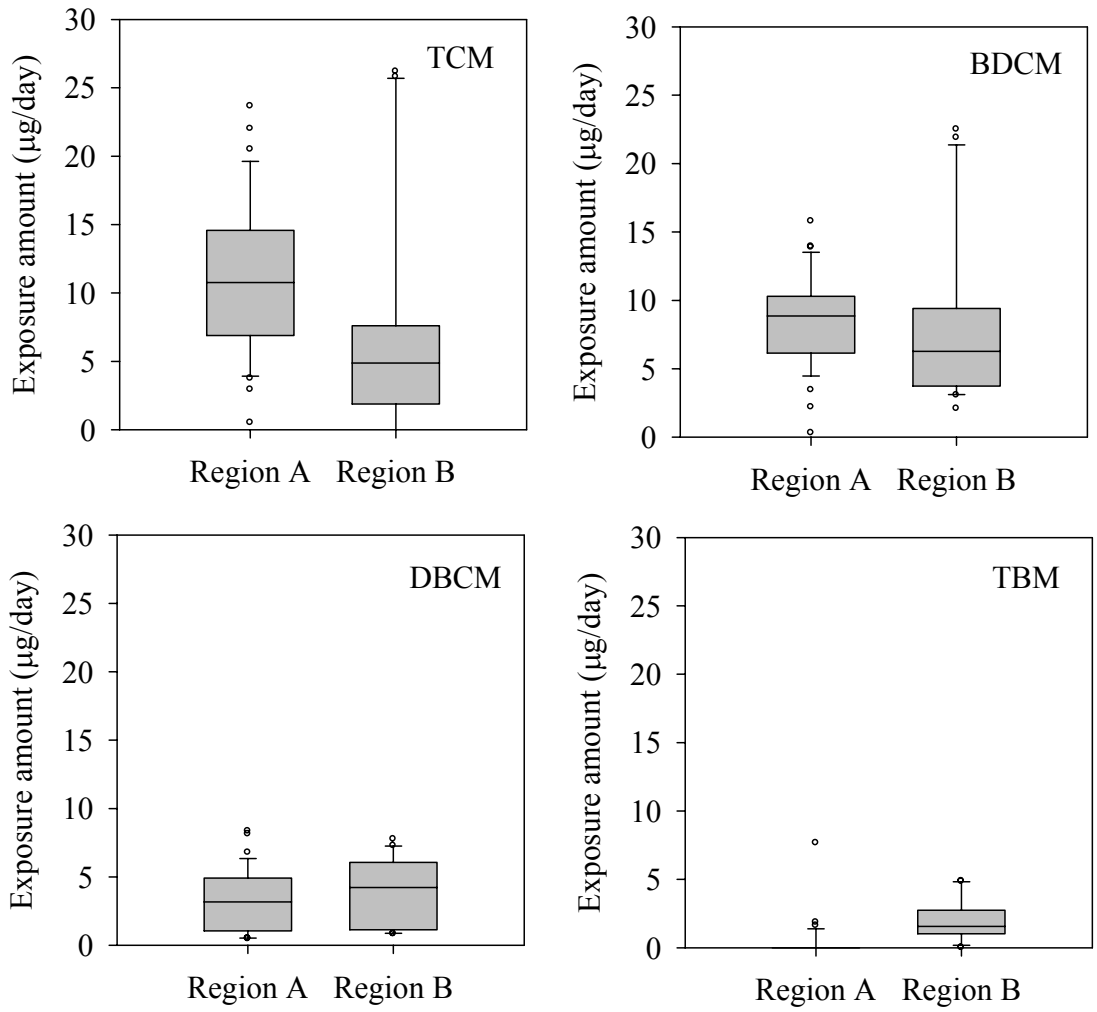

Figure 3.9 THM ingestion exposure via tap water of Regions A and B

3.3.7 THM Inhalation Exposure

Inhalation exposure in bathroom was higher than in other indoor and outdoor environments (Table 3.16 and Figure 3.10). Even THM concentrations in kitchen were higher than in living room, longer occupation time in living room (average 948 minutes) led to much higher exposure amount than that in kitchen (approximately 13-14 times higher for all THMs).

Table 3.16 THM inhalation exposure in each environment (μg/day)

Bathroom	Arithmetic mean	Median	Max	Min
TCM	6.43	2.26	29.90	0.07
BDCM	4.27	2.60	19.00	0.00
DBCM	2.42	1.63	11.80	0.00
TBM	0.42	0.21	2.92	0.00

Kitchen	Arithmetic mean	Median	Max	Min
TCM	0.69	0.37	3.32	0.00
BDCM	0.47	0.18	2.32	0.00
DBCM	0.26	0.12	2.36	0.00
TBM	0.07	0.04	0.74	0.00

Living room	Arithmetic mean	Median	Max	Min
TCM	6.75	4.79	17.30	0.00
BDCM	3.80	2.51	12.10	0.00
DBCM	2.37	1.73	7.69	0.27
TBM	0.54	0.51	2.09	0.00

Outdoor	Arithmetic mean	Median	Max	Min
TCM	0.17	0.17	0.37	0.07
BDCM	0.00	0.00	0.10	0.00
DBCM	0.00	0.00	0.05	0.00
TBM [a]	0.00	0.00	0.03	0.00

Total	Arithmetic mean	Median	Max	Min
TCM	12.90	8.38	45.20	3.64
BDCM	7.77	5.28	25.50	0.00
DBCM	4.67	3.78	19.60	0.41
TBM [a]	1.00	0.73	5.05	0.00

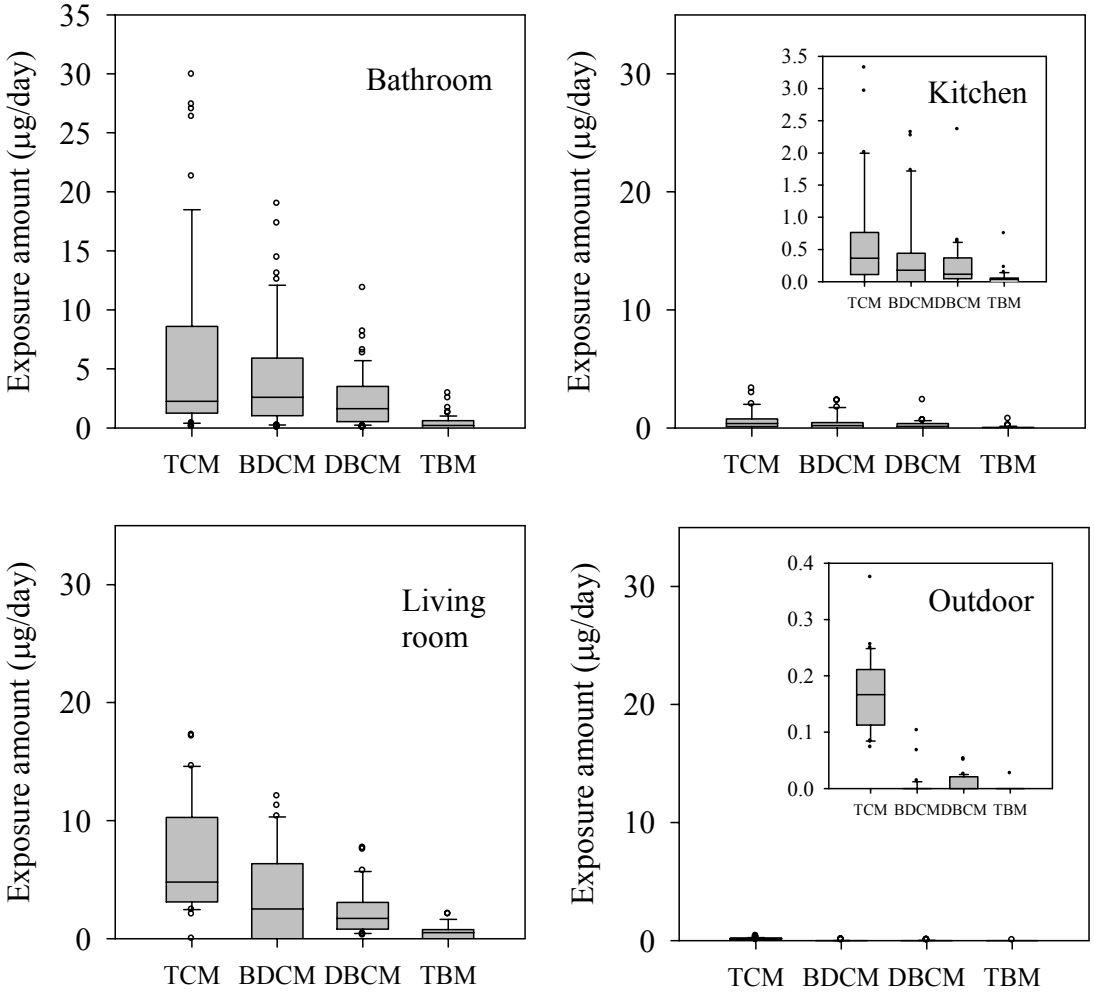

Figure 3.10 THM inhalation exposure in each environment

The total inhalation exposure was estimated through the combination of all inhalation exposure amounts (Figure 3.11). Like the ingestion exposure via tap water, subjects were exposed to TCM in the highest amounts (3.64 – 45.2 μg/day, median 12.9 μg/day), followed by BDCM (0 – 25.5 μg/day, median 7.77 μg/day), DBCM (0.41 – 19.6 μg/day, median 4.67 μg/day), and TBM (0 – 5.05 μg/day, median 1 μg/day).

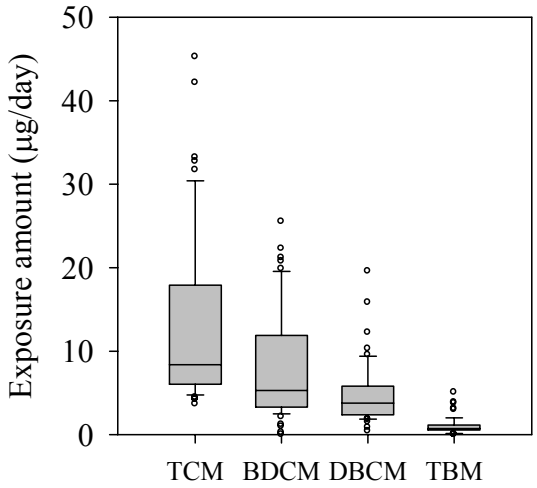

Figure 3.11 THM total inhalation exposure

The statistical differences in the total THM inhalation exposure between Regions A and B were also tested in the Mann-Whitney test. Figure 3.12 shows that in Region A, TCM and BDCM inhalation exposure amounts (median 13.5 and 7.75 μg/day) were statistically higher than those in B (median 6.63 and 4.29 μg/day), but TBM inhalation exposure was lower (median 0.55 and 1.11 μg/day). These regional differences were very similar to those of ingestion exposure estimated in 3.3.5. This observation suggests that the THM concentrations in local tap water are probably stronger factors affecting inhalation exposure than others (e.g., different lifestyles and physical conditions).

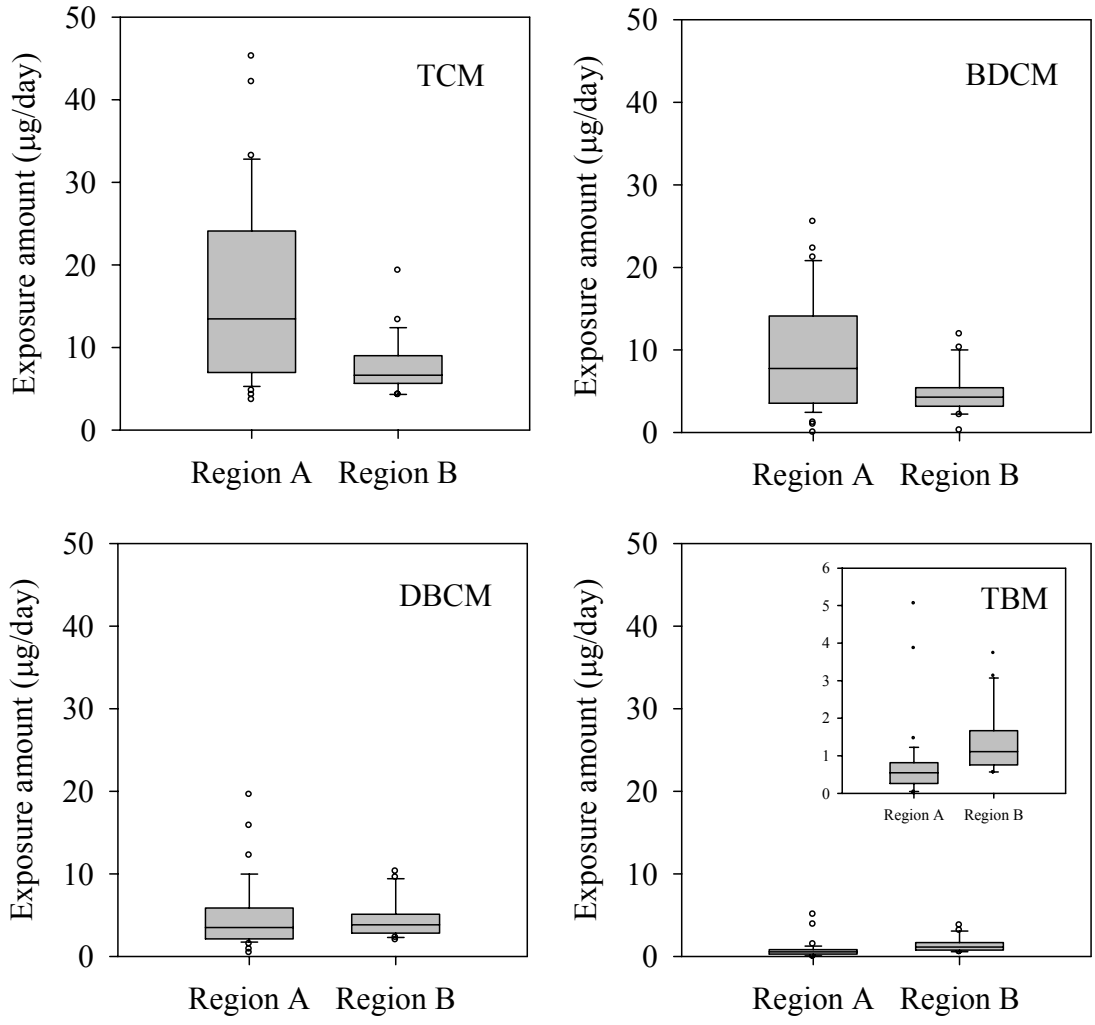

Figure 3.12 THM total inhalation exposure of subjects in Regions A and B

3.3.8 THM Transdermal Exposure

As is shown in Table 3.17 and Figure 3.13, subjects were transdermally exposed to TCM in the highest amounts (0 – 25.5 μg/day, median 8.69 μg/day), followed by BDCM (0.38 – 18.1 μg/day, median 6.21 μg/day), DBCM (0.42 – 15.6 μg/day, median 3.37 μg/day), and TBM (0 – 18.2 μg/day, median 0 μg/day).

Table 3.17 THM transdermal exposure (μg/day)

Ingestion	Arithmetic mean	Median	Max	Min
TCM	9.80	8.69	25.50	0.00
BDCA	7.01	6.21	18.10	0.38
DBCA	4.26	3.37	15.60	0.42
TBM	1.46	0.00	18.20	0.00

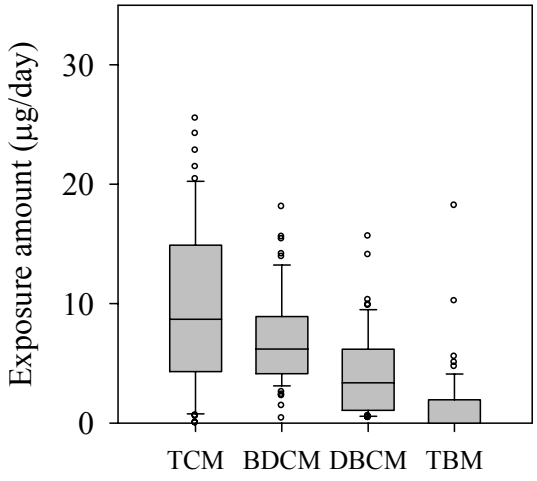

Figure 3.13 THM transdermal exposure

The results of the Mann-Whitney test showed that TCM and BDCM transdermal exposures (median 11.5 and 6.87 μg/day) were statistically higher in Region A than those in Region B (median 3.82 and 4.29 μg/day), but TBM was lower (median 0 and 1.94 μg/day) (Figure 3.14). Again, THM concentrations in local tap water may also be stronger factors affecting transdermal exposure than others (e.g., different bathing duration and skin permeability).

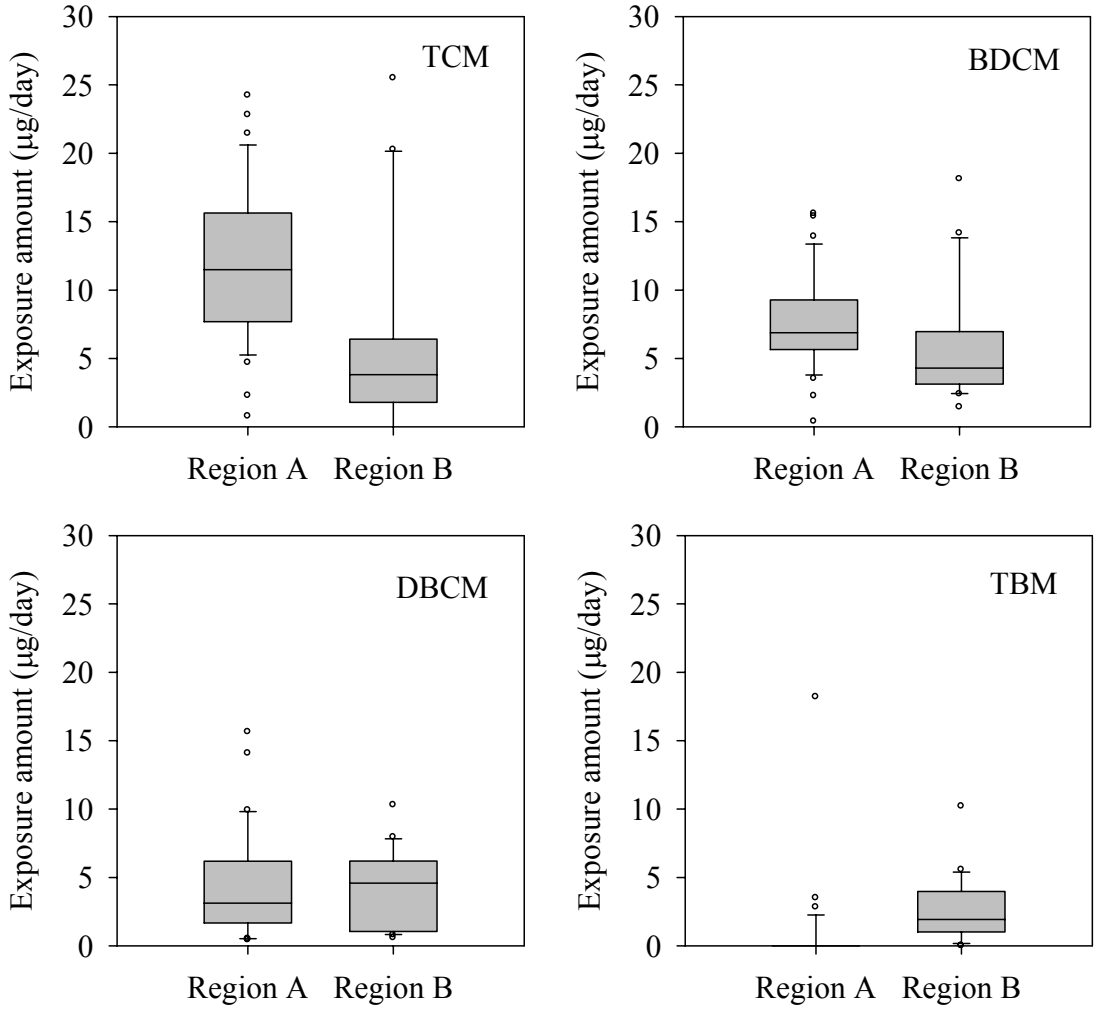

Figure 3.14 THM transdermal exposure of subjects in Regions A and B

3.3.9 THM Ingestion Exposure via Dietary

From Tables 3.18 and 3.19, it was found that the daily dietary intake amount was the main factor governing the ingestion exposure amount. Although the highest TCM concentration was detected in algae group, daily exposure amount via it was 0.41 μg/day because of its small daily intake amount. On the contrary, the much larger daily intake of beverage group led to nearly 15 times higher exposure amount (6.11 μg/day) than that of algae. For both BDCM and DBCM, the greatest contributor among dietary samples was also beverage. The estimated TCM and BDCM total ingestion exposure via dietary (12.3 and 2.64 μg/day) are lower than that those reported by Yanagibashi (2008) (173 and 3.8 μg/day).

Table 3.18 THM ingestion exposure via dietary samples without water preparation (μg/day)

Group	Intake (g/day)	TCM	BDCM	DBCM	TBM
Nut	2.1	0.00	0.00	0.00	0.00
Fruit	119.2	0.00	0.00	0.00	0.00
Seafood	82.6	0.73	0.09	0.03	0.00
Meat	77.9	0.99	0.51	0.10	0.00
Egg	34.4	0.01	0.00	0.00	0.00
dairy	135.4	1.03	0.08	0.04	0.00
Lipid	10.5	0.05	0.01	0.00	0.00
Snack	25.6	0.13	0.01	0.01	0.00
Sum		2.93	0.70	0.18	0.00

Table 3.19 THM ingestion exposure via tap water prepared dietary samples (μg/day)

Group	Intake (g/day)	TCM	BDCM	DBCM	TBM
Grain	449.5	0.04	0.16	0.07	0.00
Potato	60.5	0.15	0.03	0.00	0.00
Sweetener	7.1	0.07	0.02	0.02	0.00
Bean	61.5	0.32	0.17	0.09	0.00
Vegetable	253.9	0.42	0.08	0.11	0.00
Mushroom	15	0.08	0.02	0.01	0.00
Algae	12.9	0.41	0.01	0.01	0.00
Beverage	616.4	6.11	0.92	0.35	0.00
Seasoning	92	1.74	0.52	0.31	0.00
Sum		9.35	1.94	0.97	0.00

From the comparison of the ratios of TCM, BDCM and DBCM ingestion exposure amounts to local tap water concentrations between this research and two previous market-basket researches (Table 3.20), great difference was observed from one of them (Sasao,1996). Since the ingestion exposure via dietary confronts spatial and temporal variabilities, an annual national total diet survey is therefore necessary in the future work. However, in this research, the ingestion exposure estimated above was applied to the calculation of allocation factor because it firstly covered the whole typical dietary items according to the latest classification of National Nutrition Survey.

Table 3.20 Comparison of ratios of the THM
ingestion exposure amount to the local tap water concentration

	Present study	Previous studies	
		a	b
TCM	1.42	1.16	0.44
BDCM	0.54	0.76	0.06
DBCM	0.45	0.67	0.03

[a] Miyata *et al*., 1989

[b] Sasao, 1996

3.3.10 Comparison of THM Ingestion Exposures via Tap-water and Reagent-water Prepared Dietaries

Tables 3.19 and 3.21 show that TCM ingestion exposure via dietaries prepared with tap water was entirely higher (nearly 2-15 times) than those with reagent water in all dietary groups. For BDCM (1-23 times) and DBCM (2-26 times), the differences were greater than TCM. This observation indicates that preparing food with tap water does influence the THM ingestion exposure, and possibly that the less volatile the compound is, the greater the influence becomes. Applying the ingestion exposure via dietary prepared with tap water to the exposure assessment reflects the real-life exposure scenario, but it is not precise enough to estimate the allocation factor of drinking water because the ingestion exposure via indirect tap water from cooking is included in ingestion exposure via dietary.

Table 3.21 THM ingestion exposure via reagent water prepared dietary samples (μg/day)

Name	Intake (g/day)	TCM	BDCM	DBCM	TBM
Grain	449.50	0.00	0.01	0.01	0.00
Potato	60.50	0.03	0.03	0.00	0.00
Sweetener	7.10	0.01	0.00	0.00	0.00
Bean	61.50	0.04	0.02	0.02	0.00
Vegetable	253.90	0.08	0.01	0.03	0.00
Mushroom	15.00	0.00	0.00	0.00	0.00
Algae	12.90	0.24	0.00	0.00	0.00
Beverage	616.40	0.41	0.04	0.18	0.00
Seasoning	92.00	0.48	0.03	0.02	0.00
Sum		1.29	0.14	0.26	0.00

3.3.11 THM Total Exposure

Daily THM total exposure amounts were calculated as the summation of the exposure amounts via each route based on the results in 3.3.6 – 3.3.9. The ingestion exposure via dietaries was combined with the exposure amounts via other routes for each subject. Therefore, its spatial and temporal variation was not estimated. The results are shown in Table 3.22 and Figure 3.15.

Table 3.22 THM total exposure amounts (μg/day)

	Arithmetic mean	Median	Max	Min	n [a]
TCM	44.70	43.40	92.90	16.50	59
BDCA	25.80	24.30	55.10	3.31	59
DBCA	13.50	12.30	44.70	3.38	59
TBM	3.42	0.98	30.90	0.00	59

[a] The number of the estimated subjects in 59

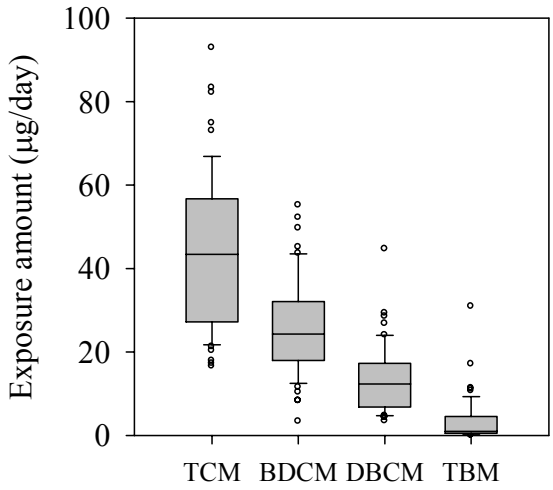

Figure 3.15 THM total exposure amounts

The maximum values of the daily THM total exposure amounts were divided by the average body weight of 50 kg. All of them (TCM, 1.86, BDCM, 1.10, DBCM, 0.89, and TBM, 0.62 μg/(kg· day)) were much smaller than their TDI values (Table 2.1). However, as was observed in 3.3.7, 3.38 and 3.3.9, higher THM concentrations in tap water led to higher ingestion, inhalation and transdermal exposure even under various lifestyles. In another word, ingestion exposure amount via tap water could roughly be in a positive proportional relationship with others. Therefore, a same or similar allocation factor could be derived from a much higher total exposure amount than that in this research. For the possibility that total exposure could approach TDI value under certain circumstances (e.g. areas with much higher THM concentrations in tap water than that in this survey) (Figure 3.16), and as was mentioned in 1.1.4, TDI approach ensures that total exposure from all sources does not exceed the TDI of each chemical. Therefore, It is very necessary to discuss and decide the allocation factors even the total exposure amounts were surveyed to be lower than TDI values.

