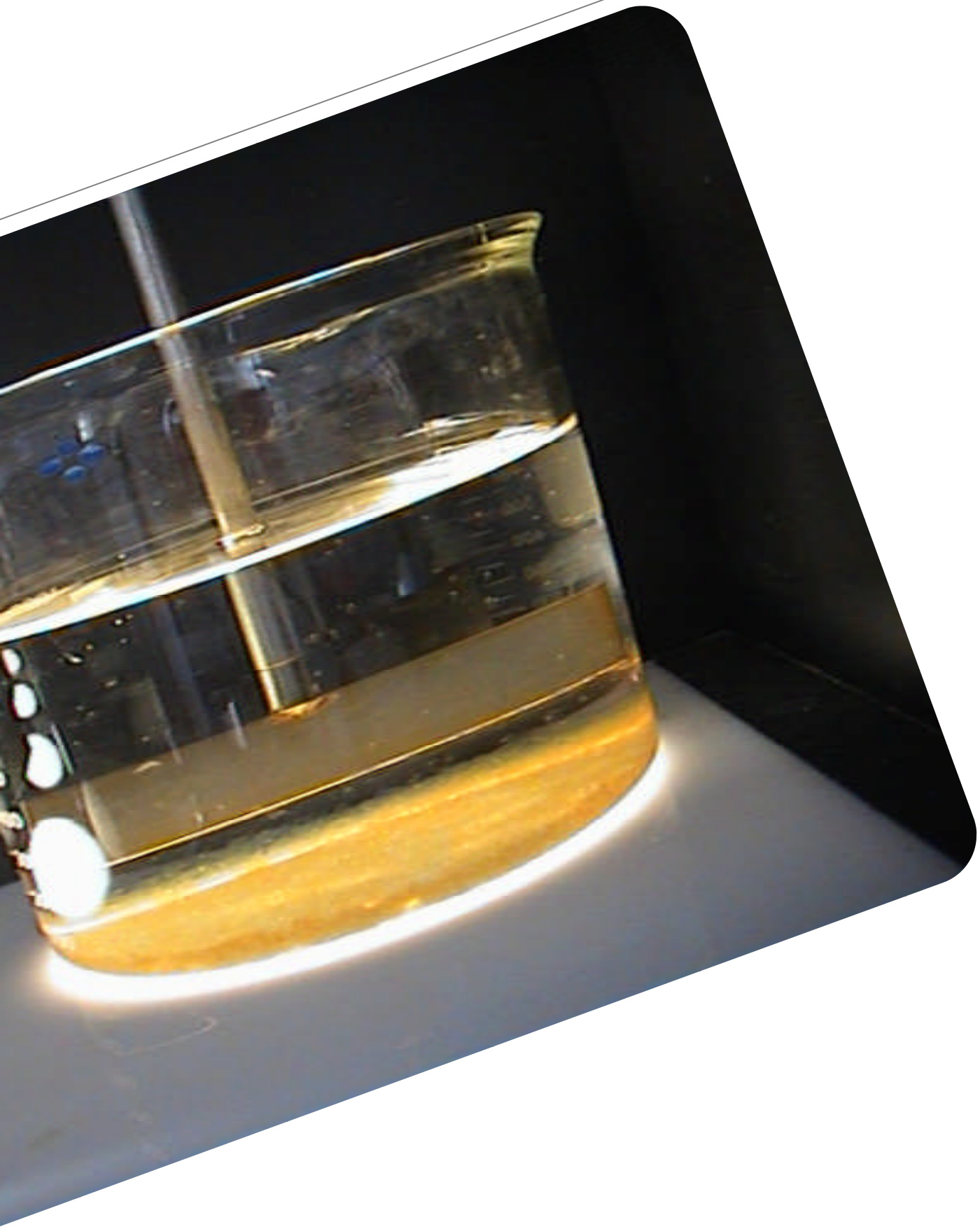
Final Report

Study into the formation of disinfection by-products of chloramination, potential health implications and techniques for minimisation