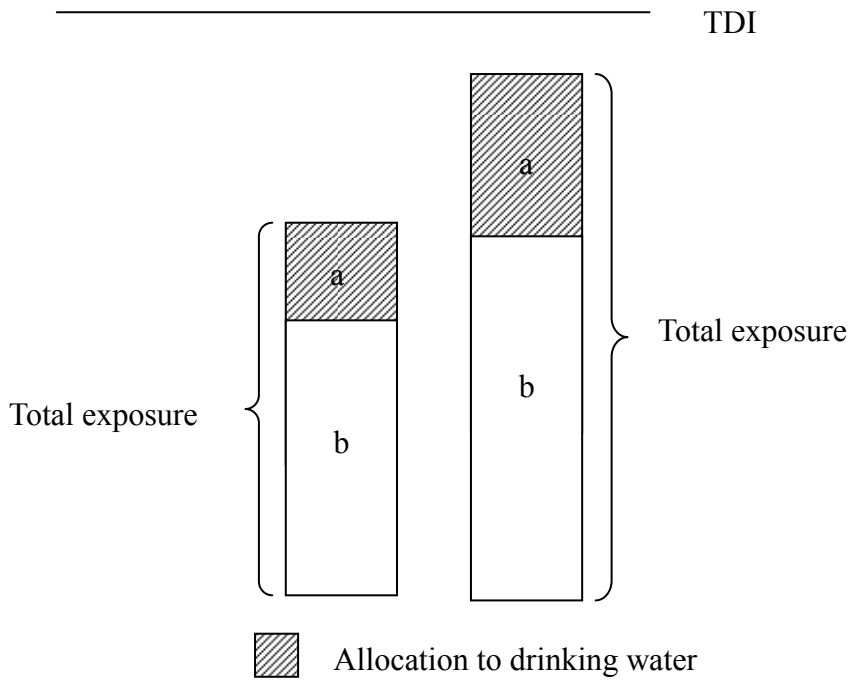

Figure 3.16 Conceptual illustration of the similar allocation to drinking water in different total exposure
(a, ingestion exposure via tap water; b, exposure via other routes)

3.4 Allocation to Drinking water

3.4.1 Estimation of Allocation Factor of Drinking water

THM allocation factors of drinking water in total exposure were calculated through following equation. This approach follows the derivations of THMs in the current standard value of Japan. It considers that ingestion exposure of consuming 2 L of tap water per day should be allocated to drinking water in total exposure. The ingestion exposures via tap water and dietary are independently considered (Figure 3.17). Therefore, the indirect tap-water-intake via prepared food discussed in 3.3.5 is not considered here. And the exposure via dietary intake is also based on the measured THM concentrations in foods prepared with tap water. Subjects who were not estimated to be exposed to THMs (total exposure amount = zero) were excluded.

Allocation factor = Ingestion exposure via tap water / Total exposure (3.6)

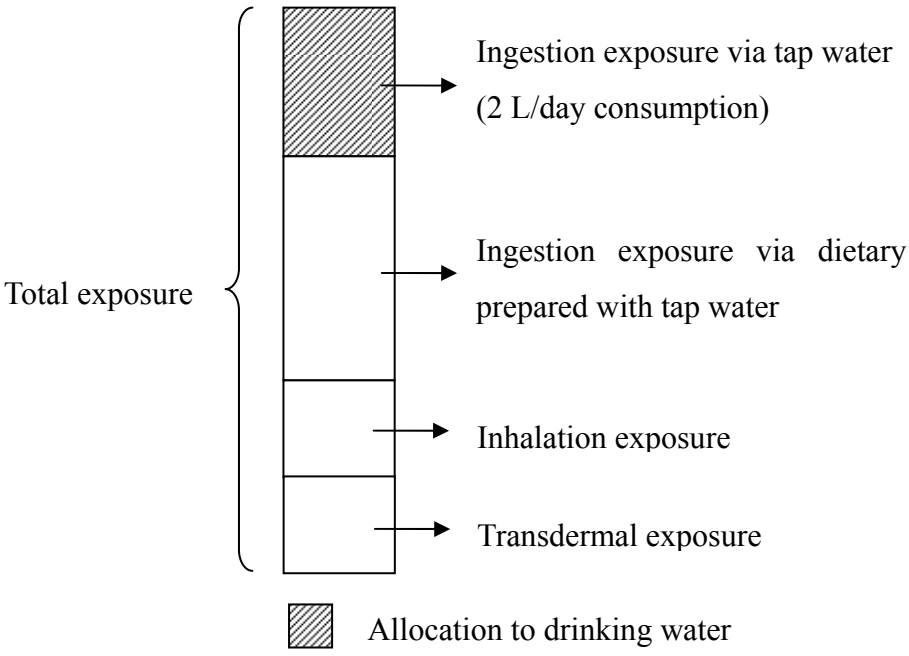

Figure 3.17 Conceptual illustration of the allocation to drinking water in the derivations of the current standard values

In the results of TCM for the 59 subjects (Table 3.23 and Figure 3.18), the minimum allocation factor was approximately 0.02, and the median value was 0.18. Thirty-three subjects were estimated to have allocation factors lower than the current applied 0.2. The minimum and median values of BDCM were estimated to be 0.9 and 0.32. Four subjects had factors lower than 0.2. In the results of BDCM, the minimum and median allocation factors were 0.6 and 0.23. Factors of 20 subjects were lower than 0.2 among 59. The minimum and median values of TBM were estimated to be 0 and 0.08. Thirty-two subjects had factors lower than 0.2 among 57 of them, and 28 of them had factors of zero.

Among the four species, BDCM had a slightly higher range of allocation factor than others. This is because that for BDCM, the ingestion exposure via tap water (median 8.19 μg/day) was the highest among the four exposure routes (median 5.28 μg/day for inhalation and median 6.20 μg/day for transermal). In case of TCM, DBCM, and TBM, ingestion exposures via tap water did not showed significant differences with other routes except dietary (e.g. for TCM, median 8.28 mg/day for ingestion via tap water, median 8.38 μg/day for inhalation, and median 8.69 μg/day for transermal). Comparing with TCM, even though the BDCM concentration in tap water (median 4.09 μg/L) was very close to it (median 4.14 μg/L), the boiling point of BDCM (90 ºC) is much higher than that of TCM (61.2 ºC), and their Henry's constants are very close (BDCM, 2.12×10^{-3} atm· m^3/mol, TCM, 3.67×10^{-3} atm· m^3/mol· 25 ºC). Therefore, under approximately the same concentration in tap water, inhalation exposure to BDCM could be less than that of TCM (i.e. allocation factor of BDCM is relatively higher than TCM). Furthermore, BDCM has the smallest Lag time (0.15 hr) among the four species. The smaller relative transdermal exposure of it also led to its higher range of allocation factor.

Table 3.23 THM allocation factors

	Geometric mean [a]	Median	Max	Min	Standard deviation	n [b]
TCM	0.18	0.18	0.4	0	0.10	59
BDCM	0.31	0.32	0.51	0.09	0.10	59
DBCM	0.22	0.23	0.43	0.06	0.10	59
TBM	0.27	0.08	0.46	0	0.16	57

[a] Those with zero value were excluded from the calculation

[b] The number of the estimated subjects in 59

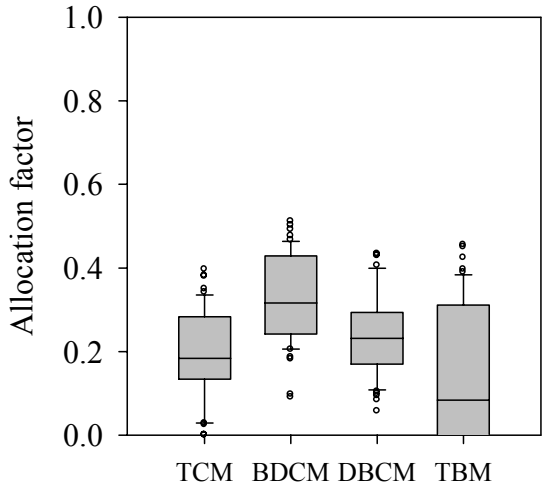

Figure 3.18 THM allocation factors

3.4.2 Attempt on Fitting Lognormal Distribution in Allocation Factor

The most important objective of this research is to discuss how the allocation factors of THMs should be established. The first attempt to answer this question should focus on the investigation of whether the current criteria are rational and appropriate. These criteria include the allocation factors recommended by WHO, and those applied to the current framework of Japan as mentioned in Chapter 2. For this purpose, it is necessary to understand the probabilistic distribution of the allocation factor first. If this distribution can be approximated by a theoretical distribution function, it is then possible to assess the probability of any given allocation factor, and oppositely the allocation factor could also be found in any given probability.

Since the derivation approach of the allocation factor (Equation 3.6) combines multiplicative, additive, and divisional effects, it is difficult to select a theoretical probability distribution based on experiences or previous examples. However, a plausible range (0 – 1) could be inferred because the ingestion exposure via tap water could never exceed the total exposure amount. An allocation factor of zero could be interpreted as there is not ingestion exposure via tap water, but via other exposure routes. Therefore, a probability distribution will be truncated at a minimum of zero.

The lognormal distribution is a uni-modal skewed distribution with an unbounded range of values. This distribution is characterized with the mean (μ) and the standard deviation (σ) of the associated normal distribution of the data. The associated normal distribution is attained by taking the logarithm of the data. The function is expressed in Equation 3.7. It is nowadays widely used in many analyses of risk assessment (e.g. chemical concentrations in various environmental media and media contact rates) (EPA, 2001). As was shown in Table 3.22, the geometric means of the allocation factors for TCM, BDCM and DBCM are very close to their medians. This is one of the most important characteristic of the lognormal distribution. Therefore, the histogram of the allocation factor was created for each THMs. In each histogram, the bins were equally spaced. The number of the bins was decided by the Sturges' rule (Equation 3.8). After the histogram was created, its shape was approximated by a lognormal probability density function with the same μ and σ values (derived from the natural-logarithm-transformed

data). A chi-square test and a Kolmogorov-Smirnov test were used to test the goodness of fit. All statistical analyses were performed with a Sigmaplot (CA, USA) software (Version 10.0).

$$f(x) = \frac{1}{\sigma x\sqrt{2\pi}} \exp\left[\frac{-(\ln(x)-\mu)^2}{2\sigma^2}\right] \tag{3.7}$$

f(x) = probability density of occurrence
x = any value (allocation factor in this research)

$$t = 1 + \frac{\log_{10} N}{\log_{10} 2} \tag{3.8}$$

t = number of the bins
N = number of the data

The results of the chi-square tests showed that it is possible that the allocation factors of all THMs are not in normal distribution. However, the factors of TCM, BDCM and DBCM also failed to pass the Kolmogorov-Smirnov tests. Therefore, it is also possible that they are not in lognormal distribution. This is probably because that the limited number of the raw data could not satisfy the precise tests. As is shown in Figure 3.19, the blank areas under the right tails of each distribution imply that there were not subjects estimated to have high allocation factors. However, the possibility could not be denied without further investigation. In case of TCM, half of the bin that located between 0 and 0.06 were not covered with the left tail of the distribution curve. Similar observation could also be found in DBCM (the bins located between 0.06 and 0.11) and TBM (the bins located between 0 and 0.07). These are probably because that the subjects who were estimated to have allocation factor equal to zero (TCM, 4; TBM, 28) were included in the histogram. An allocation factor equal to zero means no ingestion exposure via tap water. It is because that the ND values of THM concentrations in tap water were calculated as zero. But, it could never be considered as no-exposure in

reality. Since the exposure amount (allocation factor) could be very low, these subjects were included in the histogram. However, they were excluded from the calculation of the mean value and standard deviation of the lognormal function because the data had to be natural-logarithmly transformed first. Even though, the lognormal distribution curve showed an overall unsatisfactory fitting with allocation factors of TBM. Above all, the lognormal distribution could be attempted to approximate the distribution of allocation factors for TCM, BDCM and DBCM. Their cumulative probability distributions were created through the integration in Figure 3.20.

As is shown in Figure 3.20, the current factors of 0.2 applied in Japan were corresponding with relatively higher non-exceedance probabilities in TCM (0.57) and DBCM (043). This suggests that for approximately half of the population, lower allocation factors (standard values) should be established. Therefore, the current factors of TCM and DBCM should be replaced with lower ones. In case of BDCM, the factor of 0.2 is within the lower bound of the distribution (0.12 non-exceedance probability). The 5th or 95th percentiles are often of greatest interest when characterizing variability in risk assessment. In case of allocation factor, the lower tail of the distribution is of greatest concern. The highlighted 5th and 10th percentiles shown in Figure 3.20 did not have allocation factors with great difference for TCM (0.07 and 0.08), BDCM (0.17 and 0.19) and DBCM (0.11 and 0.12). The rounded values of TCM (0.1), BDCM (0.2) and DBCM (0.1) are therefore recommended. In case of TBM, since thirty-two subjects had factors lower than 0.2 among 57 of them (28 of them had factors equal to zero), a lower allocation factor should be appropriate. Since the median value of it was 0.08, along with other three species, an allocation factor of 0.1 is recommended conclusively. However, it should be noted that, (a) the estimation was based on the assumption that the allocation factors of TCM, BDCM and DBCM are lognormally distributed and (b) since the left tail (lower bound) did not quite well fit with the histogram due to limited number of samples, further efforts should be made to investigate this specific area.

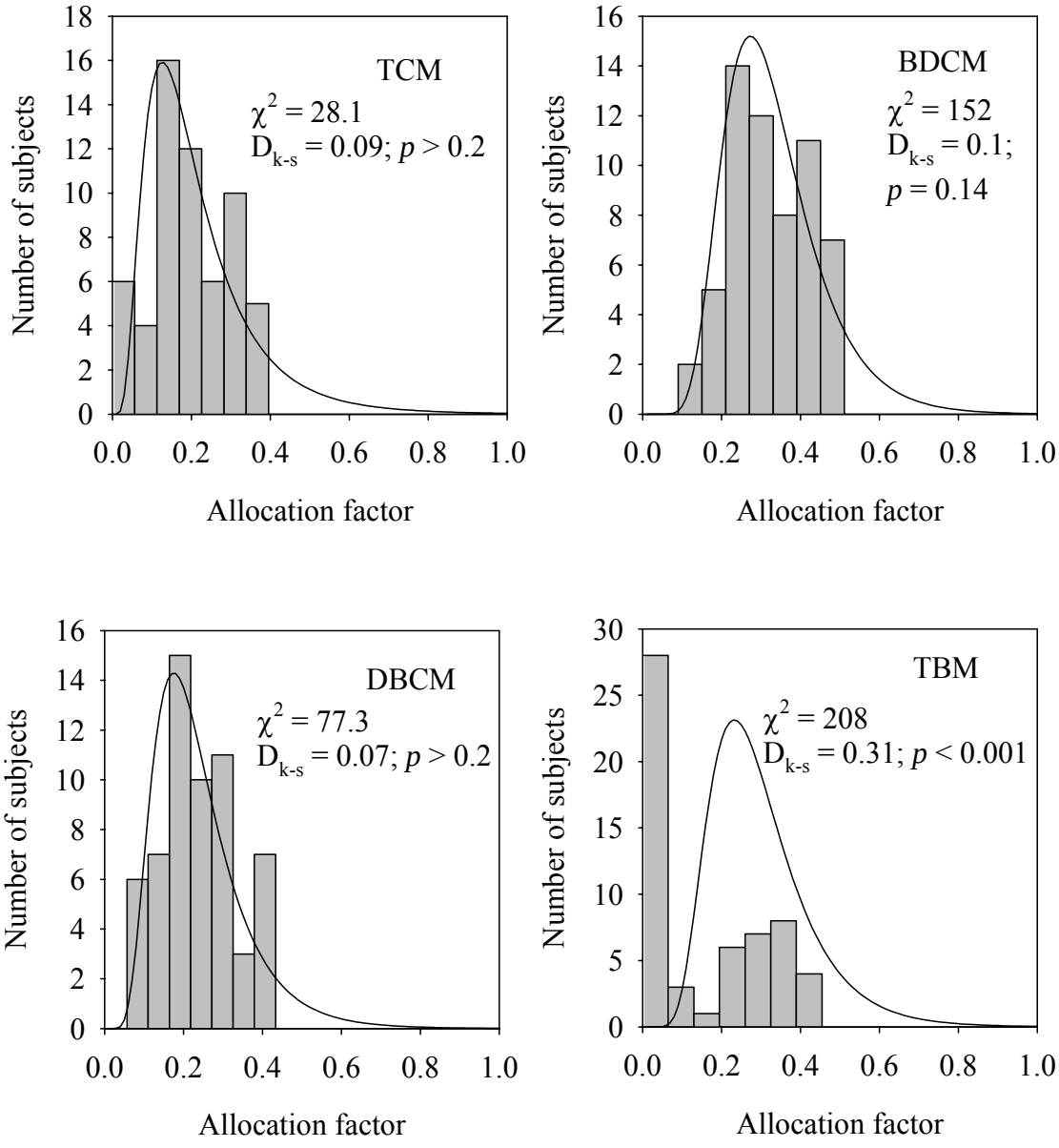

Figure 3.19 Distributions of allocation factors of THMs

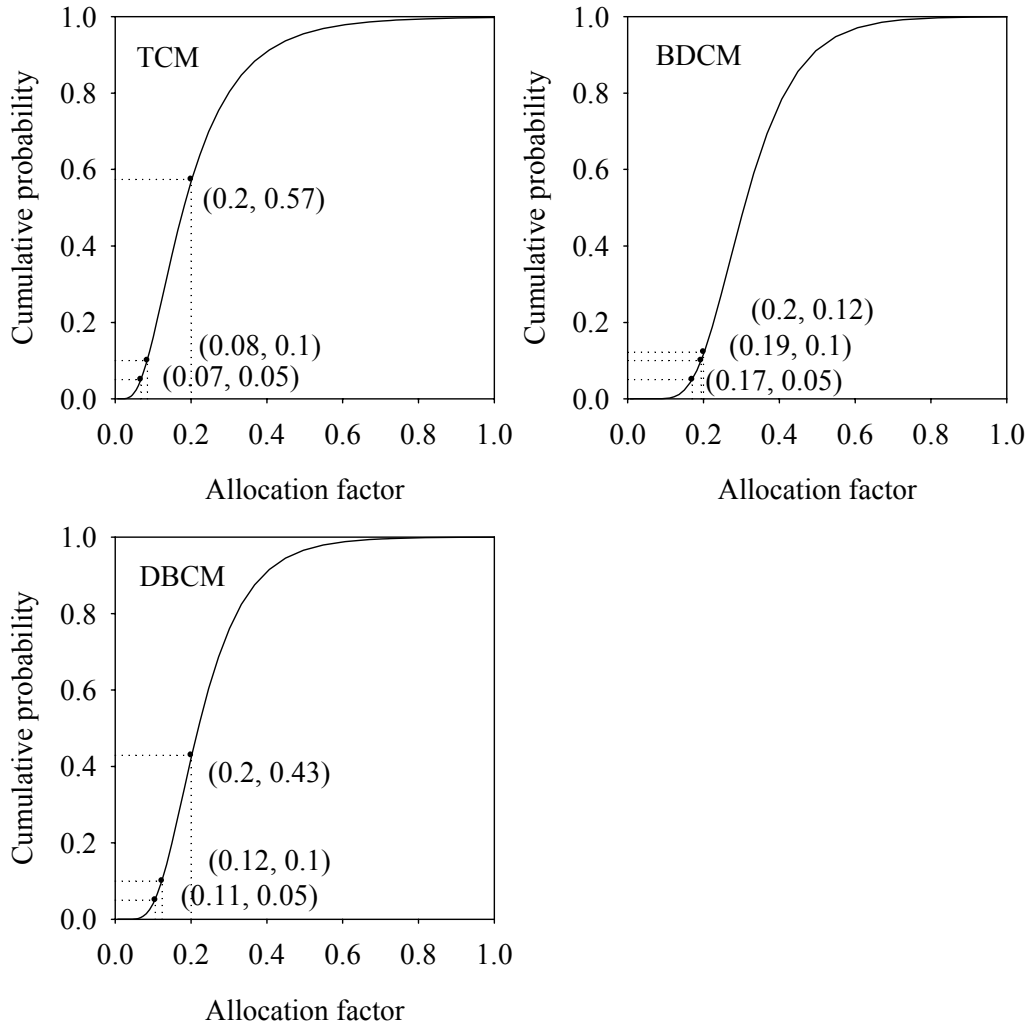

Figure 3.20 Cumulative probability of allocation factors

3.4.3 Allocations to Drinking Water in Regions A and B

The allocation factors for each subjects in Regions A and B were estimated and compared. There are not statistically differences in allocation factors of TCM (median 0.19 and 0.19), BDCM (median 0.30 and 0.36), and DBCM (median 0.22 and 0.24). But, the TBM allocation factor in Region A (median 0.20) was lower than that in B (median 0.34) (Figure 3.21). This observation suggests that even there are regional differences in the exposure to TCM, BDCM and DBCM, the allocation factors to drinking water are

unlikely to be different. Since tap water is the major emission source of airborne THMs, the ingestion and inhalation exposure could change accordingly. Therefore, when setting the allocation factors of TCM, BDCM, and DBCM, more attention should be paid in life-style than regional difference.

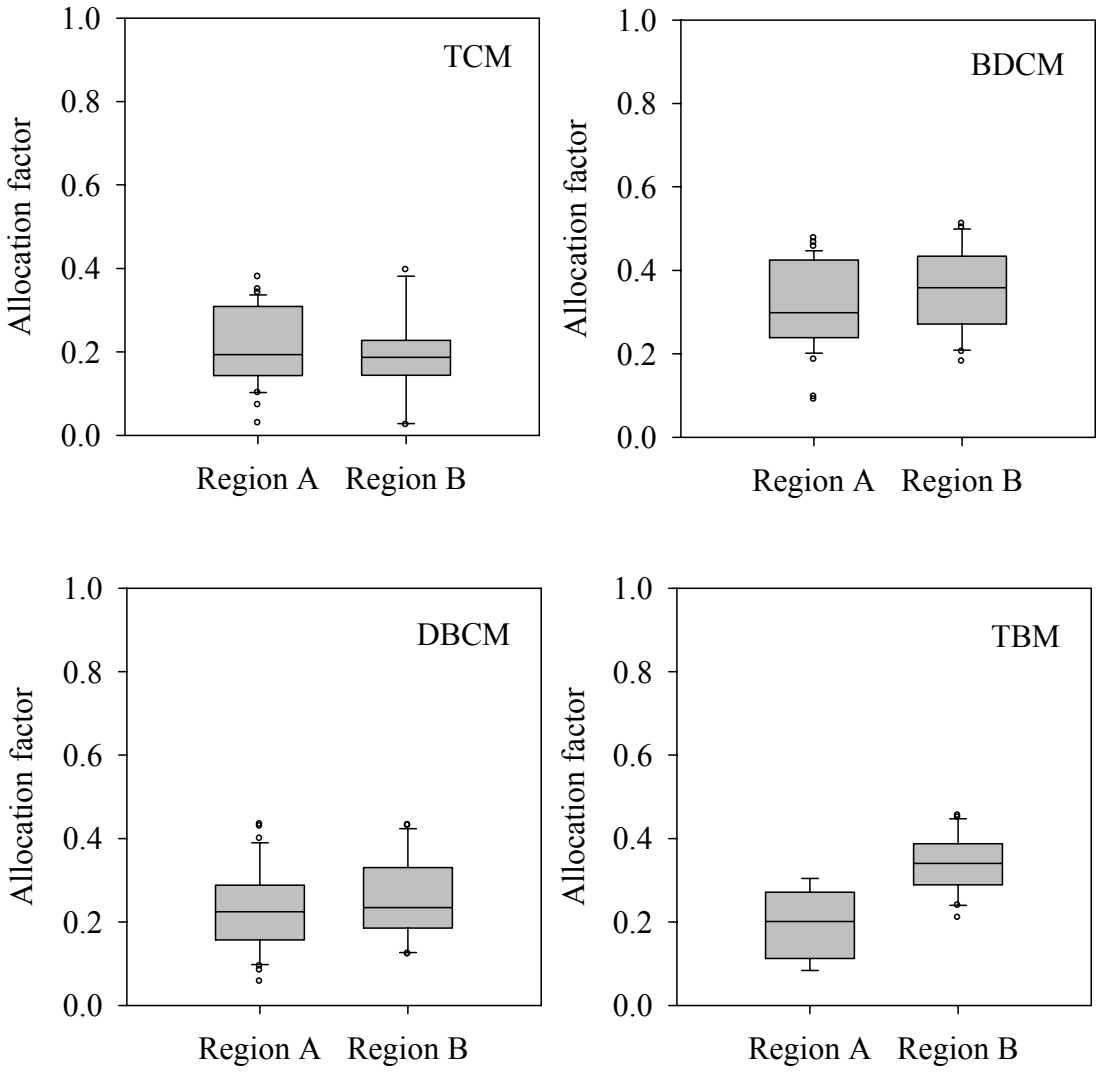

Figure 3.21 THM allocation factors of Regions A and B

3.4.4 Prediction of the High-total-exposure and Low-allocation Scenario

WHO set the guideline for TCM based on a 30-min bath exposure as the highest total exposure scenario. In this research, not only a similar high-total-exposure scenario but also a low-allocation-factor scenario was attempted under domestic environment. Understanding such scenarios could give useful information to further necessary investigation (e.g., the lower bound of the distribution mentioned in 3.4.1). To describe the scenario, affecting factors to high-total-exposure and low-allocation-factor need to be specified. A prediction of them was conducted by applying a forward stepwise multi-linear regression test using a Sigmaplot (CA, USA) software (Version 10.0). For the statistical procedure, $p \leq 0.05$ was set as the criteria. As was mentioned previously, the local tap water concentration is a strong affecting factor to exposure amount. Therefore, the total daily exposure amount of each subject was divided by the local tap water concentration. The ratios for each THMs were considered as the dependent variables in the regression test, as well as allocation factors. The potential independent variables (affecting factors) were chosen from the relevant items of the questionnaire (Table 3.24). Before the test, colinearity was checked between each pair of the independent variables. Pairs have correlation coefficients greater than 0.5 were excluded from the test.

Table 3.24 Dependent and independent variables in multi-linear regressions

Dependent variables	Independent variables
Ratios of the total daily exposure amounts to the THM concentrations in local tap water	Sexuality
Allocation factors	Number of family members [a]
	Type of residence
	Bathroom volume
	Bathing style [a]
	Bathroom occupation duration [a]
	Bathing duration
	Shower duration
	Ventilation

[a] Variable excluded from the colinearity test

The results are shown in Table 3.25. Since the objective of the regression test is not to predict a mathematical model to derive exposure amount or allocation factor, but to find the strong affecting factors, the numerical and logistic independent variables (e.g. number of family member and sexuality) were simultaneously evaluated. And, for this reason, the multiple correlation coefficients (the R) for the regression tests were not shown. However, from the coefficients of the independent variable in the predicted regression model, it is possible to understand which variable is stronger than others. For example, if the coefficient of bathing duration and shower duration to allocation factor of TCM are estimated to be -0.38 and -0.33, then bathing duration is a stronger affecting factor and the longer it is, the allocation factor is smaller. The standardized coefficients shown in Table 3.25 were the coefficients standardized to dimensionless values.

Table 3.25 Affecting factors to total daily exposure and allocation factor

	Dependent variables	Positive independent variables [a]	Negative dependent variables [b]	Standard coefficients [c]
TCM	Total daily exposure amount	Shower duration		0.44
	Allocation factor		Bathing duration	0.38
			Shower duration	0.33
BDCM	Total daily exposure amount	Bathing duration		0.37
		Shower duration		0.56
	Allocation factor		Bathing duration	0.54
			Shower duration	0.51
DBCM	Total daily exposure amount	-		
	Allocation factor		Shower duration	0.34
			Ventilation	0.28
TBM	Total daily exposure amount	Type of residence (apartment)		0.38
		Shower duration		0.51
	Allocation factor		Type of residence (apartment)	0.39
			Shower duration	0.45

[a] Variable with positive standard coefficient

[b] Variable with negative standard coefficient

[c] $p < 0.05$

The results showed that generally shower duration was predicted to be the major positive affecting factor of THM total exposure amounts except DBCM. The total exposure amount to TBM was also observed to be higher in the apartment type of residence than detached house. Longer shower and bathing duration were predicted to lead to smaller allocation factor of TCM and BDCM. And, smaller allocation factor of DBCM was probably because of the long shower duration without ventilation. Further investigation on high-exposure or low-allocation situation should pay more attention to these scenarios.

3.4.5 Alternative Considerations of Allocation to Drinking Water

Consideration of direct and indirect intake of tap water

As was introduced in 1.1.4 and 3.3.5, the daily per capita consumption could be considered as the summation of daily direct tap water intake, daily indirect tap water intake as cooking water (658 mL in this study), and daily water intake in other forms. Mons *et al*. recommend using a 3.49 glasses of water/day (349 – 523 mL/day with a consumption of 100 mL to 150 mL glass volumes) as a conservative estimation on direct tap water intake for quantitative microbiological risk assessment. In Japan, a survey of Yano *et al*. (2000) estimated the arithmetic mean value of direct tap water intake was 209.2 mL/day. This value was applied to the following estimation because it was based on a domestic investigation (Equation 3.9). In another aspect, the ingestion exposure amount via tap-water-prepared dietary was proved to be higher than that of reagent water in 3.3.10. Since this difference is probably due to the indirect intake of tap water, it should be included in the consideration of allocation to drinking water. Above all, the approach is shown as below and in Figure 3.22.

Ingestion exposure via direct tap water intake (μg/day)
= Tap water concentration (μg/L) × Direct tap water intake (L /day) (3.9)

Ingestion exposure via indirect tap water intake (μg/day)
= Ingestion exposure via dietary prepared with tap water – Ingestion exposure via dietary prepared with reagent water (3.10)

Ingestion exposure via tap water (μg/day)
= Ingestion exposure via direct tap water intake + Ingestion exposure via indirect tap water intake (3.11)

Total exposure (μg/day)
= Ingestion exposure via tap water + Ingestion exposure via dietary prepared with reagent water + Inhalation exposure + Transdermal exposure (3.12)

Allocation factor
= Ingestion exposure via tap water intake / Total exposure (3.13)

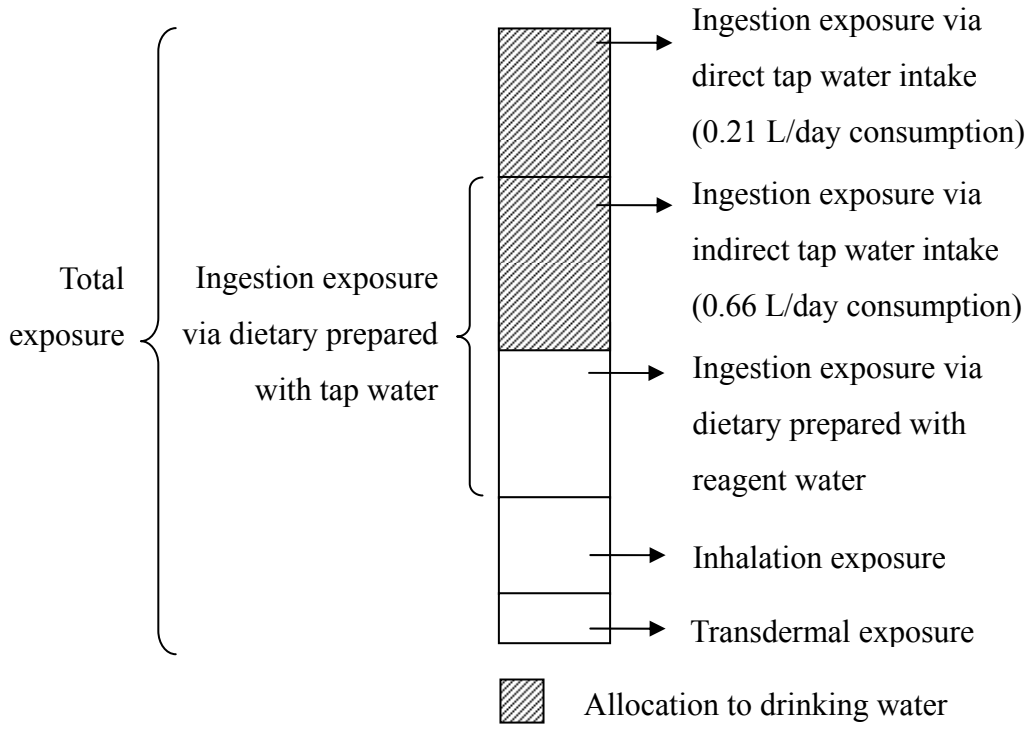

Figure 3.22 Conceptual illustration of allocation to drinking water with the consideration of direct and indirect tap water intakes

Table 3.26 and Figure 3.23 show the result of the estimation. Allocation factors to TCM (0.13 – 0.49, median 0.27) were a slightly higher than the results in 3.4.1 (0 – 0.4, median 0.18). Those of DBCM (0.12 – 0.95, median 0.81) and TBM (0 – 0.95, median0.13) were much higher than the results in 3.4.1 (0.06 – 0.43 median 0.23; 0 – 0.46, median 0.08). But for BDCM, a lower range (0.07 – 0.6, median 0.17) than the results in 3.4.1(0.09 – 0.51, median 0.32) was observed. As was mentioned previously, because applying a greater allocation factor to the derivation directly leads to a higher standard value, the allocation factors of TCM, DBCM, and TBM estimated in 3.4.2 should be sustained.

Table 3.26 THM allocation factors to drinking water in total daily exposure with the consideration of direct and indirect daily tap water intakes

Ingestion	Geometric mean	Median	Max	Min
TCM	0.27	0.27	0.49	0.13
BDCM	0.16	0.17	0.6	0.07
DBCM	0.71	0.81	0.95	0.12
TBM	0.75	0.13	0.95	0

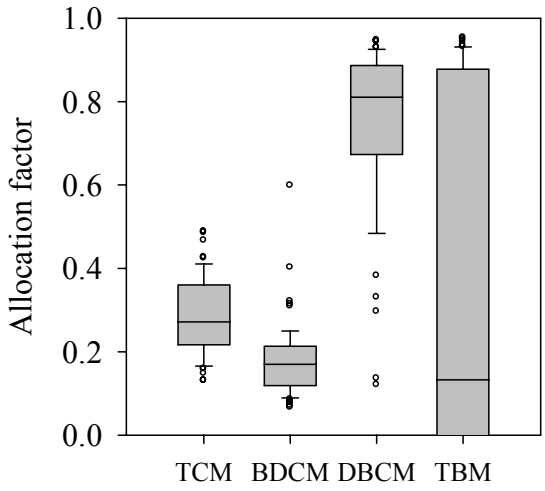

Figure 3.23 THM allocation factors derived by the consideration of direct and indirect tap water intake

The histograms of them were also created (Figure 3.24). Like in 3.4.2, a lognormal distribution was approximated to it. Since the fitting was satisfactory in BDCM, the cumulative probability curve was also created. The 5th and 10th percentiles shown in Figure 3.24 were also very close (0.08 and 0.09). The rounded value of them (0.1) was smaller than that estimated in 3.4.2 (0.2), therefore 0.1 is recommended. It should be noted that among the four species of THMs, standard value of BDCM is derived by a different approach from others. Additionally, applying the allocation factor of BDCM derived from this approach to the calculation of its standard value, the denominator of Equation 1.1 (daily drinking-water consumption) should be 0.87 L (209.2 + 658 mL) instead of 2 L. However, the calculated standard values should not have great difference with each other because the ratios between allocation factor and daily drinking-water consumption in both approaches are very close (0.1 and 0.11).

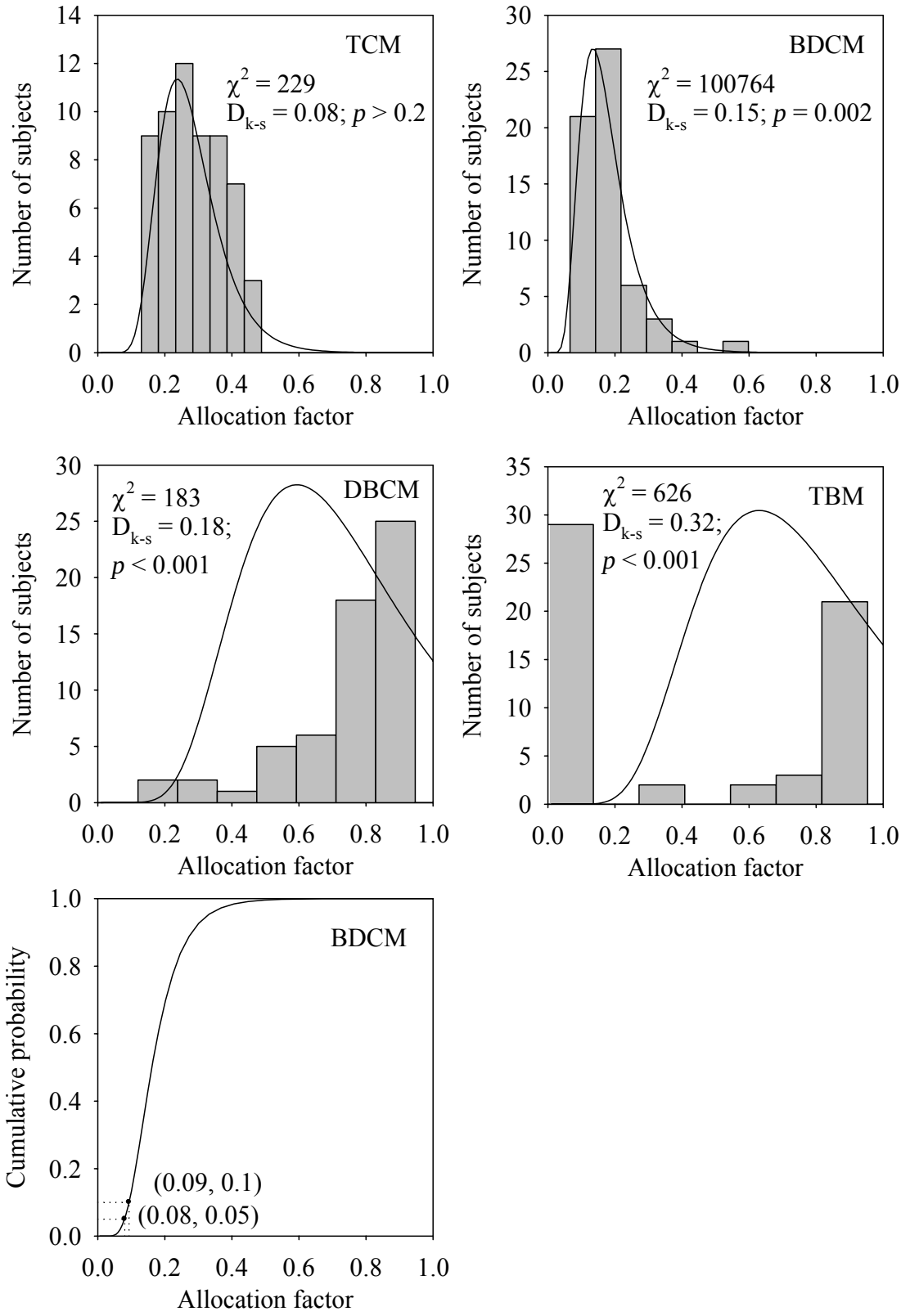

Figure 3.24 Distributions of allocation factors of THMs with the consideration of direct and indirect intake of tap water

Consideration of ingestion-equivalents (Ieq)

Since tap water was considered as the major emission source of THMs in indoor air, WHO attributed the inhalation and dermal exposure to tap water by applying the ingestion-equivalent (Ieq) of TCM. The estimated highest TCM total exposure values for drinking water were for adults in a 30-min bath scenario: 4.61 Ieq (2 litres ingestion, 1.7 litres inhalation, and 0.91 litres transdermal). The allocation factor was estimated to be 0.75. In this section, allocation factor is also attempted based on the same consideration. The derivation is shown in Figure 3.25 and Equations 3.14 – 3.16.

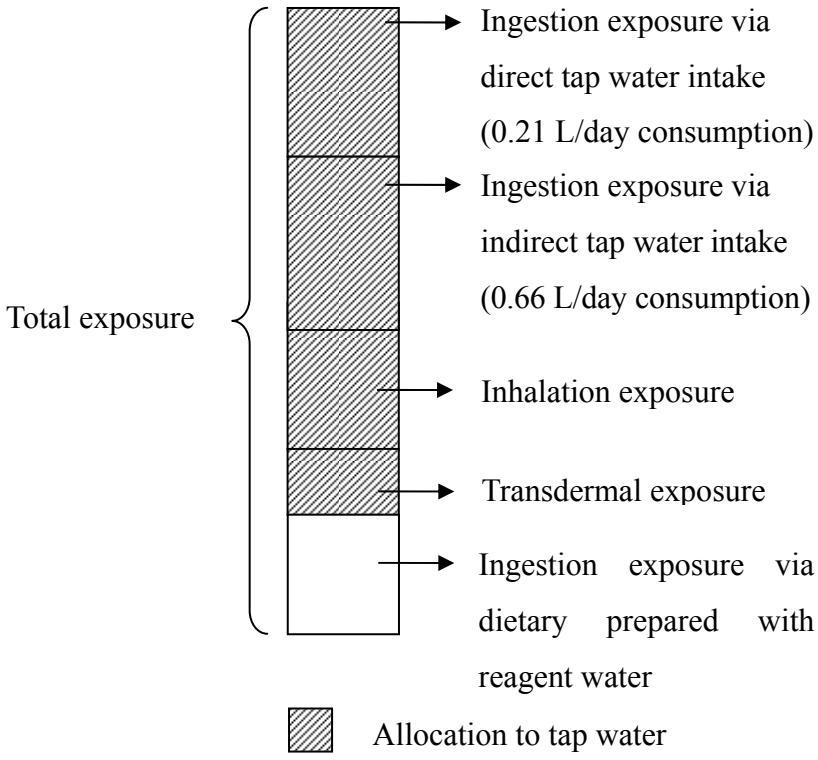

Figure 3.25 Conceptual illustration of allocation to drinking water with the consideration of ingestion-equivalents (Ieq)

Exposure amount allocated to drinking water (μg/day)
= Ingestion exposure via tap water (direct and indirect) (μg/day) + inhalation exposure (μg /day) + transdermal exposure (μg/day) (3.14)

Total exposure
= Exposure amount allocated to drinking water + ingestion exposure via dietary prepared with reagent water (3.15)

Allocation factor
= Exposure amount allocated to drinking water / Total exposure (3.16)

In the result of this estimation, allocation factors for all THMs were estimated to be very high (Table 3.27 and Figure 3.26). Minimum values for TCM, BDCM, and DBCM were greater than 0.7. As was mentioned above, if the allocation factors were derived from approach, standard values will be much higher than present. According to WHO, when a high proportion of TDI has been allocated to drinking water but concentrations in water are generally well below the guideline value, it is not appropriate to allow contamination to increase up to the guideline value (WHO, 2008). In another aspect, applying a much higher allocation factor not only looses the regulation of chemical, but also practically leads the standard value close to its TDI. Additionally, as was mentioned in chapter 2, inhalation exposure to TCM leads to higher health risk than the case of ingestion. Therefore, great uncertainty exists when directly combining inhalation exposure with ingestion and transdermal exposure as total exposure. Above all, establishing the allocation factors for THMs in this approach is not necessary at the present time.

Table 3.27 THM allocation factors of drinking water in total daily exposure with the consideration of ingestion-equivalents (Ieq)

Ingestion	Geometric mean	Median	Max	Min
TCM	0.27	0.87	0.94	0.75
BDCM	0.16	0.95	0.98	0.74
DBCM	0.71	0.99	0.99	0.94
TBM	0.75	1	1	1

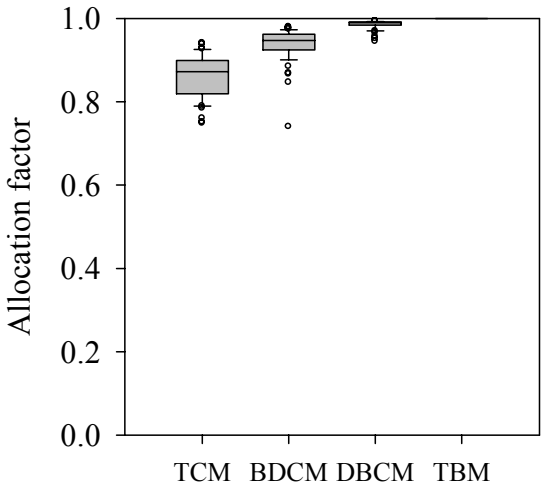

Figure 3.26 THM allocation factors derived by the consideration of ingestion-equivalents (Ieq)

3.5 Summary

In this chapter, THM concentrations in tap water, air and dietary were thoroughly surveyed in domestic environment in Japan. Based on these data, the ingestion, inhalation, and transdermal exposure were estimated. Using the above knowledge, the allocation factors of THMs to drinking water were calculated and discussed. The conclusions are summarized as below.

(a) In the tap water of 59 common residences, four species of THMs were frequently detected. Among them TCM concentration was the highest, followed by BDCM, DBCM, and TBM.
(b) TCM, BDCM, DBCM, and TBM concentrations were much higher in bathroom air than in kitchen, living room and outdoor. Their distributions in each indoor environment were similar to that of tap water. Additionally, domestic THM concentrations in bathroom air were generally higher than those reported abroad.
(c) All THMs were detected from most of the dietary samples prepared with tap water except TBM. THM concentrations were measured to be generally higher than those with reagent water.
(d) Inhalation exposure in living room was comparable to that in bathroom because of its long occupation time. Ingestion exposure via dietary prepared with tap water was higher than those prepared with reagent water.
(e) Allocation factors for the four species of THM should be considered respectively. The distribution of the factors of TCM, BDCM and DBCM were approximated by lognormal distributions. The allocation factors corresponding with 5th or 10th percentile probabilities of TCM (0.07, 0.08), and DBCM (0.11 and 0.12) were very close to 0.1. Those of BDCM (0.17, 0.19) were close to 0.2. In case of TBM, the median value of its allocation factor was 0.08.
(f) Alternative derivations were attempted based on the considerations of direct and indirect tap water intakes, and ingestion equivalent (Ieq) approach. For TCM, DBCM, and TBM, higher ranges of their allocation factors were derived. The lognormal distribution did not fit them. In case of BDCM, the allocation factor

derived from the consideration of direct and indirect tap water intake was fitted in a lognormal distribution. The correspondings with 5th or 10th percentile probabilities were 0.08 and 0.09 respectively, which were also very close to 0.1.

(g) The allocation factor recommended in this study was 0.1 for the four species of THMs. BDCM was derived from a different approach, and the daily drinking-water consumption should be applied as 0.87 L to the calculation of its standard value.

Chapter 4

Multi-route Exposure Assessment and the Allocation to Drinking Water of Haloacetic Acids

This chapter aims to survey the HAA concentrations in tap water, food, and air. A large-scale investigation was conducted in food because HAAs were assumed to be mainly exposed via this route. The HAA multi-route exposure amounts were estimated. Their allocation factors were calculated and recommended based on the obtained knowledge.

4.1 Introduction

Information on human exposure to the six species of HAAs (MCA,MBA, DCA, TCA, BCA, BDCA, DBA, DBCA, and TBA) is rather limited compared with THMs. In WHO, guidelines of only MCA, DCA, and TCA were established, and the available data are considered inadequate for the rest 6 species (WHO, 2008). In Japan, MCA, DCA, and TCA have been regulated in the standard group since 2004 mainly because their toxicological information was considered to be sufficient (Ministry of Environment, Japan, 2003). The other 6 species are temporarily classified into under-consideration group.

As was mentioned in 2.3.2, it is possible that inhalation exposure to HAAs occurs via small aerosols during bathing (Xu and Weisel, 2003). From the knowledge that abundant THMs exist in indoor environment, it was decided to survey the HAA concentrations in common residences too. Also, studies showed that HAAs were detected from dietary in abroad (Reimann *et al*., 1996). Since they are stable in aqueous phase, it is also necessary to survey HAA concentrations in domestic dietary.

Therefore, the objectives of this chapter are as follows: (a) to survey HAA concentrations in common indoor (bathroom, and living room), outdoor airs, and tap water, (b) to survey HAA concentrations in diets of the whole typical items, (c) to estimate the

inhalation, transdermal, and ingestion (drinking-water and dietary) exposures, and (d) to discuss how the allocation factors of HAAs should be established based on the obtained knowledge.

4.2 Materials and Methods

4.2.1 Reagents

Reagent water for all the experiments was purified with a Millipore (Tokyo, Japan) Academic-A10 purification system. All the reagents were purchased from Wako Pure Chemical Industries (Osaka, Japan) except haloacetic acid standards from Kanto Chemical (Tokyo, Japan). Water-analysis-grade MTBE, methanol, and 1,2,3-trichloropropane were used for preparing the calibration curves and checking the extraction recovery. Residual-pesticide-analysis-grade sodium sulfate and Japanese Industry Standard (JIS) reagent-grade sulfuric acid, sodium hydrogen carbonate, sodium dihydrogen phosphate, sodium hydrogen phosphate, copper sulfate pentahydrate, and sodium bicarbonate were used in the HAA extraction from the water and dietary samples.

4.2.2 Survey Protocol

Air and tap water sampling

Twenty-two residences were visited for the survey from August to December 2007. Permissions of the survey and cooperations were received from each of the resident. The residences were geographically scattered in a watershed area. Among the 22 residences, there were 15 single-family houses and 7 apartments. Each residence was occupied with a single family with one to six persons. Air samplings were conducted in bathrooms (during occupation), living rooms, and outdoors (from 6 p.m. to 10 a.m.). Ventilation was not controlled for all the residences during the sampling.

Air sampling in bathroom was conducted during bathing time, and an over night (from 6 p.m. to 10 a.m) sampling was conducted in living rooms and outside. Air was

passed through two glass impingers connected in series containing 50 mL (bathroom) or 60 mL (living room and outdoor) of 1 mM sodium hydroxide aqueous solution with a Sibata (Tokyo, Japan) MP-Σ300 constant flow air sampling pump. The flow rates were 5.0 L/min for bath room and 1.5 L/min for living room and outdoor, respectively. All liquid samples were stored below 5 ˚C and protected from light until extraction. During each visit, a recall questionnaire was also conducted on their lifestyles.

Concurrently, tap water samples were also collected in glass vials with Teflon-lined enclosures. Prior to sampling, 10 mg ammonium chloride was placed in the vials to quench residual free chlorine. All samples were stored below 5 ˚C and protected from light until extraction.

Dietary and cooking water sampling

Food and beverage samples were obtained from seven regions geographically scattered in Japan from June to October 2008. In four of the regions (A, B, C, D), foods were randomly purchased from the local market. Following the National Nutrition Survey (2004), raw foods were prepared with local tap water and blended according to their intake proportions. Pasted samples were stored as 13 groups (Table 4.1) at -20 °C until analysis. Samples from the other two regions (E and F) were similarly purchased, prepared, blended and stored, except that cooking waters were reagent water. The local tap water samples of Region E and F were also collected. In Region G, since diet samples were purchased based on the National Nutrition Survey 2006, they were divided into 17 groups. Additionally in Region G, both tap water and reagent water were used for cooking in the same manner respectively. All the cooking waters of the seven regions were reserved until extraction.

Table 4.1 Dietary classification in 7 areas

Regions A-F	Region G
Grain	Grain
Potato	Potato
Sweetener and snacks	Sweetener
Lipid	Bean
Bean	Nut
Fruit	Vegetable
Vegetable	Fruit
Algae	Mushroom
Beverage	Algae
Seafood	Seafood
Meat and egg	Meat
Dairy	Egg
Seasoning	Dairy
	Lipid
	Snack
	Beverage
	Seasoning

4.2.3 Extraction and Analysis of HAAs in Tap Water Samples

The aqueous samples (sodium hydroxide aqueous solution and tap tater) were both extracted in EPA Method 552.3. A Shimadzu (Kyoto, Japan) GC-14B gas chromatograph equipped with electron-capture detector (^{63} Ni) was used for analysis. The conditions are shown in Table 4.2.

Table 4.2 GC-ECD/MS analytical conditions of HAAs

	GC-ECD	GC-MS
Column	J & W DB-1701 (0.25 mm×30 m, film 0.25 μm)	J & W DB-5 (0.32 mm×30 m, film 0.25 μm)
Program of GC oven	40 ºC (10 min) - 2.5 ºC /min - 65 ºC - 10 ºC - 85 ºC - 20 ºC/min -205 ºC (7 min)	40 ºC (6 min) - 2.5 ºC/min - 65 ºC - 20 ºC - 205 ºC (5 min)
Injection	210 ºC , splitless (1min sampling)	230 ºC, splitless (0.45min sampling)
Detection	290 ºC	200 ºC
Purge gas	Nitrogen (30 mL/min)	
Carrier gas	Helium (33 cm/sec)	Helium (2.04 mL/min)

4.2.4 Extraction and Analysis of HAAs in Dietary Samples

HAAs were extracted from cooking water samples in EPA Method 552.3. The extraction procedure for the dietary sample was developed based on a literature method (Yamada *et al*., 1994) as follow.

(a) Disperse 2-g dietary sample in 10 mL of reagent water and homogenize it.
(b) Add 3 mL of 0.5 M phosphate buffer at pH 6.2. Check the pH of the solution using narrow range pH indicator strips. Add more buffer if the pH is less than 6.2.
(c) Adding 20 mL of MTBE and shaking for 15 minutes to remove the potentially interfering compounds
(d) After centrifugation, remove the separated organic layer.
(e) Adjust the pH to near zero using 0.5 mL of concentrated sulfuric acid.
(f) Add 3 g of anhydrous sodium sulfate and 0.5 g of copper sulfate pentahydrate and shake immediately until almost all of them are dissolved.
(g) Add 4 mL of MTBE with 1, 2, 3-trichloropropane as an internal standard and shake the sample for 15 minutes.

(h) After centrifugation, take out 3 mL of the MTBE layer to a conical 15-mL centrifuge tube and add 3 mL of 10% sulfuric acid in methanol.
(i) Cap and vortex the tube, and incubate it in a heating block at 50 °C for 120 minutes to form methyl esters of HAAs.
(j) Cool the sample for 10 minutes and add 7 mL of sodium sulfate aqueous solution (150 g/L).
(k) Adjust the sample pH to neutral with 1 mL of saturated sodium bicarbonate aqueous solution with frequent ventilation.
(l) Transfer 2 mL of the MTBE layer to sampler-vial.

Extract the HAAs from the Lipid samples (10 g) in reagent water (20 mL) after adjust the sample pH to 6.2. Then extract the HAAs from the same aqueous extract (10 mL) from step (a). Extract the HAAs from dairy samples after placing 1 mg of them in 40 mL of reagent water following the method in 4.2.3, due to the emulsion formation between proteinaceous material and MTBE. Extract beverage samples by using 10 mL of them and conduct the extraction from step (b). A Shimadzu (Kyoto, Japan) QP2010 Plus gas chromatograph equipped with mass spectrometry was used for the quantification of the HAAs in dietary and their cooking water samples.

4.2.5 Recovery Check and Quantification

HAA recoveries from dietary samples were investigated through the spike of HAAs dissolved in MTBE to 2 g of dietary samples dispersed in 10 mL of water (or 10 mL of beverage sample), and the entire extraction procedure. The HAAs were quantified relative to the obtained peak of 1, 2, 3-trichloropropane MTBE solution. The measured HAA concentrations were corrected with their determined recoveries. The details of the analysis are shown in Table 4. 2. Method Quantification Limits (MQL) were defined as the minimum HAA concentrations (in MTBE solution) that give the signal-to-noise ratios of 10 (Table 4.3). Concentrations below the MQL (ND) were expressed and calculated as zero in the following exposure assessment. Recoveries for tap water and reagent water prepared dietary samples were both investigated.

Table 4.3 MQLs of HAAs (μg/L in MTBE)

	MQL
MCA	10
MBA	2
DCA	1
TCA	1
BCA	2
BDCA	2
DBA	1
DBCA	5
TBA	10

4.2.6 Exposure Assessment

The exposure amounts via each route were calculated through the following equations.

Ingestion exposure via tap water (μg/day)
=Tap water concentration (μg/L) × Consumption (L /day) (4.1)

Ingestion exposure via dietary (μg/day)
= ∑ (concentration in food and beverage (μg/kg) × Intake (kg/day)) (4.2)

Inhalation exposure (μg/day)
= ∑ (Airborne concentration in each indoor and outdoor environment (μg/m^3) × Breathing rate (m^3/day) × Occupation time in each indoor and outdoor environment (hour)/24(hour)) (4.3)

Transdermal exposure amount was calculated with the equation below.

$$D = 2 \times A \times K_p \times C \times \sqrt{\frac{6 \times \tau_{event} \times t_{event}}{\pi}} \quad (4.4)$$

D = transdermal exposure (μg/day);

A = body surface area (cm^2);

K_p = permeability coefficient (cm/hr);

C = aqueous concentration (μg/L);

τ_{event} = lag time (hr);

t_{event} = bathing duration (hr)

The HAA concentrations in the tap water of the 22 residences and the 7 regions and a daily per capita water consumption of 2 liters were applied to the estimation of the ingestion exposure amounts. Intake amounts of foods and beverages were based on literature values (National Institute of Health and Nutrition, 2004 and 2006). The actual times recorded in air sampling pump were applied to the occupation times. For living room and outdoor, occupation times (948 and 72 min/day) were applied based on literal values. The rest of the times were assumed to be in unpolluted environment. Breathing rate (15 m^3/day) was based on the literature value (Ministry of Environment, Japan, 2003). Transdermal exposure was estimated based on the formula introduced by EPA (2004). Body surface area was estimated based on the formula developed by Dubois (USEPA, 1997). The transdermal exposure during bathing time was estimated with an assumption of a 100% of body area contact with water in either case of bathing and shower. Other assumptions include a body surface area of 18000 cm^2 and the contact body area of 100% in either case of bathing or shower. All the parameters were obtained from literature (Xu *et al*., 2002), except *A*, *C*, *f*, and *t*. Since the K_ps of BDCA, DBCA, and TBA remains unknown, those were compensated with that of DBAA because of their similar molecular weights (Table 4.4).

Table 4.4 Parameters of transdermal exposure assessment

	Permeability coefficient (cm/hr)	Lag time (hr)
MCA	1.1	3.67
MBA	1.4	5.67
DCA	1.9	5
TCA	1.9	4.57
BCA	1.9	6.52
BDCA [a]	-	-
DBA	2.6	4.3
DBCA [a]	-	-
TBA [a]	-	-

[a] Permeability coefficients and lag time factors were unavailable

4.3 Results and Discussion

4.3.1 HAA Concentrations in Tap water

The HAA concentrations in the tap water samples of surveyed common residences and those of the Regions A – G were shown in Table 4.5 and Figure 4.1. From these tap water samples, MCA and MBA were not detected. TBA was only found from one sample. The rest six species of HAAs were found from almost all the samples. Among them, DCA and TCA were the most abundant ones with the highest median values (1.57 – 13.10 μg/L, median 4.25 μg/L and 1.35 – 8.55 μg/L, median 2.95 μg/L, respectively), followed by BDCA (0 – 15.6 μg/L, median 1.79 μg/L), BCA (0 – 15.6 μg/L, median 1.79 μg/L), DBA ((0 – 3.55 μg/L, median 0.65 μg/L) and DBCA ((0 – 1.75 μg/L, median 0.55 μg/L). Their max/min ratios did not show great regional difference as THMs (Table 3.6).

Table 4.5 HAA concentrations in tap water (μg/L)

Bathroom	Arithmetic mean	Median	Max	Min	Max/min [a]
MCA	0.00	0.00	0.00	0.00	-
MBA	0.00	0.00	0.00	0.00	-
DCA	4.40	4.25	13.10	1.57	8
TCA	3.35	2.95	8.55	1.35	6
BCA	2.76	1.79	15.55	0.00	17
BDCA	2.75	1.85	9.30	0.00	19
DBA	0.74	0.65	3.55	0.00	12
DBCA	0.62	0.55	1.75	0.00	25
TBA	0.02	0.00	0.70	0.00	1

[a] Calculated with the minimum and max quantified value

[b] Quantified sample number in 29

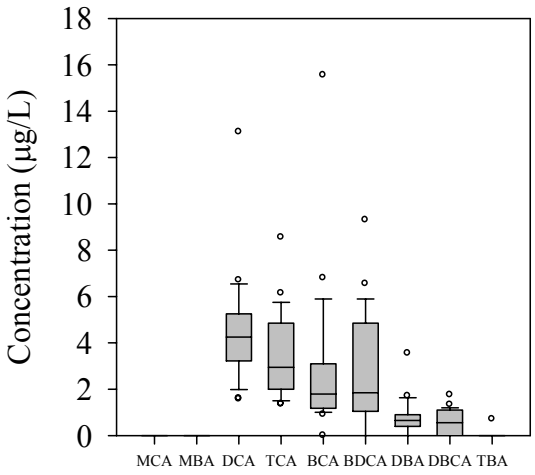

Figure 4.1 HAA concentrations in tap water

4.3.2 HAA Concentrations in Indoor and Outdoor Airs

As are shown in Table 4.6 and Figure 4.2, the most frequently detected HAAs from bathroom air were TCA (0 – 3.61 μg/L, median 0.14 μg/L), followed by DCA (0 – 3.01 μg/L, median 0.33 μg/L), DBA (0 – 0.51 μg/L, median 0 μg/L), and BCA (0 – 0.34 μg/L, median 0 μg/L). The max/min ratios showed that TCA, BCA and DCA varied probably due to the different life-styles. However, the variations were not as great as THM (Table 3.7). The abundant HAAs in living room were also DCA (0 – 0.04 μg/L, median 0 μg/L), TCA (0 – 0.09 μg/L, median 0 μg/L), DBA (0 – 0.11 μg/L, median 0 μg/L) and BDCA (0 – 0.07 μg/L, median 0 μg/L). They showed different order from the HAA concentrations in tap water and bathroom air. This implies that unlike THMs, HAAs concentration in living room air did not depend on the emission from tap water. In outdoor, lower concentration of HAAs were also detected. The major species were DCA (0 – 0.21 μg/L), TCA (0 – 0.31 μg/L) and DBA (0 – 0.58 μg/L), and their median values were all zero. Surprisingly, the max/min ratios of them were greater than those of living room. This observation implies that the HAA concentrations in outdoor air had a regional difference, and the mission source was probably in outdoor environment. Generally, comparing with different environment, bathroom air apparently had the highest concentration and detection frequency of HAAs. Based on the experience of THMs, the HAAs in bathroom air were also probably emitted from tap water, and inhalation exposure probably also occurred.

Table 4.6 HAA concentrations in air (μg/m^3) (to be continued to the next page)

Bathroom	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
MCA	0.00	0.00	0.00	0.00	-	0
MBA	0.00	0.00	0.00	0.00	-	0
DCA	0.55	0.33	3.01	0.00	19	18
TCA	0.40	0.14	3.61	0.00	33	16
BCA	0.02	0.00	0.34	0.00	34	3
BDCA	0.00	0.00	0.15	0.00	1	1
DBA	0.06	0.00	0.51	0.00	9	6
DBCA	0.00	0.00	0.12	0.00	1	1
TBA	0.00	0.00	0.00	0.00	-	0

Living room	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
MCA	0.00	0.00	0.00	0.00	-	0
MBA	0.00	0.00	0.00	0.00	-	0
DCA	0.01	0.00	0.04	0.00	4	13
TCA	0.01	0.00	0.09	0.00	9	10
BCA	0.00	0.00	0.03	0.00	3	2
BDCA	0.00	0.00	0.02	0.00	2	4
DBA	0.01	0.00	0.11	0.00	11	8
DBCA	0.00	0.00	0.07	0.00	1	1
TBA	0.00	0.00	0.00	0.00	-	0

[a] Calculated with the minimum and max quantified value

[b] Detection frequency of individual HAA (out of 22 residents)

Table 4.6 HAA concentrations in air (μg/m^3) (continues from the previous page)

Outdoor	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
MCA	0.00	0.00	0.00	0.00	-	0
MBA	0.00	0.00	0.00	0.00	-	0
DCA	0.02	0.00	0.21	0.00	21	14
TCA	0.03	0.00	0.31	0.00	31	12
BCA	0.00	0.00	0.00	0.00	-	0
BDCA	0.00	0.00	0.06	0.00	-	0
DBA	0.03	0.00	0.58	0.00	58	4
DBCA	0.00	0.00	0.00	0.00	-	0
TBA	0.06	0.06	0.06	0.06	1	1

[a] Calculated with the minimum and max quantified values

[b] Detection frequency of individual HAA (out of 22 residents)

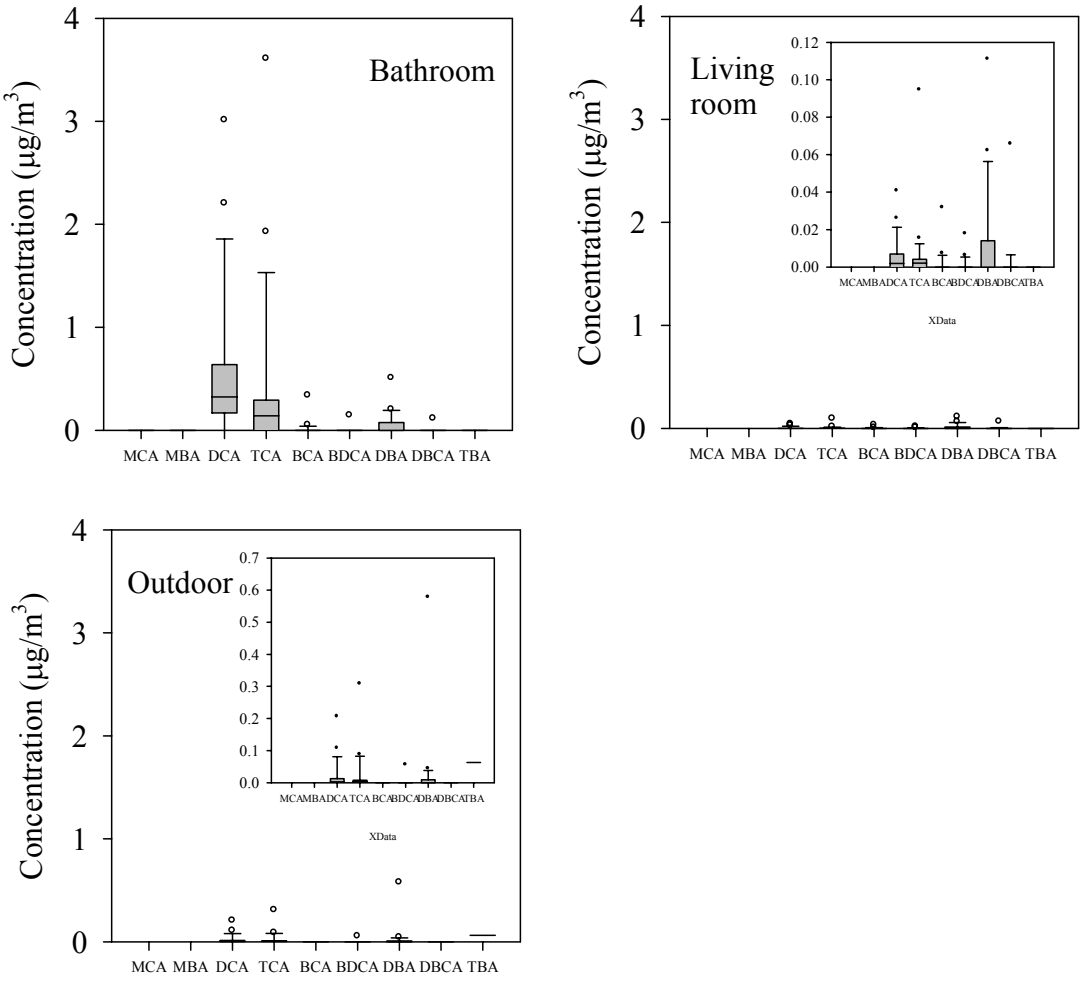

Figure 4.2 HAA concentrations in air of each environment

4.3.3 HAA Concentrations in Dietary Sample

The HAA recoveries from all the dietary samples were greatly different. However, all their relative standard deviations were less than 30% (Appendix). Therefore, measured HAA concentrations were corrected through the division of them with their determined recoveries. The HAA concentrations in cooking waters are shown in Table 4.7. In the dietary samples from the Regions A – D and G (samples prepared with tap water), DCA (0 – 20.2 ng/g) and TCA (0 – 37.1 ng/g) were most frequently detected, followed by BCA (0 – 60.9 ng/g), BDCA (0 – 20.3 ng/g), DBA (0 – 9.29 ng/g) and DBCA (0 –

18.09 ng/g) (Table 4.8 and Figure 4.3). The HAA concentrations in the tap water samples collected from those areas were also in the same order with that of the dietary samples, but their concentrations in dietaries showed greater variability than those in tap water. Their max/min ratios imply that MBA (560) had a great regional difference than others, followed by BCA (55) and TCA (25). TBA, MCA, DBA, DBCA and BDCA were not detected from all or most of the dietary samples except from a few specific items such as seasoning (MCA, 4.37 ng/g), algae (DBCA, 18.1 ng/g, TBM 89.6 ng/g) and lipids (BDCA, 20.3 ng/g). HAAs (except DCA, TCA and BCA) were not generally contained in the dietary, but could be found in specific items.

Table 4.7 HAA concentrations in tap water (cooking water) samples (μg/L)

	Region A	Region B	Region C	Region D	Region E	Region F	Region G
MCA	0.00	0.00	0.00	0.00	0.00	0.00	0.00
MBA	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DCA	2.32	1.57	3.30	3.57	1.98	2.32	5.20
TCA	1.36	2.82	5.10	5.15	2.69	1.36	6.14
BCA	1.16	1.79	4.60	2.32	1.36	1.16	3.87
BDCA	0.77	1.04	0.00	1.09	0.00	0.77	5.30
DBA	0.39	1.63	0.36	0.00	0.00	0.39	0.00
DBCA	0.00	1.32	0.00	1.13	0.00	0.00	0.07
TBA	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Table 4.8 HAA concentrations in dietary samples of Region A-D and G [a] (ng/g)

Bathroom	Arithmetic mean	Median	Max	Min	Max/min [b]	n [c]
MCA	0.11	0.00	4.37	0.00	1	2
MBA	2.06	0.00	89.60	0.00	560	12
DCA	3.41	0.00	20.20	0.00	11	27
TCA	3.49	0.00	37.10	0.00	25	25
BCA	3.00	0.00	60.90	0.00	55	22
BDCA	0.84	0.00	20.30	0.00	3	4
DBA	0.17	0.00	9.29	0.00	3	2
DBCA	0.59	0.00	18.10	0.00	2	3
TBA	0.00	0.00	0.00	0.00	-	0

[a] Tap water prepared samples

[b] Calculated with the minimum and max quantified values

[c] Quantified sample number in 69

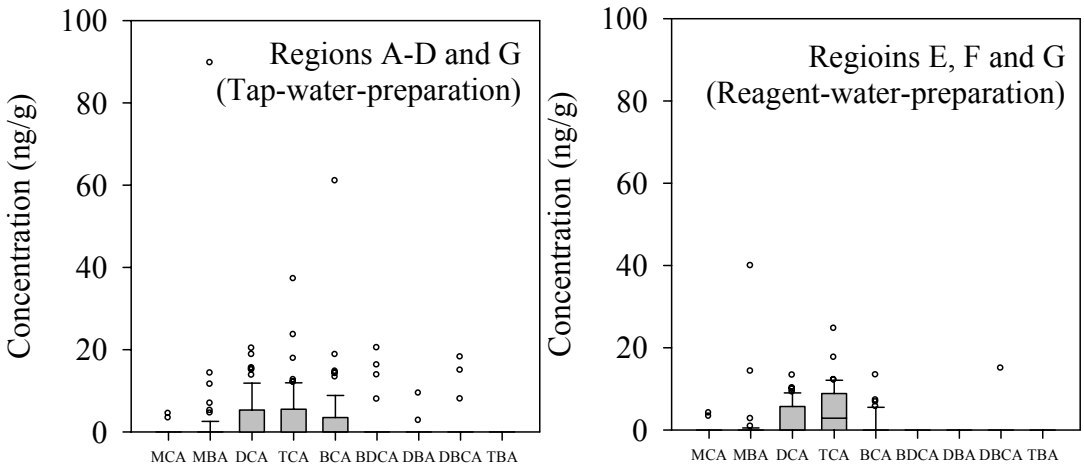

Figure 4.3 HAA concentrations in tap water and reagent water prepared dietaries

4.3.4 Comparison of HAA concentrations between Tap-water and Reagent-water Prepared Dietary Samples

In case of Regions E, F and G (samples prepared with reagent water) (Table 4.9), TCA (0 – 24.6 ng/g), DCA (0 – 13.3 ng/g) and BCA (0 – 13.3 ng/g) were also detected in the dietary samples in lower ranges comparing with that of Regions A – D. MBA was detected from only 3 items of 43, but with the highest concentration in algae group again (39.9 ng/g). However, the result of this comparison is bounded with great uncertainty because the possible HAA concentrations in raw food could be different in different regions. In Region G, since the same raw foods were prepared with both tap and reagent water in the same manner and time, it could help to understand HAA concentrations in tap water and reagent water prepared dietary better. As is shown in Table 4.10, almost all the HAAs detected in tap-water-prepared dietary were in higher concentrations than that of reagent water, except for BCA (potato group), DBCA (bean group) and MBA (beverage group). These observations imply that preparing food with tap water led some samples to higher contamination levels of major HAAs. However, Krasner and Wright (2005) had found that increased mono- and di-haloganated acetic acids formation occurs when boiling the chlorinated tap water and the degradation of tri-haloganated acetic acids. They suggested that the change of the HAA concentration in tap water due to heating or boiling should be taken into account in the estimation of ingestion exposure to them. Compared with chlorinated tap water, much more complicated composite of dietary may contained more HAA precursors such as amino acids and more dissolved organic carbon. Therefore, the observed higher HAA concentrations of the tap-water-prepared samples in this research were probably more complicated than simple traveling of HAAs from tap water to raw food. However, since the information on this point is very insufficient, in this research, tap-water-preparation was considered as the explanation for the increasing HAA concentrations.

Table 4.9 HAA concentrations in the dietary samples of Regions E, F, and G [a] (ng/g)

Bathroom	Arithmetic mean	Median	Max	Min	Max/min [b]	n [c]
MCA	0.17	0.00	4.06	0.00	1	2
MBA	1.34	0.00	39.9	0.00	15	3
DCA	2.94	0.00	13.3	0.00	5	20
TCA	4.79	2.88	24.6	0.00	10	24
BCA	1.15	0.00	13.30	0.00	4	7
BDCA	0.00	0.00	0.00	0.00	-	-
DBA	0.00	0.00	0.00	0.00	-	-
DBCA	0.35	0.00	14.9	0.00	1	1
TBA	0.00	0.00	0.00	0.00	-	-

[a] Reagent water prepared samples

[b] Calculated with the minimum and max quantified values

[c] Quantified sample number in 43

Table 4.10 HAA concentrations in dietary samples prepared with tap water and reagent water of region G

	Grain		Potato		Sweetener		Bean		Vegetable	
	Tap water preparation	Reagent water preparation	Tap water preparation	Reagent water preparation	Tap water preparation	Reagent water preparation	Tap water preparation	Reagent water preparation	Tap water preparation	Reagent water preparation
MCA	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
MBA	0.00	0.00	0.00	0.00	6.88	0.00	0.00	0.00	0.00	0.00
DCA	11.26	0.00	13.68	3.92	0.00	0.00	0.00	0.00	3.38	0.00
TCA	11.68	5.50	9.79	6.06	12.59	5.40	1.47	0.00	5.65	2.48
BCA	0.00	0.00	0.00	4.02	0.00	0.00	0.00	0.00	0.00	0.00
BDCA	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DBA	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
DBCA	0.00	0.00	0.00	0.00	0.00	0.00	0.00	14.91	0.00	0.00
TBA	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

4.3.5 Water Absorption of Food

The same as 3.3.5, the water absorption ratios of the dietaries in Region G were calculated, and the indirect daily tap water intake was evaluated to be 702 mL (Table 4.11). The food samples were randomly selected for both of these two surveys. Therefore, even for the same classification, different choice of food items could lead to slightly different water absorption ratios and the result of indirect daily tap water intake.

Table 4.11 Water absorption of food

Group	Weight of raw food (g)	Weight of prepared food (g)	Water absorption ratio raw food relative	Dietary intake (g/day)	Water intake via dietary (mL/day)
Grain	500	610	22%	449.5	91
Potato	500	632	26%	60.5	13
Sweetener [a]	500	1000	not calculated	7.1	0
Bean	500	650	30%	61.5	14
Vegetable	500	531	6%	253.9	15
Mushroom	500	587	17%	15	2
Algae	500	4698	840%	12.9	12
Beverage [a]	100	1020	not calculated	616.4	556
Seasoning [a]	500	1000	not calculated	92	0
Sum					702

[a] Not calculated because the sample was in solution form

4.3.6 HAA Ingestion Exposure via Tap Water

HAA ingestion exposure via tap water is shown in Table 4.12 and Figure 4.4. DCA had the highest exposure amount (3.14 – 26.2 μg/day, median 8.5 μg/day), followed by TCA (2.7 – 17.1 μg/day, median 5.9 μg/day), BCA (0 – 31.1 μg/day, median 3.59 μg/day), BDCA (0 – 18.6 μg/day, median 3.7 μg/day), DBA (0 – 7.1 μg/day, median 1.3 μg/day), and DBCA (0 – 3.5 μg/day, median 1.10 μg/day).

Table 4.12 HAA ingestion exposure via tap water (μg/day)

Bathroom	Arithmetic mean	Median	Max	Min	Max/min [a]
MCA	0.00	0.00	0.00	0.00	-
MBA	0.00	0.00	0.00	0.00	-
DCA	8.81	8.50	26.20	3.14	8
TCA	6.70	5.90	17.10	2.70	6
BCA	5.51	3.59	31.10	0.00	17
BDCA	5.49	3.70	18.60	0.00	19
DBA	1.48	1.30	7.10	0.00	12
DBCA	1.23	1.10	3.50	0.00	25
TBA	0.05	0.00	1.40	0.00	1

[a] Calculated with the minimum and max quantified values

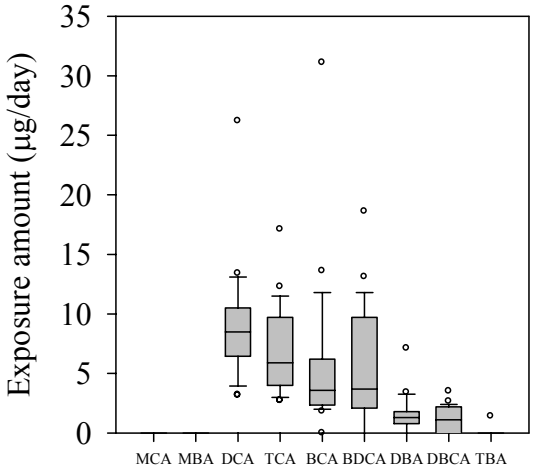

Figure 4.4 HAA ingestion exposure via tap water

4.3.7 HAA Ingestion Exposure via Dietaries

HAA ingestion exposure via dietaries is shown in Table 4.13. The max/min ratios of total HAA ingestion exposure via dietary (15) implied that there was a regional difference. DCA and BCA ingestion exposure were estimated in all five regions, followed by TCA (4), MBA (3), DBCA (3), BDCA (2), DBA (2), MCA (1) and TBA (0). The exposure amount of DCA was the highest (9.66 μg/day), followed by TCA (8.82 μg/day) and BCA (4.18 μg/day). In the following estimation of HAA total exposure amount, the choice of representative value (among Regions A – D and G) of the ingestion exposure via dietaries was guided with the example of establishing standard value of boron in Japan (Ministry of Health, Labor and Welfare, Japan, 2003). Ingestion is the major exposure route of boron, and seawater desalination may lead to high concentration of boron in tap-water-prepared dietaries. A market-basket survey of the boron concentration in the dietaries and tap water in nine domestic regions was conducted from 1994 to 1997. The standard value was established based on an allocation factor (0.4) which was derived from a high-exposure region (seawater desalination treatment region). Therefore, in this research, the ninety-five percentile values of ingestion exposure via dietaries of the five regions for each HAAs were used. In another aspect, the standard value of boron is also a good example of making independent decision on establishing standard value of drinking water based on domestic situation.

Table 4.13 HAA ingestion exposure via dietary (μg/day)

	Region A	Region B	Region C	Region D	Region G	Average	Max/min [a]
MCA	0.00	0.00	0.00	0.00	0.66	0.13	-
MBA	0.00	0.40	2.16	0.00	1.67	0.85	-
DCA	2.85	8.13	15.61	0.89	20.82	9.66	23
TCA	8.31	3.54	9.33	0.00	22.91	8.82	6
BCA	1.98	5.07	11.58	2.27	0.03	4.18	414
BDCA	4.84	0.00	0.14	0.00	0.00	1.00	34
DBA	0.03	0.00	0.00	0.00	0.77	0.16	-
DBCA	0.19	0.19	0.00	0.00	0.10	0.10	2
TBA	0.00	0.00	0.00	0.00	0.00	0.00	-
Total	18.20	17.33	38.82	3.16	46.96	-	15

[a] Calculated by the minimum quantified value

4.3.8 Comparison of HAA Ingestion Exposures via Tap-water and Reagent-water Prepared Dietaries

Table 4.14 shows the results of the comparison between HAA ingestion exposure via tap water and reagent water prepared dietary in Region G. DCA and TCA ingestion exposure amounts via tap-water-prepared dietaries were approximately as three times and twice high as those of reagent water. Similar observation was found in DBA, too. No great difference was observed for MCA, MBA, BDCA and TBA. However, in the case of BCA and DBCA, exposure amount via reagent-water-prepared dietaries was higher than that of tap water, but not in a very high level. In a generally way, preparing food with tap water also causes higher ingestion exposure amounts.

Table 4.14 HAA ingestion exposure via dietary prepared with tap water and reagent water of region G (μg/day)

	Tap-water-preparation	Reagent-water-preparation
MCA	0.66	0.63
MBA	1.67	1.38
DCA	20.82	7.25
TCA	22.91	11.76
BCA	0.03	0.27
BDCA	0.00	0.00
DBA	0.77	0.00
DBCA	0.10	0.92
TBA	0.00	0.00

4.3.9 HAA Inhalation Exposure

As is shown in Figure 4.5, since overwhelming long duration time is spent in living room (948 min/day), inhalation exposure to DCA (0 – 1.725 μg/day, median 0.12 μg/day), TCA (0 – 1.96 μg/day, median 0.04 μg/day), and DBA (0 – 0.55 μg/day, median 0 μg/day) were higher or comparable to those of bathroom (DCA, 0 – 1.03 μg/day, median 0.07 μg/day; TCA 0 – 1.24 μg/day, median 0.03 μg/day; DBA 0 – 0.17 μg/day, median 0 μg/day). Great difference was not observed for other HAAs between the inhalation exposures in bathroom and living room. HAA inhalation exposure amounts in outdoor were estimated to be generally lower than indoor environment (DCA 0 – 0.66 μg/day, median 0 μg/day; TCA 0 – 0.48 μg/day, median 0 μg/day, DBA 0 – 0.13 μg/day, median 0 μg/day). Unlike THMs, bathing behavior did not lead to much higher HAA inhalation exposure than other environments.

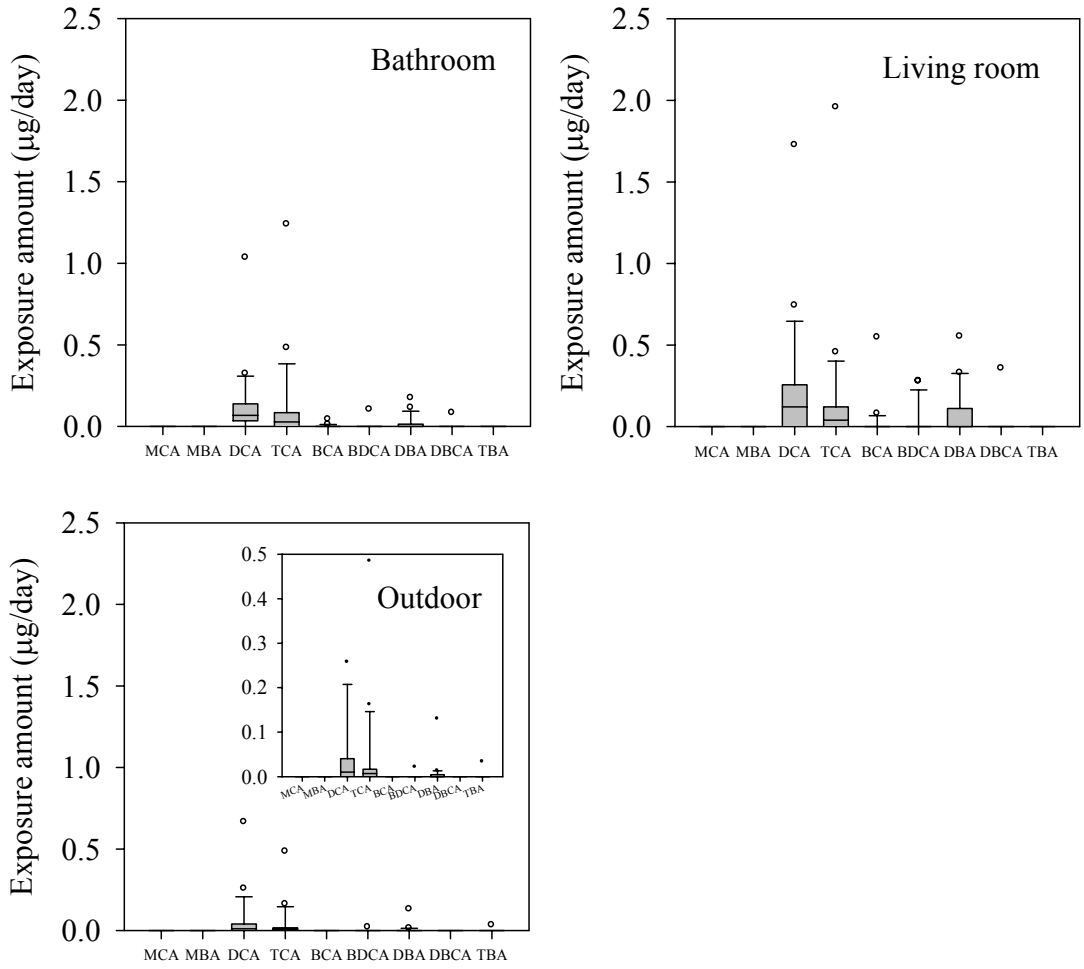

Figure 4.5 HAA inhalation exposure in each environment

In total HAA inhalation exposure (Table 4.15 and Figure 4.6), DCA, TCA, BCA, BDCA, and DBA showed regional difference in their max/min values. However, even their max values were generally smaller than the ingestion exposure estimated previously. This means inhalation is not the major exposure route to HAAs. Along with the knowledge obtained from THM exposure, it can be understood that human could be exposed to various disinfection byproducts in different scenario due to their different properties even though they share the same emission source of tap water.

Table 4.15 HAA total inhalation exposure (μg/day)

	Arithmetic mean	Median	Max	Min	Max/min [a]
MCA	0.00	0.00	0.00	0.00	-
MBA	0.00	0.00	0.00	0.00	-
DCA	0.42	0.30	3.42	0.00	428
TCA	0.32	0.09	3.68	0.00	368
BCA	0.03	0.00	0.59	0.00	59
BDCA	0.04	0.00	0.38	0.00	76
DBA	0.11	0.02	0.63	0.00	63
DBCA	0.02	0.00	0.44	0.00	1
TBA	0.00	0.00	0.03	0.00	1

[a] Calculated with the minimum and max quantified values

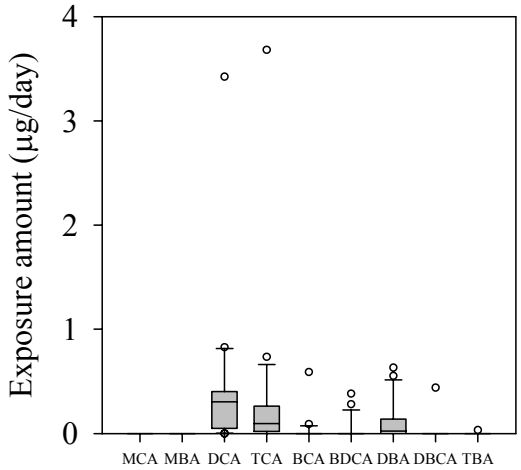

Figure 4.6 HAA total inhalation exposure

4.3.10 HAA Transdermal Exposure

As is shown in Table 4.16 and Figure 4.7, subjects were transdermally exposed to DCA in the highest amounts (0 – 0.01 μg/day, median 0 μg/day). Transdermal exposure amounts were generally much lower than other exposure routes.

Table 4.16 HAA transdermal exposure (μg/day)

	Arithmetic mean	Median	Max	Min	Max/min [a]
MCA	0.00	0.00	0.00	0.00	-
MBA	0.00	0.00	0.00	0.00	-
DCA	0.00	0.00	0.01	0.00	7
TCA	0.00	0.00	0.00	0.00	8
BCA	0.00	0.00	0.01	0.00	27
BDCA	0.00	0.00	0.00	0.00	24
DBA	0.00	0.00	0.00	0.00	14
DBCA	0.00	0.00	0.00	0.00	7
TBA	0.00	0.00	0.00	0.00	1

[a] Calculated with the minimum and max quantified values

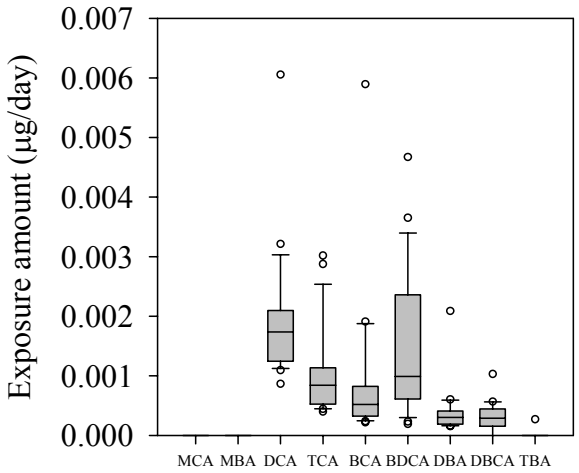

Figure 4.7 HAA transdermal exposure

4.3.11 HAA Total Exposure

Daily HAA total exposure amounts were calculated as the summation of the exposure amounts via each route based on the results of 4.3.6 – 4.3.10. As was mentioned in 4.3.7, the maximum value of ingestion exposure via dietaries in Regions A – D and G were applied to the 22 subjects to compare with HAA TDI values (if available). The results are shown in Table 4.17 and Figure 4.8. The maximum values of the daily HAA total exposure amounts were divided by the average body weight of 50 kg. The results of MCA (MCA 0.08 μg/(kg· day) and TCA (MCA 1.05 μg/(kg· day) were much smaller than their TDI values (3.5 and 32.5 μg/(kg· day)). Similarly as was discussed in 3.3.11, higher HAA concentrations in tap water led to higher ingestion exposure via tap water and dietaries. Therefore, a same or similar allocation factor could be derived from a much higher total exposure amount than this research. For the possibility that the total exposure could approach TDI value under certain circumstances (e.g. areas with much higher HAA concentrations in tap water than this survey), it is necessary to discuss and decide the allocation factors even the total exposure amounts were surveyed to be lower than TDI values. For those HAAs which do not have TDI values, it is also important to understand the total exposure amount and the proportional relationship among various exposure routes.

Table 4.17 HAA total exposure (μg/day)

	Arithmetic mean	Median	Max	Min	Max/min [a]
MCA	4.16	4.16	4.16	4.16	1.0
MBA	85.16	85.16	85.16	85.16	1.0
DCA	29.29	28.38	45.80	22.61	2.0
TCA	42.10	41.76	52.67	38.03	1.4
BCA	63.83	61.84	89.00	59.73	1.5
BDCA	25.86	23.97	37.92	20.34	1.9
DBA	10.66	10.42	15.93	9.77	1.6
DBCA	18.60	18.70	20.68	17.18	1.2
TBA	0.07	0.00	1.43	0.00	-

[a] Calculated with the minimum and max quantified values

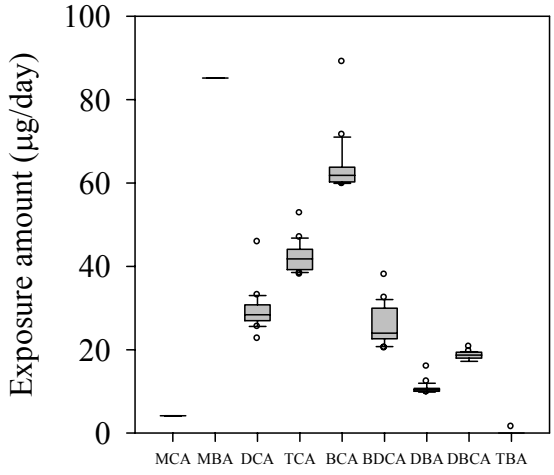

Figure 4.8 HAA total exposure

4.4 Allocation to Drinking Water

4.4.1 Estimation of the Allocation to Drinking Water

HAA allocation factors of drinking water (direct ingestion) in total exposure were estimated with Equotion 4.5. This approach followed the derivations of MCA and TCA in the current standard value of Japan. It considers that the ingestion exposure of consuming 2 L of tap water per day should be allocated to drinking water in total exposure. Since it is possible to regulate the other seven species of HAAs in TDI approach in the future, their allocation factors were also derived. The subjects who were not estimated to be exposed to HAAs (total exposure amount = zero) were excluded from the estimation.

Allocation factor = Ingestion exposure via tap water / Total exposure (4.5)

In the results of the 22 subjects (Table 4.18 and Figure 4.9), no distributions of allocation factor for MCA, MBA, and TBA was obtained. This is because that the ingestion exposure via tap water was zero for all the subjects (MCA and MBA). In case of TBA, only one subject was estimated to have ingestions exposure via tap water. Therefore, it is considered not necessary to calculate their allocation factors in the present stage. For the other six species of HAAs, except DCA (0.31), the median values of their allocation factors were all below 0.2 (DCA, 0.31; TCA, 0.14; BCA, 0.06; BDCA, 0.19; DBA, 0.14; and DBCA, 0.08, respectively). Further investigation on their distributions is necessary.

Table 4.18 HAA allocation factors

	Geometric mean [a]	Median	Max	Min	Standard deviation	n [b]
MCA	-	0.00	0.00	0.00	-	0
MBA	-	0.00	0.00	0.00	-	0
DCA	0.31	0.31	0.57	0.14	0.08	22
TCA	0.14	0.14	0.33	0.07	0.07	22
BCA	0.07	0.06	0.35	0.03	0.07	22
BDCA	0.20	0.19	0.49	0.05	0.12	22
DBA	0.14	0.14	0.45	0.06	0.08	22
DBCA	0.08	0.08	0.17	0.00	0.05	18
TBA	0.98	0.98	0.98	0.98	-	1

[a] Zero value were excluded from the calculation

[b] Number of estimated subjects in 22

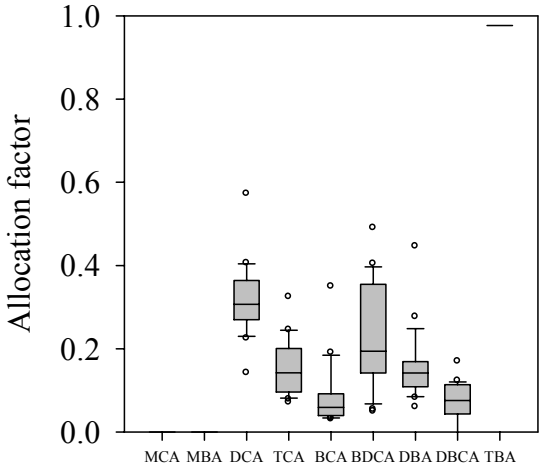

Figure 4.9 HAA allocation factors

4.4.2 Attempt on Fitting Lognormal Distribution in Allocation Factor

As was introduced in 3.4.2, since the geometric means of the allocation factors for DCA, TCA, BCA, BDCA, DBA, and DBCA (Table 4.18) are very close to their medians, fitting the lognormal function on their distributions was attempted. The histogram of the allocation factor was created for each HAA (Figure 4.10). Consequently, its shape was approximated to a lognormal probability density function with the same average values and standard deviations (derived from the natural-logarithm-transformed data). A chi-square test and a Kolmogorov-Smirnov test were used to test the goodness of fit. All statistical analyses were performed with a Sigmaplot (CA, USA) software (Version 10.0).

The results of the chi-square tests showed that it is possible that the allocation factors of TCA, BCA, DBA, and DBCA are in lognormal distributions. The possibilities that DCA and BDCA are not in lognormal distributions remained. The results of the Kolmogorov Smirnov test implies that only factors of BCA and DBA are possibly in lognormal distribution. Therefore, it is possible that allocation factors of HAAs are not all in lognormal distributions. However, from Figure 4.10, it was visually observed that lognormal function could be fitted in the distribution of allocation factors. There were also specific areas such as the peak parts of TCA, BDCA, and DBA, left parts of DCA, BDCA and DBCA were not covered with the curve of lognormal functions. These are probably because of the limited number of samples (18 – 22) in this research. The

uncovered bin located between 0 – 0.03 in DBCA was probably because of the four subjects who had allocation factor equal to zero. As was mentioned in 3.4.2, since the exposure amount of zero is impossible in reality, the allocation could be much lower. Therefore, they were included in the histogram. However, they were excluded from the calculation of the mean value and standard deviation of the lognormal function because the data needed to be natural-logarithmly transformed first. Above all, the lognormal distribution could be attempted to approximate the distribution of allocation factors for the six HAAs. The cumulative probability distributions of them are created by integration in Figure 4.11.

The current factors of 0.2 applied for DBPs in Japan were corresponding with relatively higher non-exceedance probabilities in TCA (0.83), BCA (0.96), DBA (0.82) and DBCA (0.99). This suggests that for more than eighty percent of the population, lower allocation factors (standard values) should be established. Especially, in case of TCA, since it has been regulated in the current standard value, its allocation factor (0.2) should be adjusted. In case of BDCA, since the non-exceedance probability corresponded with 0.2 was 0.52, a smaller factor than 0.2 is therefore necessary too. In case of DCA, since the allocation factor of 0.2 corresponded with a probability of 0.06, which is within the common acceptable range in risk assessment (0.05 – 0.1), the 0.2 should be sustained. As was mentioned in chapter 2, standard value of DCA was derived from VSD approach. However, if it is considered more appropriate to use the TDI approach, the allocation estimated here could be applied. Similarly with THM, the 5th and 10th percentile of the cumulative probability were also estimated. In case of TCA, BDCA and DBA, since the corresponding allocation factors did not show clear difference from each other, the rounded value of 0.1 is recommended. In case of DBCA and BCA, the corresponding allocation factors to 5^{th} and 10th cumulative probability were both very small (0.02 – 0.05). Giving consideration on the practical aspects of water-quality management, 0.05 is recommended for them. However, it should be noted that, (a) the estimation was based on the assumption that the allocation factors of DCA, TCA, BCA, BDCA, DBA and DBCA are lognormally distributed; (b) since the histogram did not perfectly fit with the lognormal distribution in certain areas, further efforts should be made to specificly investigate them.

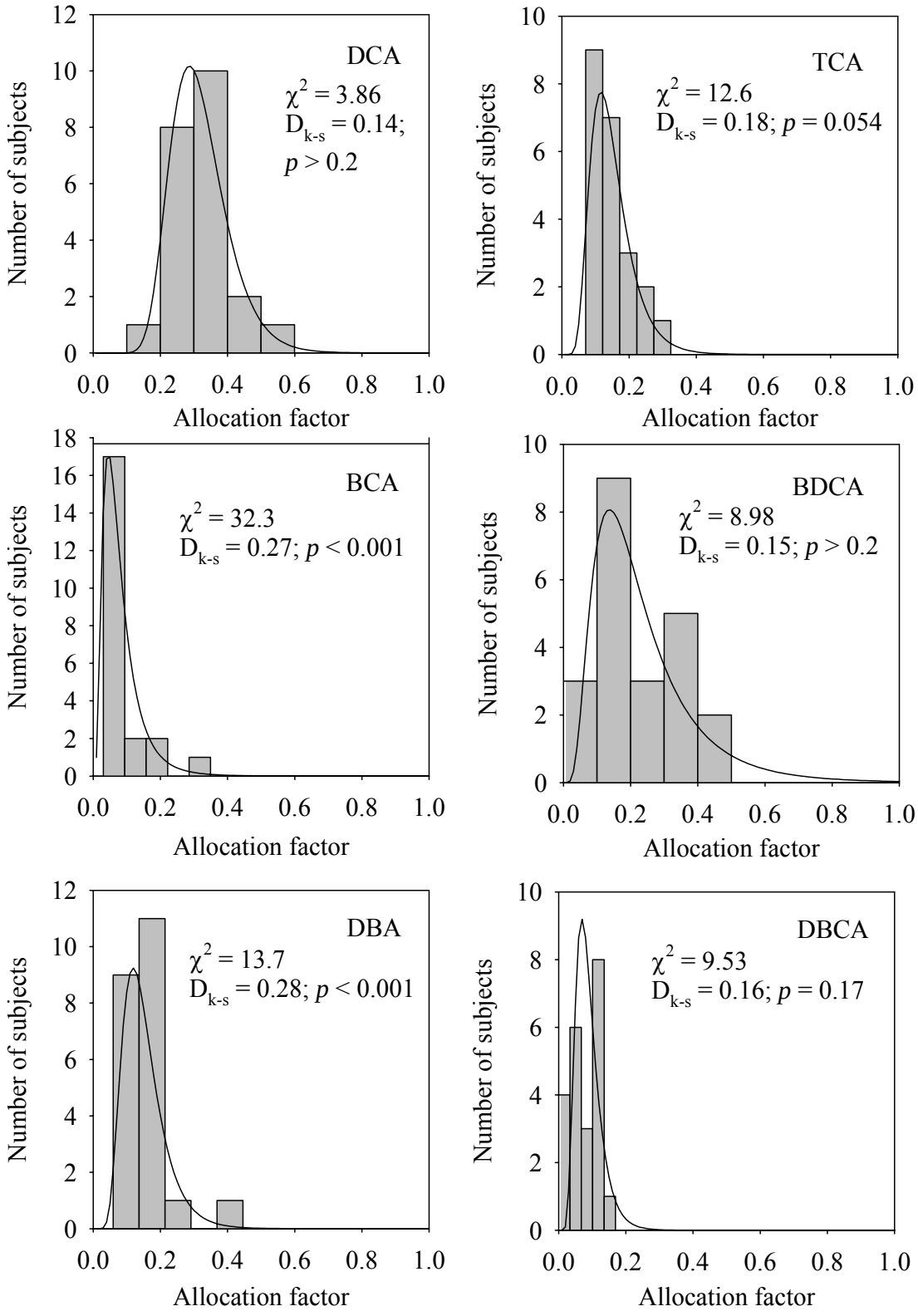

Figure 4.10 Distributions of the allocation factors of HAAs

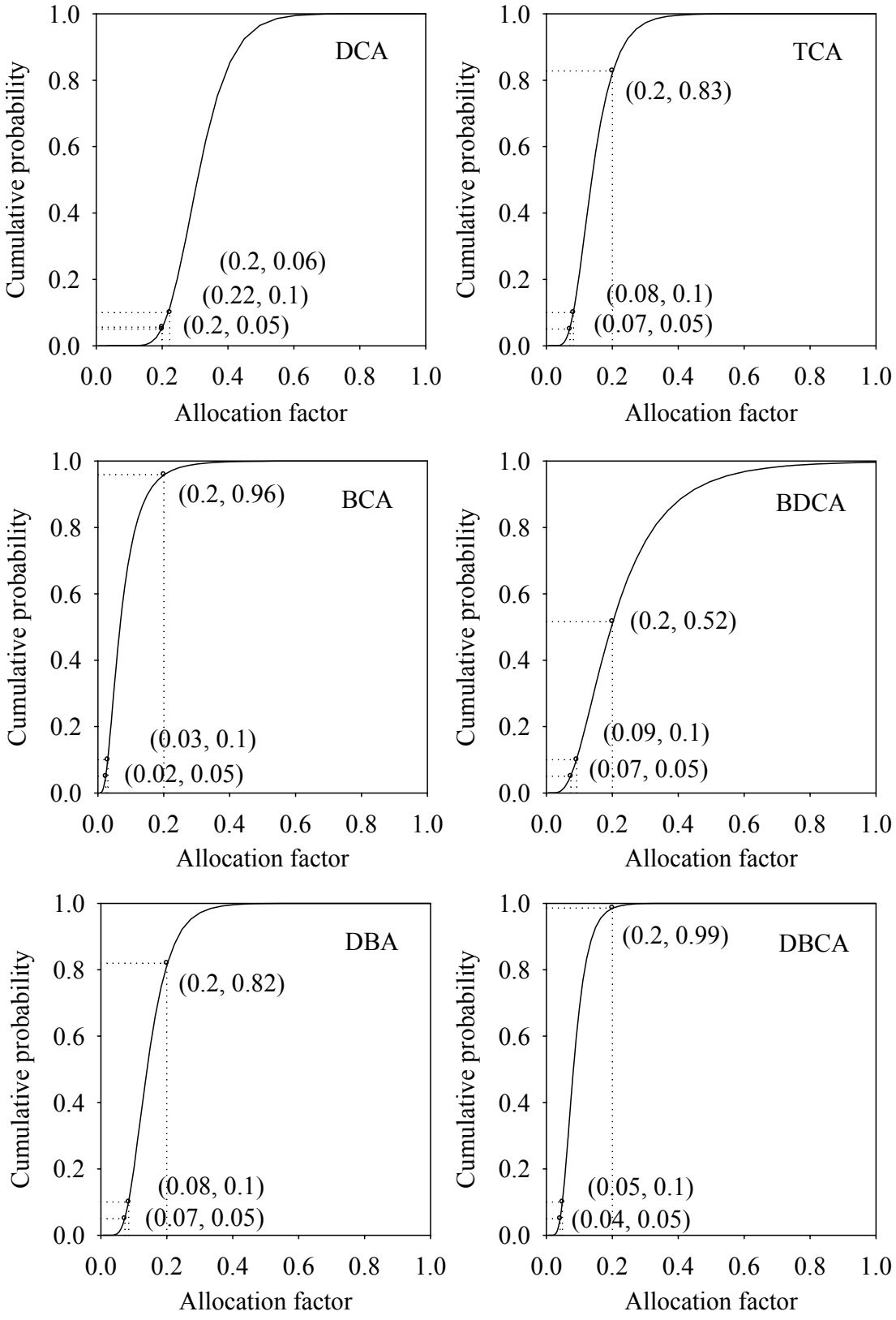

Figure 4.11 Cumulative probability of allocation factors

4.4.3 Alternative Consideration on Allocation to Drinking water

Consideration on direct and indirect intake of tap water

As was mentioned in 3.4.5, the daily per capita consumption of two liters could be considered as the summation of direct and indirect tap water intakes, and water intake in other forms. In 4.3.8, it was observed that preparing food with tap water generally raises the HAA ingestion exposure level. If we make the assumption that this is due to the indirect intake of tap water (as cooking water), the allocation to drinking water could be derived from the approach introduced in 3.4.5.

The results are shown in Table 4.19. In case of MCA, MBA, and TBA, since the ingestion exposure via one or two specific dietaries represents the total exposure amounts, the allocation factors of them were not estimated in this research. Because that the allocation factors of the rest six HAAs did not have great variations, median values were focused in the discussion. In case of BCA and BDCA, because almost no inhalation, transdermal and ingestion exposure (via reagent-water-prepared dietary) were estimated to them, intake of tap water (direct and indirect intakes) was estimated to be the only exposure routes. Similar observation could also be found in TCA. The allocation factors were (or close to) 1. The allocation factor of DCA was in the range of 0.4 – 0.49 (median 0.45). In case of DBA and DBCA, except the minimums, all the allocation factors estimated were above 0.4. For these HAAs, all the factors estimated in this approach were higher than those recommended in 4.4.2. Therefore, the recommendations should be sustained. Additionally, it should also be noted that in this approach, the derived standard value will become greater because the daily water consumption is 0.91 L (209.2 + 702 ml) instead of 2 L.

Table 4.19 HAA allocation factors with the consideration of direct and indirect daily tap water intake amount

Ingestion	Arithmetic mean	Median	Max	Min
MCA	-	-	-	-
MBA	-	-	-	-
DCA	0.45	0.45	0.49	0.40
TCA	0.93	0.94	0.94	0.81
BCA	0.95	1.00	1.00	0.36
BDCA	0.95	1.00	1.00	0.54
DBA	0.65	0.69	0.82	0.38
DBCA	0.48	0.59	0.78	0.00
TBA	-	-	-	-

Consideration on ingestion-equivalents (Ieq)

Like THMs (3.4.5), the allocation factors were also estimated based on the consideration of the Ieq. The results are shown in Table 4.20. The allocation factor of MCA, MBA and TBA were not included in the estimation for the reason mentioned previously. Because more exposure amounts were allocated to tap water, the results were very close to that in Table 4.19 and even higher than that. The minimum values were all higher than those recommended 4.4.2. In case of DBCA, there were four subjects who had allocation equal to zero, and the lowest factor above 0.4. In general, the allocation facotors derived in this approach were higher than those in 4.4.2. Therefore, the allocation factor recommended in 4.4.2 should also be sustained.

Table 4.20 HAA allocation factors with the consideration of ingestion-equivalent (Ieq)

Ingestion	Arithmetic mean	Median	Max	Min
MCA	-	-	-	-
MBA	–	–	–	–
DCA	0.47	0.47	0.53	0.45
TCA	0.94	0.94	0.95	0.94
BCA	1.00	1.00	1.00	1.00
BDCA	1.00	1.00	1.00	1.00
DBA	0.73	0.72	0.82	0.69
DBCA	0.51	0.61	0.85	0.00
TBA	–	–	–	–

4.5 Summary

In this chapter, HAA concentrations in tap water, air and dietaries were surveyed in domestic environment. Based on them, the ingestion, inhalation, and transdermal exposure were estimated. Using the above knowledge, the allocation of HAAs to drinking water were calculated and discussed. The conclusions are summarized as below.

(a) In the tap water samples, DCA concentration was the highest, followed by TCA and BDCA.
(b) DCA, TCA, and DBA were most frequently detected from bathroom air although most HAAs were not detected from living room and outdoor. The ranges of DCA, TCA, and DBA concentrations in outdoor were higher than that in living room, but the median values were all zero.
(c) In dietary samples, DCA and TCA were frequently detected, followed by BCA, BDCA, DBA, and DBCA. Preparing food with tap water led sample to higher contamination levels of major HAAs.
(d) Ingestion via dietaries was proved to be the major exposure route to HAAs, followed by ingestion via tap water, inhalation, and transdermal exposure.
(e) Distribution of the allocation factors of HAAs (except MCA, MBA, and TBA) approximated lognormal distributions. For TCA, BDCA, and DBA, since the corresponding allocation factor of 5th and 10th cumulative probabilities did not show clear difference from each other, the rounded value of 0.1 is recommended to them. For DCA, since the allocation factor of 0.2 was corresponded with a probability of 0.06, the current applied factor of 0.2 should be sustained. In case of DBCA and BCA, the corresponding allocation factors with 5th and 10th cumulative probabilities were both very small (0.02 – 0.05). Giving consideration on the practical aspects of water-quality management, 0.05 is recommended for them conclusively. Since total exposure to MCA, MBA and TBA was estimated to be or near zero, the allocation factors for them were not attempted.
(f) The results of the evaluation based on the consideration of direct and indirect tap

water intakes, and ingestion equivalents (Ieq) approach implied that the allocation factors for HAAs estimated in (e) were appropriate.

Chapter 5

Inhalation Exposure Assessment and the Allocation to Drinking Water of Haloacetonitriles

This chapter aims to decide the method of measuring HANs in the air at first, and to survey the HAN concentrations in tap water and air. The ingestion exposure and inhalation were only estimated because the information on transdermal exposure assessment was insufficient and ingestion exposure via dietary was considered unlikely occurs. The allocation factors of them were calculated and recommended based on the obtained knowledge.

5.1 Introduction

Since available data are insufficient to serve as the basis for the derivation of guidelines or provisional standard values for trichloroacetonitrile (TCAN) and bromochloroacetonitrile (BCAN), only dichloroacetonitrile (DCAN) and dibromoacetonitrile (DBAN) were suggested in WHO and regulated in Japan (WHO, 2008; Ministry of Health, Labor and Welfare, Japan, 2003). Both WHO and Japan considered that it is appropriate to derive the guideline (provisional standard value) of DCAN in TDI approach. However, its provisional standard value (in Japan) significantly differs from that of WHO. In the current Japanese drinking-water quality regulation, DCAN was classified into the management target group, and its provisional standard value was derived from a NOAEL of 8 mg/(kg·day) based on the same study of WHO. A composite uncertainty factor of 1000 was used. Recently, DCAN was reevaluated based on a different viewpoint with the same toxicological information. Since it is considered being appropriate to apply a LOAEL instead of NOAEL, an uncertainty factor of 3000 is used. Consequently, the provisional standard value was revised from the current 0.04 mg/L to 0.01 mg/L (Ministry of Health, Labor and Welfare, Japan, 2009). DBAN was also

considered appropriate to derive the guideline (provisional standard value) in TDI approach. Therefore, WHO and Japan used the same NOAEL of 11.3 mg/(kg·day).

Very less or even no domestic or abroad information on HAN concentrations in water, air, and food could be obtained. However, their physical and chemical properties show that HANs are semi-volatile and very sensitive to pH and temperature. DCAN concentrations were found to dramatically decrease upon 5-minute boiling of chlroraminated (96%) and chlorinated water (98%). After one-hour heating at 65 °C, residual DCAN concentration in water was found to be more than 30% relative to the original concentration (Krasner and Wright, 2005). These facts imply that in human exposure, the ingestion via dietaries is likely to be minimal, and inhalation during hot water bathing should be the primary route. Because the method of monitoring HAN in the air has not been generally established, it is necessary to determine a suitable sampling method first.

The objectives of this research are: (a) to decide suitable sampling methods to collect HANs in bathroom air; (b) to survey HAN concentrations in bathroom air and tap water; (c) to estimate the ingestion, inhalation and transdermal exposure to HANs; (d) to propose rational suggestions on setting the allocation to drinking water of HANs.

5.2 Materials and Methods

5.2.1 Reagents

Reagent water for all the experiments was treated with a Millipore (Tokyo, Japan) Academic A10 purification system. All the reagents were purchased from Wako Pure Chemical Industries (Osaka, Japan). Haloacetonitrile standards were from KANTO CHEMICAL (Tokyo, Japan). Water-analysis-grade MTBE and 1,2,3-trichloropropane were used for the preparation of the calibration curves and the extraction recovery check as the internal standard. Residual-pesticide analysis-grade sodium sulfate and sodium chloride were used in the extraction of HANs from water samples.

5.2.2 Survey Protocol

Preliminary experiment

To find a suitable sampling method, air samplings were conducted in three bathrooms (two in common apartments and one in the University) and two kitchens (the two apartments mentioned above). Two sets of air sampling apparatus were operated simultaneously in bathrooms and kitchens. One was using imipingers (with reagent water) connected with the Sibata (Tokyo, Japan) MP-Σ300 air sampling pump to collect HANs as described in 4.2.2. The other one was with Supelco (PA, USA) glass tubes containing Tenax-TA adsorbents connected with the GL Science (Tokyo, Japan) SP208-100 Dual air sampling pump introduced in 3.2.2. Sampling conditions are shown in Table 5.1.

Table 5.1 Air sampling conditions in preliminary experiment

	Tenax-TA		Impinger	
	Flow rate (mL/min)	Air volumn (L)	Flow rate (mL/min)	Air volumn (L)
Bathroom 1	40	0.8	3000	60
Bathroom 2	40	0.8	3000	60
Bathroom 3	40	0.8	3000	60
Kitchen 1	30	0.97	3000	97
Kitchen 2	30	0.6	3000	60

Air and tap water samplings

Twenty-nine residences were visited for the main survey from August to September 2009. Permissions of the survey and cooperation were received from the residents. The residences were geographically scattered in a watershed area. In this area, Region A is located upstream of Region B. The characteristics of this watershed area were similar to those in 3.2.2, but there was not duplication between the two surveys. Among the 29

residences, 15 were detached houses and 14 were apartments. Each residence was occupied with a single family with one to six persons. Air samplings were conducted in the bathrooms (during occupation). Ventilation was not controlled for all residences. Humidity during sampling was also monitored with a T&D monitor (T&D, Nagano, Japan). During the visit, a recall questionnaire was also conducted.

Concurrently, cold and hot tap water samples were collected in glass vials with Teflon-lined enclosures. Prior to sampling, 10 mg ammonium chloride was placed in the vials to quench residual chlorine. All samples were stored below 5 °C until HAN extraction.

5.2.3 Desorption and Analysis of HANs

The desorption and analytical method of HANs were the same as was mentioned in 3.2.3 (Table 5.2).

Table 5.2 Analytical conditions

	GC-MS-QP2010 Plus	GC-MS-QP2010
Preparation	-	thermal desorption 280 ºC (10 min)
Column	J & W DB-1 (0.32 mm×30 m, film 1.0 μm)	Restek Rtx-1 (0.32 mm×60 m, film 1 μm)
Program of GC oven	40 ºC (10 min) - 20 ºC /min - 200 ºC (5 min)	40 ºC - 3 ºC /min - 100 ºC - 20 ºC /min - 250 ºC
Injection	200 ºC, splitless	250 ºC, split (25:1)
Detection	200 ºC	250 ºC
Carrier gas	Helium (2.7 mL/min)	Helium (2.35 mL/min)

5.2.4 Extraction and Analysis of HANs in Tap Water Samples

The procedure below was developed based on the Standard Methods for Examination of Water (Japan Water Works Association, 2001).

(a) Add 16 g sodium chloride and 4 mL of MTBE to 40 mL of the water sample.
(b) Shake for 15 minutes and allow the phases to separate.
(c) Transfer approximately 3 mL of the MTBE layer to a conical 15-mL centrifuge tube.
(d) Add approximately 2 g sodium sulfate to remove the remaining water.
(e) Transfer 2 mL of the upper phase to a sampler-vial, and add 4 mL of 1,2,3 trichloropropane MTBE solution (0.5 mg/L). Analyze solution using a Shimadzu (Kyoto, Japan) QP2010-Plus gas chromatograph equipped with mass spectrometry. The conditions are shown in Table 5.2.

5.2.5 Extraction Recovery Check and Quantifications

Since the calibration curve of HAN were generated through the entire extraction procedure after appropriate amount of analytes dissolved 40 μL of MTBE introduced to 40 mL of water, the extraction recoveries were not investigated.

HANs in tap water were quantified relative to the obtained peaks of the internal standard (1,2,3-trichloropropane). Method Quantification Limit (MQL) was defined as the HAN concentrations (in water) that give the signal-to-noise ratios of 10. The MQL for HAN in air was the minimum absolute amount (Table 5.3). ND values were expressed and calculated as zero.

Table 5.3 MQLs of HANs

Water (μg/L)	MQL
DCAN	0.2
BCAN	0.3
DBAN	0.3

Air (ng)	MQL
DCAN	0.1
BCAN	0.1
DBAN	0.2

5.2.6 Exposure Assessment

The exposure amounts via were calculated with the following equations.

Ingestion exposure via tap water (μg/day)
= Tap water concentration (μg/L) × Consumption (L /day) (5.1)

Inhalation exposure (μg/day)
= Airborne concentration in bathroom air (μg/m^3) × Breathing Rate (m^3/day) (5.2)

In a recent report of USEPA (2000), the permeability coefficients of HANs were estimated to be uniformly about 0.1 cm/hour in steady state methods, which is very close to that of THMs (about 0.2 cm/hour) and much greater than that of HAAs (about 0.002 cm/hour). However, there was no information on their respective coefficients and lag time factors. Therefore, the transdermal exposure was not estimated in this study.
As was mentioned previously, ingestion exposure via dietaries was considered unlikely occurs. Therefore, the total exposure was estimated as the sum of ingestion and inhalation exposure amount in this research.

5.3 Results and Discussion

5.3.1 Determination of Sampling Strategy

As is shown in Table 5.4, in the preliminary experiment, the Supelco Tube containing Tenax-TA collected more DCAN and BCAN than impingers in all bathrooms. No clear difference on the collection efficiency on DBAN between them was observed. Therefore, Supelco Tube was selected to use in the main survey of HAN concentrations in bathroom air. Furthermore, no HANs was detected in the kitchens. Therefore, survey on the HAN concentrations in kitchen air was excluded from this survey. Based on the experience of THMs, tap water was assumed as the major emission source of HANs in common indoor environments. Since HANs were not detected from the kitchens, where tap water was used intentionally, possibility of detecting any HAN in living room became very low. Therefore, the investigation focused only bathrooms in this research.

Table 5.4 HAN concentrations in bathroom and kitchen air (preliminary experiment) (μg/m^3)

	DCAN		BCAN		DBAN	
	Tenax-TA	Impinger	Tenax-TA	Impinger	Tenax-TA	Impinger
Bathroom 1	3.68	0.75	0.85	0.59	ND	ND
Bathroom 2	1.64	ND	0.71	0.57	ND	ND
Bathroom 3	2.91	ND	1.16	ND	0.48	ND
Kitchen 1	ND	ND	ND	ND	ND	ND
Kitchen 2	ND	ND	ND	ND	ND	ND

5.3.2 HAN Concentrations in Tap Water

In the 29 tap water samples of the visited residences, DCAN, BCAN and DBAN were detected from most samples (Table 5.5 and Figure 5.1). DCAN showed the widest concentration range of (0 – 1.81 μg/L) with the highest median value (0.88 μg/L), followed by BCAN (0.37 – 1.08 μg/L, median 0.79 μg/L) and DBAN (0 – 0.61 μg/L,

median 0.35 μg/L). The small max/min values showed weak regional difference in the HAN concentrations in tap water.

Table 5.5 HAN concentrations in tap water samples (μg/L)

	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
DCAN	0.79	0.88	1.81	0.00	8	23
BCAN	0.78	0.79	1.08	0.37	3	29
DBAN	0.28	0.35	0.61	0.00	2	18

[a] calculated with the minimum and max quantified value

[b] quantified sample number

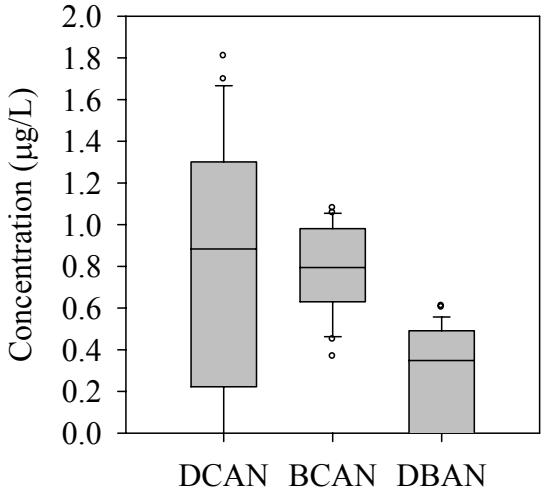

Figure 5.1 HAN concentration in tap water

The statistical differences in the HAN concentrations of the tap waters between Regions A and B were tested in the nonparametric Mann-Whitney test since the data failed to pass the normality tests ($p \leq 0.05$). All statistical analyses were performed with a Sigmaplot (CA, USA) software (Version 10.0). As is shown in Figure 5.2, DCAN and BCAN concentrations in Region A (median 1.29 and 0.97 μg/L) were statistically higher than those in Region B (median 0.22 and 0.63 μg/L), and DBAN concentration

(median 0 μg/L) were statistically lower than those in Region B (median 0.49 μg/L).

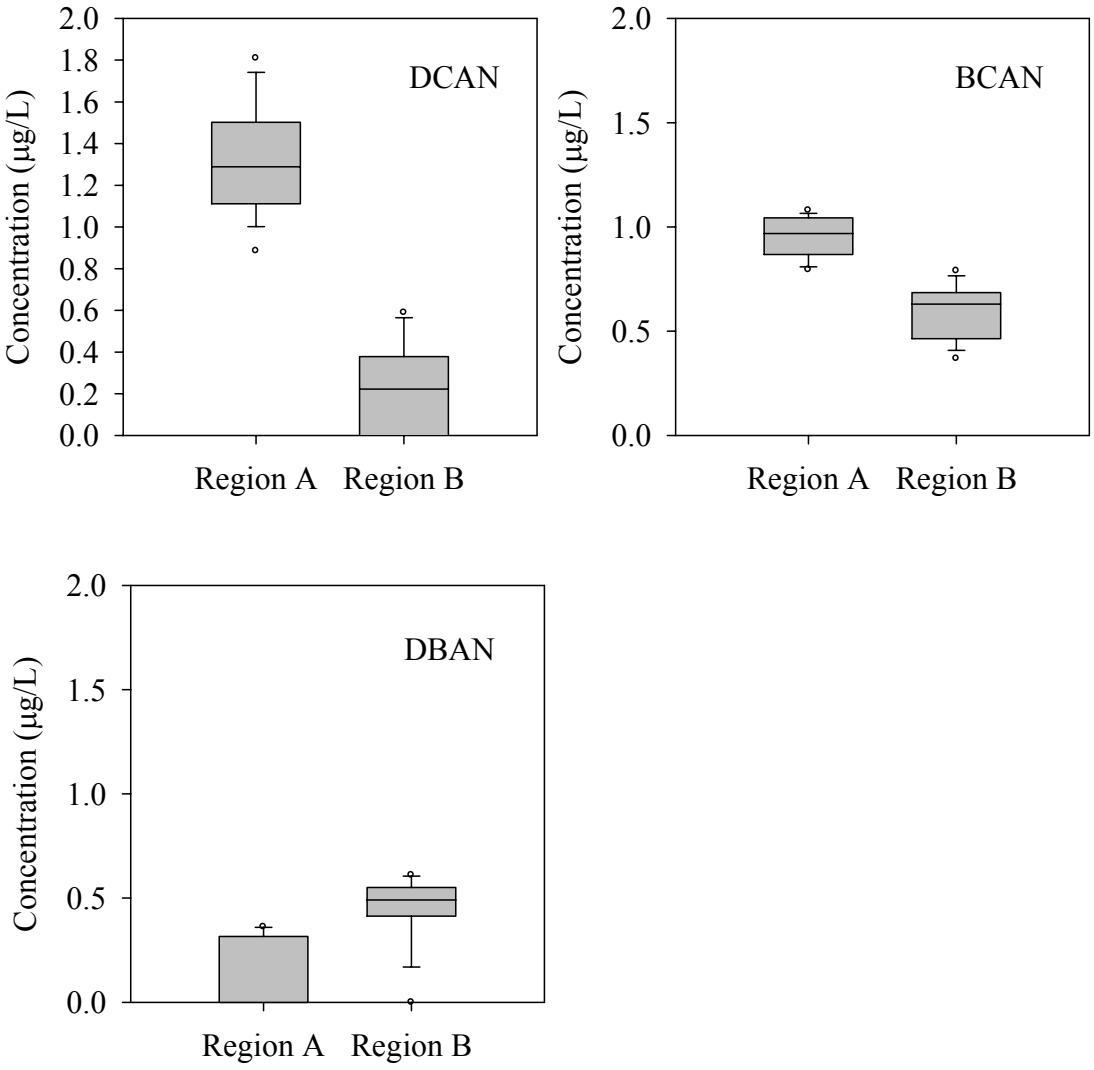

Figure 5.2 HAN concentrations in tap water of Regions A and B

In the cold and tap water samples of the same residence, no statistical difference of DCAN (median 0.88 and 0.70 μg/L), BCAN (median 0.79 and 0.75 μg/L), and DBAN (median 0.35 and 0.31 μg/L) were observed (Figure 5.3). The following ingestion exposure estimation was based on cold tap water concentration.

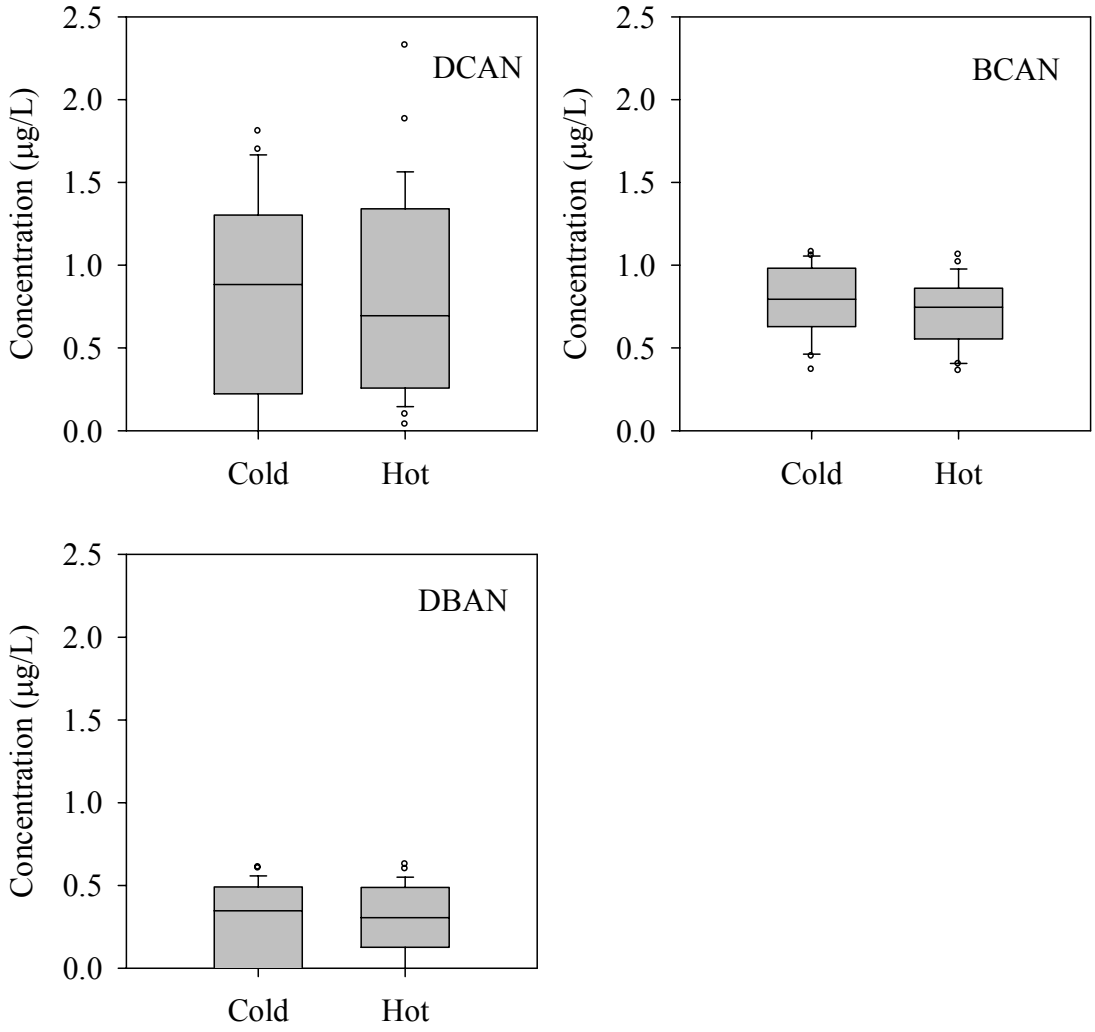

Figure 5.3 HAN concentrations in cold and hot tap water

5.3.3 HAN Concentrations in Bathroom Air

DCAN and BCAN were more frequently detected from common bathroom air than DBAN (Table 5.6 and Figure 5.4). DCAN had the highest concentration range (0 – 1.81 μg/L, median 0.88 μg/L), followed by BCAN (0– 1.08 μg/L, median 0.79 μg/L) and DBAN (0 – 0.61 μg/L, median 0.35 μg/L). The statistical differences of the airborne HAN concentrations in bathrooms between Regions A and B were tested in the nonparametric Mann-Whitney test. The results of the HAN concentrations in the

bathrooms of Regions A and B are shown in Figure 5.5. No statistically difference of the HAN concentrations between Regions A and B was observed.

Table 5.6 HAN concentrations in bathroom air (μg/m3)

	Arithmetic mean	Median	Max	Min	Max/min [a]	n [b]
DCAN	0.84	0.30	6.62	0.00	25	17
BCAN	0.35	0.00	2.10	0.00	7	13
DBAN	0.09	0.00	1.00	0.00	2	3

[a] Calculated with the minimum and max quantified values

[b] Quantified sample nuber

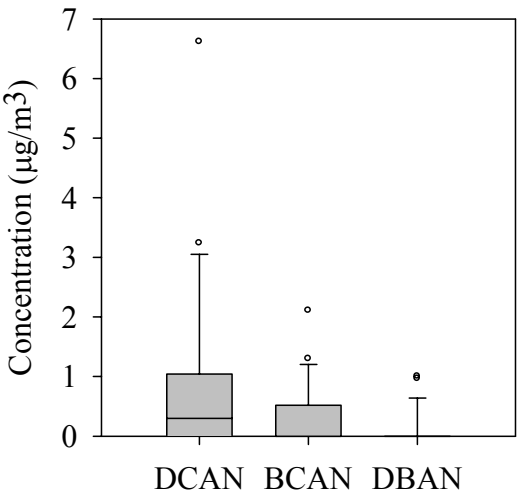

Figure 5.4 HAN concentrations in bathroom air

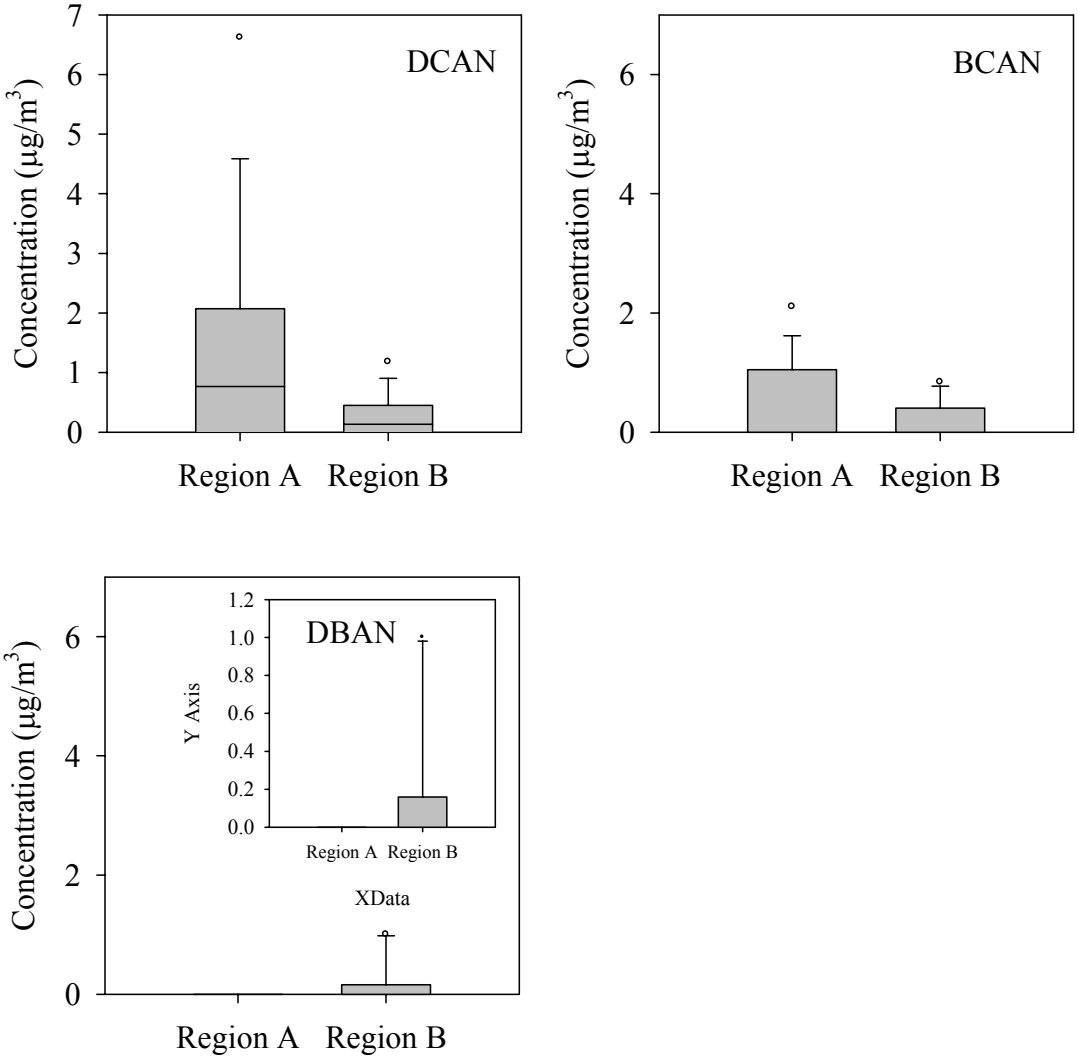

Figure 5.5 HAN concentration in the bathroom air of Regions A and B

5.3.4 HAN Ingestion Exposure

Ingestion exposures to HANs were shown in Table 5.7 and Figure 5.6. The subjects were mostly exposed to DCAN (0 – 3.62 μg/day, median 1.77 μg/day), followed by BCAN (0 – 2.16 μg/day, median 1.59 μg/day) and DBAN (0 – 1.22 μg/day, median 0.7 μg/day). Weak regional differences of HAN ingestion exposure were also observed from their max/min values. The DCAN and BCAN ingestion exposures in Region A

(median 2.58 and 1.94 μg/day) are statistically higher than those of Region B (median 0.44 and 1.26 μg/day), and DBAN ingestion exposure (median 0 μg/day) is statistically lower than that in Region B (median 0.98 μg/day).

Table 5.7 HAN ingestion exposure (μg/day)

	Arithmetic mean	Median	Max	Min	Max/min [a]
DCAN	1.58	1.77	3.62	0.00	8
BCAN	1.57	1.59	2.16	0.74	3
DBAN	0.56	0.70	1.22	0.00	2

[a] Calculated with the minimum and max quantified values

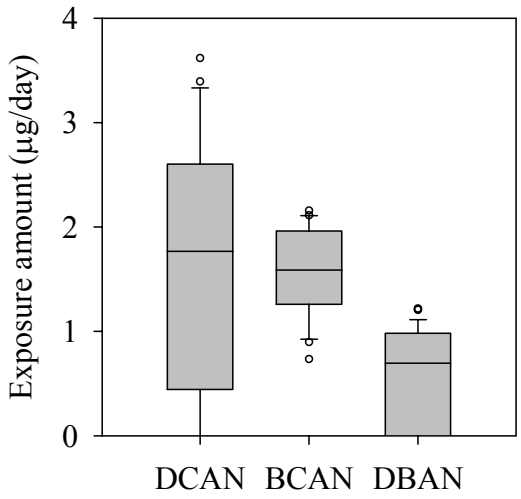

Figure 5.6 HAN ingestion exposure

5.3.5 HAN Inhalation Exposure

Inhalation exposure to HANs were shown in Table 5.8 and Figure 5.7. Like the ingestion exposure via tap water, the subjects were mostly exposed to DCAN (0 – 1.38 μg/day, median 0.05 μg/day), followed by BCAN (0 – 0.44 μg/day, median 0 μg/day) and DBAN (0 – 0.17 μg/day, median 0 μg/day). The statistical differences in the HAN

inhalation exposures between Regions A and B were also tested in the Mann-Whitney test. Figure 5.8 shows no statistically difference of inhalation exposure between two regions in DCAN (median 0.08 and 0.02 μg/day), BCAN (median 0 μg/day in both regions), and DBAN (median 0 μg/day in both regions). This is not in accordance with ingestion exposure. The observation suggests that the HAN concentrations in local tap water are probably weaker factors affecting inhalation exposure than others (e.g., different lifestyles and physical conditions).

Table 5.8 HAN inhalation exposure (μg/day)

	Arithmetic mean	Median	Max	Min	Max/min [a]
DCAN	0.15	0.05	1.38	0.00	34
BCAN	0.06	0.00	0.44	0.00	7
DBAN	0.02	0.00	0.17	0.00	1

[a] Calculated with the minimum and max quantified values

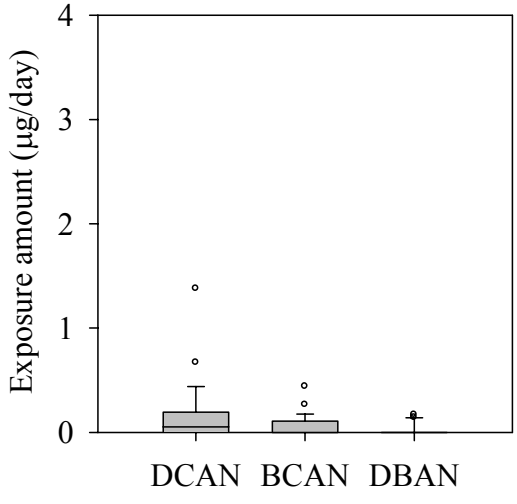

Figure 5.7 HAN inhalation exposure

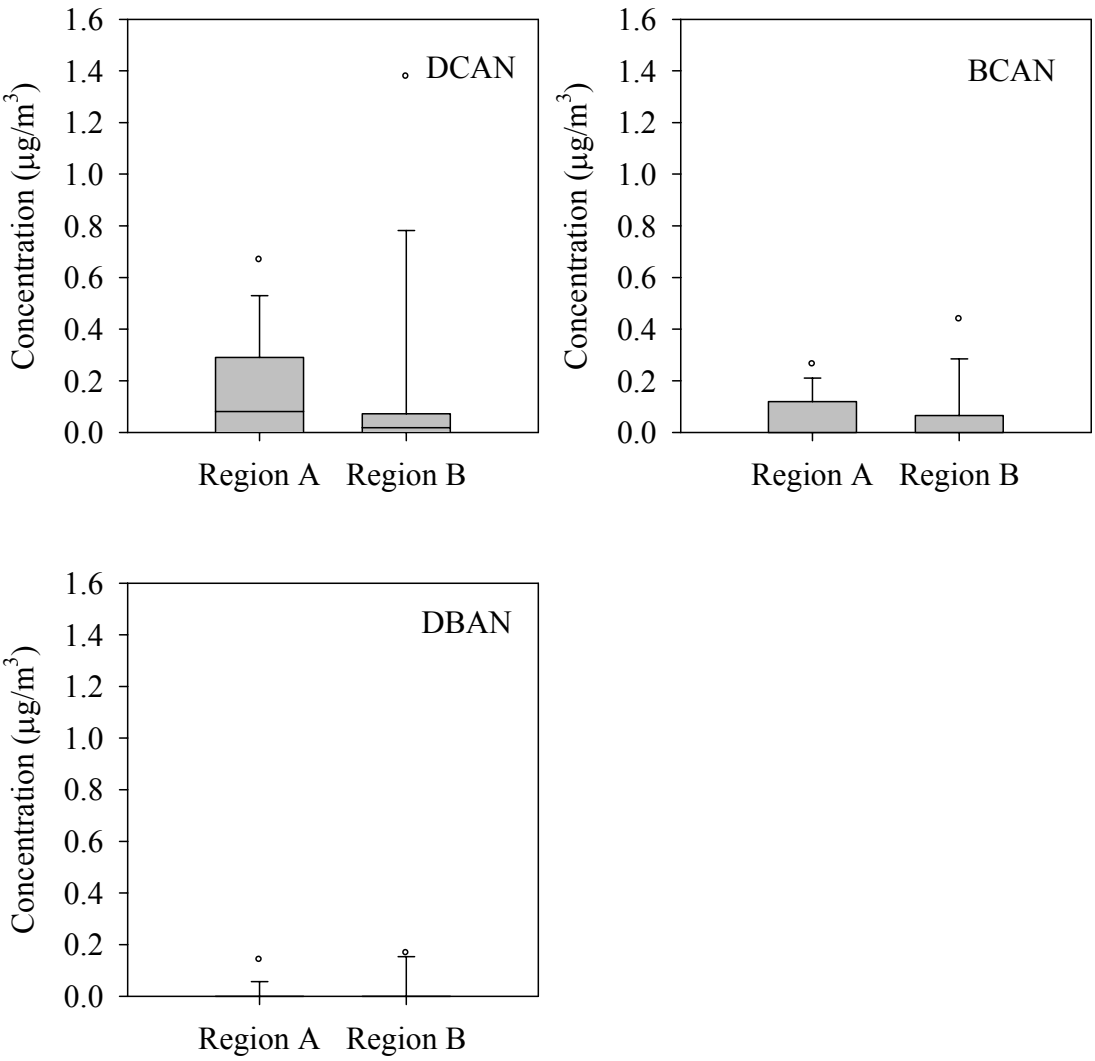

Figure 5.8 HAN inhalation exposure of Regions A and B

5.3.6 HAN Total Exposure

Daily HAN total exposure amounts were calculated as the summation of the ingestion and inhalation exposure amounts. The results are shown in Table 5.9 and Figure 5.9. The max values of the daily HAN total exposure amounts were divided by the average body weight of 50 kg. All of them (DCAN, 0.09 and BCAN, 0.05 μg/(kg· day)) were much smaller than their TDI values (Table 2.1). For the same reason mentioned

previously (3.3.11), it is necessary to discuss and decide the allocation factors even the total exposure amounts were surveyed to be lower than TDI values.

Table 5.9 HAN total exposure (μg/day)

	Arithmetic mean	Median	Max	Min	Max/min [a]
DCAN	1.73	1.77	4.71	0.00	72
BCAN	1.63	1.64	2.43	0.74	3
DBAN	0.58	0.70	1.22	0.00	2

[a] Calculated with the minimum and max quantified values

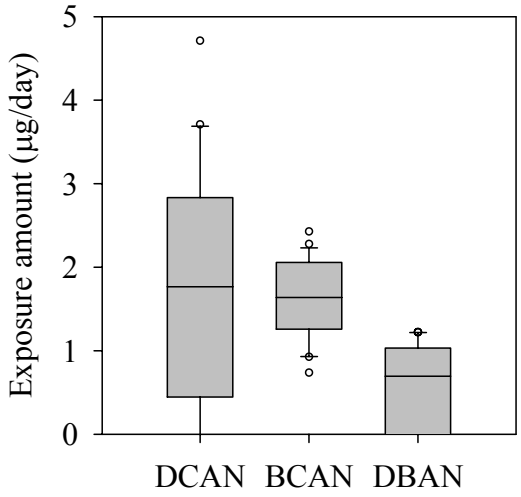

Figure 5.9 HAN total exposure

5.4 Allocation to Drinking Water

5.4.1 Estimation of Allocation to Drinking Water

HAN allocation factors were calculated with Equation 5.1. This approach considers that the ingestion exposure of consuming 2 L of tap water per day should be allocated to drinking water in total exposure to HANs. The subjects who were not estimated to be exposed to HANs (total exposure amount = zero) were excluded.

Allocation factor = Ingestion exposure via tap water / Total exposure (5.1)

In the results of DCAN for the 29 subjects (Table 5.10 and Figure 5.10), the minimum allocation factor was 0, and the median value was 0.92. Two subjects were estimated to have allocation factors lower than the currently applied 0.2. The minimum and median values of BCAN were estimated to be 0.82 and 1, respectively. In the results of DBAN, the minimum and median allocation factors were 0.86 and 1. HAN ingestion exposure via tap water was estimated to be much greater than inhalation. Furthermore, the ingestion exposure via dietaries is considered to be very low (Raymer, 2001). For such cases, WHO (2008) specifically recommended applying allocation factors of 0.8 as was mentioned in 1.1.4. It is therefore recommended in this research.

Table 5.10 HAN allocation factors

	Geometric mean [a]	Median	Max	Min	Standard deviation	n [b]
DCAN	0.86	0.92	1.00	0.00	0.27	25
BCAN	0.97	1.00	1.00	0.82	0.05	29
DBAN	0.98	1.00	1.00	0.86	0.05	18

[a] Those with zero value were excluded from the calculation

[b] The number of the estimated subjects in 29

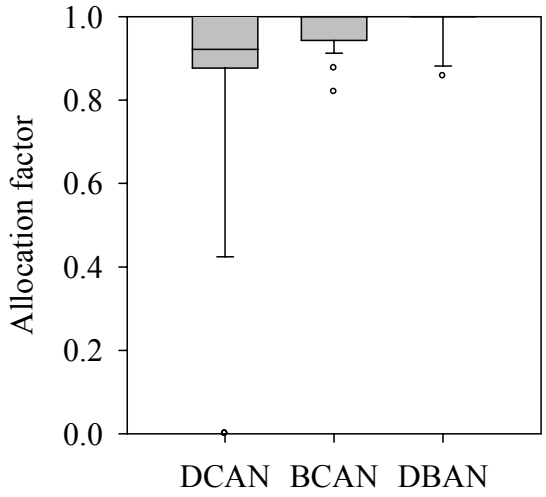

Figure 5.10 HAN allocation facotr

5.4.2 Allocations to Drinking Water of Regions A and B

The allocation factors for each subjects in Region A and B were estimated and compared. There are no statistical difference in allocation factors of DCAN (median 0.96 and 0.92), BCAN (median 1 for both regions), and DBAN (median 1 for both regions). This observation suggests that even there are regional differences in the ingestion exposure of HANs, and that the allocation factors to drinking water are unlikely to be different. Since tap water is possibly the major emission source of HANs in air, the ingestion and inhalation exposure could change accordingly. Therefore, when setting the allocation factors of HANs, more attention should be paid to life-style than regional difference.

5.4.3 Prediction of the Low-allocation Scenario

Although the allocation factors were estimated to be very high in this research, it is still possible that under certain life-style (long bathing duration or poor ventilation), the total exposure amount could be higher and allocation factor could be lower too. Therefore, a prediction of the high-exposure and low-allocation affecting factors was conducted by applying a forward stepwise multi-linear regression test. The ratios of the total daily

exposure amounts to the THM concentrations in the local tap water (to exclude influence from regional difference of tap water) were calculated, and allocation factors for each subject were considered as dependent variables. The potential independent variables were the items of the questionnaire (Table 5.11).

Before the test, colinearity was check between each pair of the independent variables. Pairs have correlation coefficients greater than 0.5 were excluded from the test. The results showed that generally shower duration and bathroom volume were the major positive contributing factors of high HAA total exposure amounts and low allocation factors (Table 5.12). Further investigation on the high-exposure or low-allocation situation should pay more attention to these scenarios.

Table 5.11 Dependent and independent variables in multi-linear regression

Dependent variables	Independent variables
Ratios of the total daily exposure amounts to the THM concentrations in the local tap water	Sexuality
Allocation factors	Number of family members [a]
	Type of residence
	Bathroom volume
	Bathing style [a]
	Bathroom occupation duration [a]
	Bathing duration
	Shower duration
	Ventilation

[a] Variable excluded from the colinearity test

Table 5.12 Contributing factors to total daily exposure and allocation factor

	Dependent variables	Positive independent variables [a]	Negative dependent variables [b]	Standard coefficients [c]
DCAN	Total daily exposure amount	Shower duration		0.46
	Allocation factor		Bathroom volume	0.41
BCAN	Total daily exposure amount	Shower duration		0.18
	Allocation factor		Shower duration	0.41
DBAN	Total daily exposure amount	Bathroom volume		0.46
	Allocation factor		Bathroom volume	0.46

[a] Variable with positive standard coefficient

[b] Variable with negative standard coefficient

[c] $p < 0.05$

5.5 Overview of THM, HAA, and HAN Exposure Assessments

So far, the exposure assessments have been conducted for THMs, HAAs, and HANs to establish their allocation factors. From these results, it could be concluded that human are exposed to different DBPs in different level via each exposure route. Physical and chemical properties of the compounds were found to be the most important factors to determine the exposure scenarios. For volatile compounds such as THMs, the inhalation is one of the major exposure routes. For semi-volatile (or non-volatile) compounds such

as HANs and HAAs, ingestion exposure is much more important. For compounds completely ionized at neutral pH such as HAAs, the transdermal exposure is much lower than others because the skin is an efficient barrier to ionic species. However, it could also be observed that when the DBP concentration in tap water is higher, its concentration in other environmental media (e.g., air and dietaries) generally tends to become higher, too. This is significantly different from most of the other compounds. The knowledge should be applied to the exposure assessment of other DBPs.

5.6 Summary

In this chapter, HAN concentrations in tap water and bathroom air were thoroughly surveyed in domestic environment. Based on them, the ingestion and inhalation exposure were estimated. Using the above knowledge, allocation to the drinking water of HANs were calculated and discussed. The conclusions are summarized below.

(a) Supelco tube containing Tenax-TA showed satisfactory collection efficiency in collecting airborne DCAN and BCAN.
(b) In the 29 tap water samples of the visited residences, DCAN, BCAN and DBAN were detected from almost all of them. DCAN concentration was the highest, followed by BCAN and DBAN.
(c) Airborne DCAN and BCAN were more frequently detected from common bathrooms than DBAN. Similarly, DCAN had the highest concentration in air, followed by BCAN and DBAN. Unlike THMs, HAN tap water concentrations were observed not to be strong affecting factors to the HAN concentrations in bathroom air.
(d) Since the allocation factors of HANs were estimated to be close to 1, according to the recommendation of WHO, an allocation factors of 0.8 can be recommended.
(e) Shower duration and bathroom volume were the major affecting factors to high-total-exposure and low-allocation-factor. Further investigation should focused on these situations.
(f) In investigating other DBPs, major exposure route to them could be predicted with

their physical and chemical properties. Higher DBP concentrations in tap water may lead to higher concentrations in other environmental media.

Chapter 6

Conclusions

This research has addressed various aspects based on the establishment of the allocation factors of drinking water for THMs, HAAs, and HANs. The major findings are summarized as below.

Chapter 2 reviewed the current regulatory framworks of major three species of disinfection byproducts (THMs, HAAs, and HANs) in drinking water of WHO and Japan. The obtained knowledge, existing challenges, and the position of this research are summarized as below:

(a) When setting the national standard for target chemicals in drinking water, variety of domestic environmental, social, cultural conditions affecting potential exposure should be taken into account.
(b) To estimate the allocation factors of drinking water for THMs, HAAs and HANs, it is necessary to investigate their total exposures first through multi-route exposure assessment.
(c) This research is designed to conduct the unprecedented multi-route exposure assessments to THMs, HAAs, and HANs under the domestic environment, and discusses how to reevaluate their allocation factors.

Chapter 3 thoroughly surveyed the THM concentrations in tap water, air, and dietaries in the domestic environment. Based on the results, the ingestion, inhalation, transdermal exposure were estimated. Then, the allocation factor of THMs were calculated and discussed. The conclusions are summarized below.

(a) In the tap water of 59 residences, TCM, BDCM, DBCM and TBM concentrations were much higher in bathroom air than in kitchen, living room, and outdoor. Their distributions in each indoor environment were similar to that of tap water. Additionally,

domestic THM concentrations in bathroom air were generally higher than those reported abroad. All THMs were detected from most of the dietary samples prepared with tap water except TBM. THM concentrations were measured to be generally higher than those with reagent water.

(b) Inhalation exposure in living room was comparable to that in bathroom because of its long occupation time. Ingestion exposure via dietary prepared with tap water was higher than those prepared with reagent water.

(c) Allocation factors for the four THMs were conclusively recommended 0.1. BDCM was derived from a different approach, and the daily drinking-water consumption 0.87 L should be applied in the calculation of its standard value.

Chapter 4 surveyed HAA concentrations in tap water, air and dietaries in domestic environment. Based on the results, the ingestion, inhalation, transdermal exposure were estimated. And, the allocation factors of HAAs were calculated and discussed. The conclusions are summarized below.

(a) DCA, TCA and DBA were most frequently detected from bathroom air. Most HAAs were not detected from living room and outdoor airs. In dietary samples, DCA and TCA were frequently detected, followed by BCA, BDCA, DBA, and DBCA. Preparing food with tap water led sample to higher contamination levels of major HAAs.

(b) Ingestion via dietaries was the major exposure route to HAAs, followed by ingestion via tap water, inhalation, and transdermal exposure.

(c) Allocation factors for the six species of HAA (except MCA, MBA and TBA) were conclusively recommended as DCA (0.2), TCA (0.1), BCA (0.05), BDCA (0.1), DBA (0.1), and DBCA (0.05).

Chapter 5 surveyed HAN concentrations in tap water, air and dietary in domestic environment. Based on them, the ingestion and inhalation exposure were estimated. The allocation factors of HANs were calculated and discussed. The conclusions are summarized below.

(a) Supelco tube containing Tenax-TA showed satisfactory collection efficiency in collecting airborne DCAN and BCAN.

(b) DCAN, BCAN and DBAN were detected from all the tap water samples (22). DCAN concentration was the highest, followed by BCAN and DBAN. Airborne DCAN and BCAN were more frequently detected from common bathrooms than DBAN. Similarly, DCAN had the highest concentration in air, followed by BCAN and DBAN.

(c) Since the allocation factors of HANs were estimated to be close to 1, an allocation factor of 0.8 can be recommended.

(d) Shower duration and bathroom volume were the major affecting factors to high-total-exposure and low-allocation-factor. Further investigation should focus on these situations.

(e) In investigating other DBPs, major exposure route to them could be predicted with their physical and chemical properties. Higher DBP concentrations in tap water may lead to higher concentrations in other environmental media.

Chapter 7

Future Research

This research has evaluated and recommended appropriate allocation factors of drinking water to THMs, HAAs, and HANs. However, to reach the final goal of setting their standard values of drinking water, several new research topics uprised and are needed to be completed.

(a) In the multi-route exposure assessment of THMs of this research, the results of a one-point survey was applied to the ingestion exposure via dietaries. However, by comparing the results with the previous researches, it was found that the ingestion exposure via dietaries may also have considerable spatial and temporal variabilities. Therefore, more comprehensive surveys on the THM concentrations in dietaries (e.g. an annually national total diet study) should be conducted.

(b) Since the low allocation areas (the tails of the distribution) of THMs and HAAs were not completely covered with the lognormal distributions, further investigation should be made based on the predicted affecting factors of the low-allocation scenario. A more precise fitting of distribution should be specifically made to this low-allocation population.

(c) In this research, the distributions of allocation factors were all based on the observed values. Therefore, uncertainties were unavoidably involved. To evaluate them in a wider viewpoint beyond this limit, simulations (e.g., Monte Carlo Analysis) are very useful tools. Grasping the distributions of every variables (e.g., concentration in tap water and daily per capita consumption) in the derivation approaches of the allocation factors as the inputs of the simulation, the estimated allocation factors and standard values of drinking water (output) could be more persuasive and rational.

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Table 1 HAA extraction recoveries of dietary samples of Region A

	Grain		Potato		Sweetener and snacks		Lipid		Bean		Fruit		Vegetable	
Region A	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.22	0.03	0.27	0.04	0.28	0.03	0.17	0.10	0.28	0.03	0.31	0.05	0.39	0.04
MBA	0.52	0.03	0.68	0.10	0.68	0.07	1.64	0.27	0.78	0.02	0.78	0.04	0.49	0.10
DCA	0.64	0.04	0.69	0.02	0.84	0.04	0.62	0.15	0.80	0.05	0.82	0.03	0.89	0.03
TCA	0.98	0.22	1.37	0.18	2.15	0.14	0.21	0.13	1.13	0.12	2.34	0.11	0.78	0.12
BCA	0.80	0.13	1.06	0.09	2.09	0.29	1.36	0.17	1.53	0.10	2.13	0.15	2.51	0.10
BDCA	0.80	0.09	0.85	0.04	1.02	0.03	0.35	0.08	1.13	0.04	0.68	0.03	1.05	0.06
DBA	0.60	0.05	0.76	0.05	1.03	0.09	0.76	0.17	1.00	0.10	1.08	0.07	1.39	0.04
DBCA	0.76	0.05	0.91	0.05	1.38	0.17	0.50	0.19	1.11	0.11	1.11	0.04	1.21	0.21
TBA	0.83	0.06	0.85	0.03	1.10	0.01	0.41	0.25	1.02	0.03	0.82	0.04	1.28	0.10

	Algae		Beverage		Seafood		Meat and egg		dairy		Seasoning			
Region A	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.34	0.01	0.34	0.01	0.54	0.02	0.52	0.09	0.44	0.01	0.45	0.02	-	-
MBA	1.39	0.06	1.39	0.06	1.90	0.08	1.47	0.02	1.67	0.15	1.67	0.15	-	-
DCA	0.95	0.02	0.95	0.02	0.96	0.04	0.75	0.02	0.94	0.04	0.94	0.04	-	-
TCA	1.10	0.26	1.10	0.26	1.34	0.14	1.60	0.28	1.24	0.17	1.24	0.17	-	-
BCA	2.26	0.06	2.26	0.06	1.37	0.14	1.68	0.05	2.76	0.04	2.76	0.04	-	-
BDCA	1.03	0.03	1.08	0.04	0.94	0.26	0.16	0.27	0.45	0.01	0.46	0.03	-	-
DBA	1.33	0.10	1.33	0.10	1.91	0.18	1.28	0.03	1.39	0.12	1.39	0.12	-	-
DBCA	1.45	0.07	1.45	0.07	1.21	0.04	0.32	0.12	0.82	0.09	0.82	0.09	-	-
TBA	1.21	0.02	1.21	0.02	0.50	0.04	0.23	0.06	0.81	0.11	0.81	0.11	-	-

Table 2 HAA extraction recoveries of dietary samples of Region B

Region B	Grain		Potato		Sweetener and snacks		Lipid		Bean		Fruit		Vegetable	
	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.16	0.14	0.32	0.00	0.48	0.09	0.49	0.10	0.52	0.11	0.28	0.01	0.28	0.03
MBA	1.16	0.07	1.13	0.08	1.52	0.12	1.47	0.02	1.59	0.19	1.29	0.23	0.49	0.04
DCA	0.87	0.04	0.81	0.05	0.95	0.04	0.75	0.02	0.89	0.03	0.96	0.01	0.86	0.04
TCA	0.38	0.13	1.27	0.15	0.59	0.30	1.01	0.20	1.22	0.19	1.97	0.10	2.50	0.08
BCA	1.85	0.16	1.84	0.16	2.52	0.20	1.68	0.05	2.80	0.21	2.68	0.09	2.38	0.17
BDCA	0.41	0.04	0.40	0.03	0.48	0.04	0.13	0.23	1.13	0.04	0.38	0.01	1.09	0.04
DBA	0.96	0.11	1.21	0.04	1.34	0.18	1.28	0.03	1.61	0.11	1.46	0.05	1.17	0.02
DBCA	0.69	0.27	0.66	0.16	0.16	0.02	0.32	0.12	0.56	0.17	0.84	0.11	1.10	0.07
TBA	0.77	0.12	0.69	0.00	0.63	0.10	0.24	0.05	0.57	0.08	0.78	0.05	1.68	0.06

Region B	Algae		Beverage		Seafood		Meat and egg		dairy		Seasoning		-	-
	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)		
MCA	0.28	0.01	0.34	0.01	0.32	0.05	0.38	0.06	0.34	0.04	0.46	0.04	-	-
MBA	1.14	0.16	1.39	0.06	1.38	0.05	1.39	0.04	1.38	0.05	1.45	0.30	-	-
DCA	0.89	0.08	0.95	0.02	0.81	0.02	0.81	0.05	0.81	0.02	0.75	0.02	-	-
TCA	0.84	0.12	1.10	0.26	0.87	0.09	0.92	0.17	1.63	0.03	1.20	0.16	-	-
BCA	2.35	0.16	2.26	0.06	1.91	0.18	2.15	0.13	2.19	0.07	2.19	0.13	-	-
BDCA	1.18	0.01	1.08	0.04	0.56	0.08	0.34	0.05	0.65	0.03	0.37	0.02	-	-
DBA	1.26	0.12	1.33	0.10	1.03	0.15	0.99	0.13	0.94	0.02	1.03	0.10	-	-
DBCA	0.92	0.19	1.45	0.07	0.89	0.16	0.49	0.18	0.97	0.06	0.55	0.17	-	-
TBA	1.59	0.14	1.21	0.02	0.71	0.12	0.64	0.01	0.80	0.03	0.72	0.09	-	-

Table 3 HAA extraction recoveries of dietary samples of Region C

	Grain		Potato		Sweetener and snacks		Lipid		Bean		Fruit		Vegetable	
Region C	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.22	0.03	0.31	0.01	0.33	0.02	0.34	0.04	0.28	0.03	0.31	0.05	0.40	0.03
MBA	0.52	0.03	1.13	0.08	1.06	0.04	1.06	0.04	0.78	0.02	0.78	0.04	0.51	0.13
DCA	0.64	0.04	0.81	0.05	0.67	0.04	0.67	0.04	0.80	0.05	0.82	0.03	0.89	0.03
TCA	0.98	0.22	1.13	0.18	0.25	0.08	0.25	0.08	1.13	0.12	2.34	0.11	0.31	0.17
BCA	0.80	0.13	1.68	0.14	1.90	0.15	1.90	0.15	1.53	0.10	2.13	0.15	2.51	0.10
BDCA	0.80	0.09	0.40	0.03	0.27	0.07	0.25	0.07	1.13	0.04	0.68	0.03	1.05	0.06
DBA	0.60	0.05	1.21	0.04	0.87	0.09	0.87	0.09	1.00	0.10	1.08	0.07	1.39	0.04
DBCA	0.76	0.05	0.66	0.16	1.34	0.13	1.36	0.11	1.11	0.11	1.11	0.04	1.21	0.21
TBA	0.83	0.06	0.69	0.00	0.38	0.02	0.38	0.02	1.02	0.03	0.82	0.04	1.28	0.10

	Algae		Beverage		Seafood		Meat and egg		dairy		Seasoning			
Region C	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.33	0.01	0.39	0.05	0.33	0.03	0.49	0.10	0.27	0.04	0.43	0.01	-	-
MBA	1.39	0.06	1.39	0.04	1.38	0.05	1.47	0.02	0.68	0.10	1.67	0.15	-	-
DCA	0.95	0.02	0.81	0.05	0.81	0.02	0.75	0.02	0.69	0.02	0.94	0.04	-	-
TCA	1.23	0.18	0.89	0.20	2.02	0.11	1.01	0.20	1.37	0.18	1.28	0.19	-	-
BCA	2.26	0.06	2.15	0.13	1.91	0.18	1.68	0.05	1.06	0.09	2.76	0.04	-	-
BDCA	1.04	0.08	0.35	0.05	0.59	0.11	0.13	0.23	0.85	0.04	0.44	0.05	-	-
DBA	1.33	0.10	0.99	0.13	1.18	0.22	1.28	0.03	0.76	0.05	1.39	0.12	-	-
DBCA	1.45	0.07	0.51	0.16	0.89	0.16	0.32	0.12	0.91	0.05	0.82	0.09	-	-
TBA	1.21	0.02	0.64	0.01	0.71	0.12	0.24	0.05	0.85	0.03	0.81	0.11	-	-

Table 4 HAA extraction recoveries of dietary samples of Region D

	Grain		Potato		Sweetener and snacks		Lipid		Bean		Fruit		Vegetable	
Region D	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.26	0.01	0.33	0.01	0.49	0.08	0.39	0.02	0.39	0.03	0.28	0.01	0.30	0.01
MBA	0.80	0.04	1.13	0.08	1.52	0.12	1.44	0.05	1.53	0.08	1.29	0.23	0.49	0.03
DCA	0.87	0.04	0.81	0.05	0.95	0.04	0.89	0.03	0.89	0.03	0.96	0.01	0.86	0.04
TCA	1.61	0.23	2.24	0.39	0.91	0.03	1.16	0.10	1.22	0.19	1.79	0.30	2.50	0.08
BCA	1.87	0.10	1.93	0.14	2.52	0.20	3.04	0.49	2.94	0.34	2.68	0.09	2.38	0.17
BDCA	0.45	0.02	0.40	0.03	0.58	0.09	0.79	0.18	0.74	0.23	0.40	0.02	1.09	0.04
DBA	1.16	0.08	1.18	0.04	1.38	0.05	1.61	0.11	1.68	0.22	1.46	0.05	1.17	0.02
DBCA	0.94	0.12	0.78	0.05	0.21	0.02	0.69	0.13	0.60	0.10	1.17	0.07	1.10	0.07
TBA	0.74	0.15	0.69	0.00	0.56	0.04	0.56	0.10	0.57	0.08	0.78	0.05	1.62	0.10

	Algae		Beverage		Seafood		Meat and egg		dairy		Seasoning			
Region D	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.28	0.01	0.37	0.02	0.34	0.04	0.40	0.05	0.37	0.02	0.46	0.04	-	-
MBA	1.22	0.02	1.36	0.06	1.38	0.05	1.39	0.04	1.36	0.05	1.45	0.30	-	-
DCA	0.82	0.13	0.79	0.03	0.81	0.02	0.81	0.05	0.79	0.02	0.75	0.02	-	-
TCA	1.90	0.01	0.82	0.10	1.63	0.03	0.81	0.08	0.80	0.07	1.11	0.14	-	-
BCA	2.23	0.24	2.13	0.11	2.19	0.07	2.15	0.13	2.09	0.07	2.14	0.05	-	-
BDCA	1.14	0.04	0.40	0.05	0.65	0.03	0.40	0.01	0.39	0.00	0.66	0.11	-	-
DBA	1.15	0.15	1.24	0.09	0.94	0.02	1.22	0.09	1.20	0.11	0.96	0.15	-	-
DBCA	1.12	0.04	0.69	0.04	0.97	0.06	0.74	0.08	0.73	0.08	0.45	0.04	-	-
TBA	1.56	0.18	0.64	0.01	0.80	0.03	0.64	0.01	0.65	0.02	0.79	0.16	-	-

Table 5 HAA extraction recoveries of dietary samples of Region E

	Grain		Potato		Sweetener and snacks		Lipid		Bean		Fruit		Vegetable	
Region E	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.24	0.04	0.28	0.02	0.32	0.02	0.39	0.02	0.33	0.04	0.25	0.01	0.30	0.06
MBA	1.34	0.13	1.08	0.10	1.06	0.04	1.59	0.19	1.31	0.13	0.99	0.03	0.45	0.07
DCA	0.84	0.03	0.76	0.05	0.67	0.04	0.89	0.03	0.87	0.05	0.75	0.04	0.87	0.06
TCA	0.31	0.16	0.84	0.28	0.93	0.21	1.04	0.14	0.65	0.30	0.53	0.41	2.67	0.04
BCA	1.97	0.12	1.93	0.13	1.90	0.15	2.80	0.21	2.32	0.20	2.14	0.12	2.31	0.18
BDCA	0.32	0.02	0.26	0.04	0.25	0.05	0.79	0.18	0.41	0.05	0.46	0.33	0.71	0.10
DBA	1.07	0.12	1.00	0.10	0.87	0.09	1.61	0.11	1.40	0.15	1.01	0.06	0.93	0.36
DBCA	0.61	0.15	0.41	0.06	1.36	0.11	0.69	0.13	0.40	0.05	0.26	0.25	1.01	0.44
TBA	0.57	0.06	0.41	0.05	0.38	0.02	0.49	0.22	0.61	0.04	0.53	0.02	1.20	0.13

	Algae		Beverage		Seafood		Meat and egg		dairy		Seasoning			
Region E	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.28	0.02	0.39	0.05	0.41	0.02	0.53	0.01	0.46	0.04	0.44	0.04	-	-
MBA	1.48	0.05	1.39	0.04	1.85	0.15	1.50	0.13	1.45	0.30	1.04	0.18	-	-
DCA	0.85	0.05	0.81	0.05	0.88	0.03	0.74	0.05	0.75	0.02	0.87	0.06	-	-
TCA	1.13	0.06	0.89	0.20	1.33	0.29	0.97	0.20	1.11	0.14	1.48	0.14	-	-
BCA	2.13	0.04	2.15	0.13	2.46	0.09	1.81	0.10	2.14	0.05	1.97	0.11	-	-
BDCA	0.62	0.01	0.35	0.05	0.43	0.13	0.29	0.06	0.66	0.11	0.50	0.03	-	-
DBA	1.09	0.17	0.99	0.13	1.02	0.17	0.98	0.25	0.96	0.15	1.25	0.12	-	-
DBCA	0.64	0.17	0.51	0.16	0.89	0.16	0.33	0.13	0.45	0.04	0.69	0.10	-	-
TBA	0.90	0.07	0.64	0.01	0.54	0.08	0.45	0.02	0.79	0.16	0.72	0.08	-	-

Table 6 HAA extraction recoveries of dietary samples of Region F

	Grain		Potato		Sweetener and snacks		Lipid		Bean		Fruit		Vegetable	
Region F	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.24	0.04	0.28	0.02	0.32	0.02	0.39	0.02	0.33	0.04	0.25	0.01	0.30	0.06
MBA	1.34	0.13	1.08	0.10	1.06	0.04	1.59	0.19	1.31	0.13	0.99	0.03	0.45	0.07
DCA	0.84	0.03	0.76	0.05	0.67	0.04	0.89	0.03	0.87	0.05	0.75	0.04	0.87	0.06
TCA	0.31	0.16	0.84	0.28	0.93	0.21	1.04	0.14	0.65	0.30	0.53	0.11	2.67	0.04
BCA	1.97	0.12	1.93	0.13	1.90	0.15	2.80	0.21	2.32	0.20	2.14	0.12	2.31	0.18
BDCA	0.32	0.02	0.26	0.04	0.25	0.05	0.79	0.18	0.41	0.05	0.46	0.13	0.71	0.10
DBA	1.07	0.12	1.00	0.10	0.87	0.09	1.61	0.11	1.40	0.15	1.01	0.06	0.93	0.16
DBCA	0.61	0.15	0.41	0.06	1.36	0.11	0.69	0.13	0.40	0.05	0.26	0.25	1.01	0.14
TBA	0.57	0.06	0.41	0.05	0.38	0.02	0.49	0.22	0.61	0.04	0.53	0.02	1.20	0.13

	Algae		Beverage		Seafood		Meat and egg		dairy		Seasoning			
Region F	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.28	0.02	0.39	0.05	0.41	0.02	0.53	0.01	0.46	0.04	0.44	0.04	-	-
MBA	1.48	0.05	1.39	0.04	1.85	0.15	1.50	0.13	1.45	0.30	1.04	0.18	-	-
DCA	0.85	0.05	0.81	0.05	0.88	0.03	0.74	0.05	0.75	0.02	0.87	0.06	-	-
TCA	1.13	0.06	0.89	0.20	1.33	0.29	0.97	0.20	1.11	0.14	1.48	0.14	-	-
BCA	2.13	0.04	2.15	0.13	2.46	0.09	1.81	0.10	2.14	0.05	1.97	0.11	-	-
BDCA	0.62	0.01	0.35	0.05	0.43	0.13	0.29	0.06	0.66	0.11	0.50	0.03	-	-
DBA	1.09	0.17	0.99	0.13	1.02	0.17	0.98	0.25	0.96	0.15	1.25	0.12	-	-
DBCA	0.64	0.17	0.51	0.16	0.89	0.16	0.33	0.13	0.45	0.04	0.69	0.10	-	-
TBA	0.90	0.07	0.64	0.01	0.54	0.08	0.45	0.02	0.79	0.16	0.72	0.08	-	-

Table 7 HAA extraction recoveries of dietary samples without water preparation of Region G

	Nut		Fruit		Seafood		Meat	
Region G (dietaries without preparation)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.71	0.09	0.68	0.04	0.70	0.27	0.80	0.04
MBA	1.40	0.02	0.75	0.03	0.47	0.10	0.28	0.01
DCA	0.58	0.07	0.81	0.04	1.17	0.06	0.93	0.03
TCA	1.76	0.03	0.86	0.02	1.89	0.06	0.89	0.14
BCA	2.40	0.06	1.48	0.06	1.90	0.11	1.33	0.03
BDCA	0.89	0.14	0.75	0.21	0.99	0.04	0.73	0.08
DBA	0.53	0.22	0.28	0.17	0.71	0.18	1.54	0.16
DBCA	1.08	0.15	1.00	0.02	1.53	0.11	1.57	0.03
TBA	1.13	0.14	1.01	0.04	1.59	0.19	1.01	0.18

	Egg		dairy		Lipid		Snack	
Region G (dietaries without preparation)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.62	0.08	0.37	0.02	0.48	0.09	0.81	0.07
MBA	0.24	0.01	1.36	0.05	0.30	0.04	0.38	0.04
DCA	0.65	0.07	0.79	0.02	0.37	0.04	0.65	0.01
TCA	0.82	0.02	0.80	0.07	0.26	0.05	0.73	0.01
BCA	1.39	0.02	2.09	0.07	0.26	0.08	1.30	0.08
BDCA	0.49	0.10	0.39	0.00	0.28	0.11	0.68	0.15
DBA	1.44	0.06	1.20	0.11	1.13	0.12	1.07	0.18
DBCA	0.59	0.04	0.73	0.08	0.41	0.07	0.83	0.15
TBA	0.56	0.08	0.65	0.02	0.18	0.09	0.71	0.11

Table 8 HAA extraction recoveries of dietary samples prepared with tap water of Region G

	Grain		Potato		Sweetener		Bean		Vegetable	
Region G (dietaries prepared with tap water)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.78	0.09	0.77	0.07	0.57	0.08	0.65	0.06	0.70	0.09
MBA	0.25	0.01	0.25	0.01	0.32	0.01	0.56	0.04	0.35	0.01
DCA	0.89	0.03	0.73	0.00	0.92	0.04	0.76	0.02	0.83	0.02
TCA	1.19	0.03	0.99	0.12	0.91	0.04	0.91	0.04	1.13	0.04
BCA	1.35	0.06	1.68	0.04	1.15	0.00	0.98	0.06	1.41	0.10
BDCA	0.73	0.01	0.74	0.04	0.87	0.03	0.91	0.22	0.67	0.01
DBA	1.29	0.02	1.48	0.09	1.39	0.04	1.69	0.19	1.48	0.07
DBCA	0.89	0.14	0.76	0.09	1.15	0.11	0.78	0.04	0.82	0.08
TBA	0.97	0.11	0.93	0.06	0.92	0.11	0.74	0.04	0.98	0.10

	Mushroom		Algae		Beverage		Seasoning			
Region G (dietaries prepared with tap water)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.40	0.00	0.53	0.13	0.61	0.06	0.80	0.14	-	-
MBA	0.48	0.03	0.59	0.20	0.90	0.03	0.24	0.01	-	-
DCA	0.80	0.05	0.78	0.07	0.63	0.03	0.80	0.07	-	-
TCA	1.86	0.06	1.17	0.03	0.86	0.03	1.03	0.04	-	-
BCA	1.75	0.09	1.91	0.09	1.13	0.17	1.63	0.09	-	-
BDCA	1.22	0.14	1.52	0.01	0.71	0.09	1.07	0.15	-	-
DBA	0.36	0.14	2.00	0.15	1.17	0.12	1.73	0.09	-	-
DBCA	1.35	0.09	1.04	0.02	0.97	0.05	1.22	0.15	-	-
TBA	1.07	0.19	0.90	0.03	1.06	0.02	1.15	0.03	-	-

Table 9 HAA extraction recoveries of dietary samples prepared with reagent water of Region G

	Grain		Potato		Sweetener		Bean		Vegetable	
Region G (dietaries prepared with reagent water)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)
MCA	0.80	0.09	0.78	0.10	0.70	0.06	0.74	0.08	0.84	0.10
MBA	0.17	0.09	0.25	0.05	0.27	0.02	0.65	0.01	0.39	0.01
DCA	1.04	0.01	0.79	0.10	0.78	0.03	0.61	0.04	0.86	0.02
TCA	1.54	0.04	0.88	0.05	0.77	0.01	0.60	0.07	1.15	0.01
BCA	1.75	0.20	1.33	0.04	1.29	0.12	0.90	0.07	1.54	0.07
BDCA	0.75	0.12	0.60	0.07	0.74	0.04	0.66	0.11	0.77	0.11
DBA	1.44	0.02	1.27	0.06	0.98	0.13	1.11	0.16	1.17	0.17
DBCA	0.93	0.07	0.73	0.10	1.14	0.10	1.00	0.06	0.89	0.03
TBA	0.92	0.03	0.83	0.05	0.97	0.09	0.73	0.07	0.90	0.09

	Mushroom		Algae		Beverage		Seasoning			
Region G (dietaries prepared with reagent water)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	Average extraction recovery (n=3)	Relative standard deviation (n=3)	-	-
MCA	0.37	0.16	0.59	0.09	0.67	0.10	0.84	0.13	-	-
MBA	0.37	0.03	0.69	0.07	0.94	0.01	0.23	0.03	-	-
DCA	0.92	0.11	0.81	0.07	0.63	0.06	0.77	0.02	-	-
TCA	1.43	0.08	1.44	0.13	0.77	0.02	0.78	0.01	-	-
BCA	1.70	0.03	1.67	0.06	0.96	0.02	1.01	0.12	-	-
BDCA	1.04	0.30	1.22	0.24	0.65	0.13	0.90	0.13	-	-
DBA	0.38	0.11	2.09	0.10	1.16	0.10	1.29	0.27	-	-
DBCA	1.69	0.03	0.83	0.03	1.06	0.06	0.84	0.04	-	-
TBA	1.09	0.08	1.35	0.06	1.02	0.27	0.73	0.04	-	-