Cranfield UNIVERSITY

STUDY INTO THE FORMATION OF DISINFECTION BY-PRODUCTS OF CHLORAMINATION, POTENTIAL HEALTH IMPLICATIONS AND TECHNIQUES FOR MINIMISATION

FINAL REPORT

STUDY INTO THE FORMATION OF DISINFECTION BY-PRODUCTS OF CHLORAMINATION, POTENTIAL HEALTH IMPLICATIONS AND TECHNIQUES FOR MINIMISATION

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DISCLAIMER

FINAL REPORT

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EXECUTIVE SUMMARY

BACKGROUND

Drinking water disinfection by-products (DBPs) are formed when a disinfectant reacts with natural organic matter and/or bromide/iodide present in a raw water source. In the UK only one group of DBPs are regulated, the trihalomethanes (THMs). A maximum concentration value of 100 μg L^{-1} at a consumers tap has been set for the sum of the concentrations of the four THMs. In order to comply with the THM target an increasing number of water utilities are switching from chlorine to chloramine disinfection. Whilst chloramination is a well understood and widely applied disinfection processes and there is considerable literature that shows' switching from chlorine to chloramine is an effective process for controlling the formation of THMs there are concerns over the formation of different groups of disinfection by-products including haloacetic acids, haloacetronitriles, halonitromethanes, cyanogen halides and nitrosamines.

RESEARCH OBJECTIVES

The aim of this research project was to investigate the formation of disinfection by-products during chloramination and to review potential health implications and techniques for minimising generation of these by-products

The research objectives for this project are to provide:

a) Evaluate and summarise the extent of previous work undertaken in the UK and abroad to quantify the extent of disinfection by-product formation due to chloramination and identify the compounds formed;

b) Through sampling and analysis of a range of Scottish drinking water supplies identify the compounds formed as by-products of the chloramination process;

c) Using published toxicological and odour threshold data and by consulting health professionals, assess the health and aesthetic implications of the main by-products identified;

d) Suggest methods of formation and practical ways in which by-product formation (of regulated and emerging unregulated species) could be minimised and balanced through the treatment process and beyond.

APPROACH

To meet the project objectives, the approach taken in this 12 month long project was to combine both practical and literature investigations, firstly to provide real data on the levels of disinfection by-products measures in chlorinated and chloraminated water samples but to allow a link between exposure and risks.

SAMPLING SURVEY

Seven water treatment works (works) were selected for the occurrence survey to allow comparison of (i) different water sources, (ii) different treatment processes and (iii) different disinfection practices. Sampling surveys were carried out in January (winter), May (spring) and August (summer) of 2008. An initial literature review identified the DBPs most likely to be found in chloraminated waters were trihalomethanes (THMs), haloacetic acids (HAAs), haloacetonitriles (HANs), halonitromethanes (HNMs), cyanogen halides, nitrosamines and also the two main iodinated THMs, dichloroiodomethane and bromochloroiodomethane.

THM4 levels identified during the survey ranged from a low of 12 μg L^{-1} to a maximum of 418 μg L^{-1} and a number of works had levels of THM4 consistently higher than the 100 μg L^{-1} MCL. The use of chloramines at four of the surveyed works led to significantly lower levels of THM4 and these typically did not increase as they went into distribution. Levels of iodinated THMs increased in line with increasing iodine levels which increased from a median of 2 μg L^{-1} in winter and spring to 6 μg L^{-1} in summer. No difference was observed between chlorinated and chloraminated works.

As with the THMs there was considerable variation between the individual waters with HAA levels ranging from 11 μg L^{-1} to 134 μg L^{-1}. The impact of chloramination was to reduce the overall levels but to also change speciation towards dihalogenated HAAs. The effect of using chloramines as a disinfectant was less pronounced for HANs and CP where the median concentration of HAN4 changed from 1.7 μg L^{-1} for chlorinated water to 1.3 μg L^{-1} when using chloramines.

Samples were analysed for nitrosamines during the spring and summer surveys and NDMA was only found at one works in spring which uses chloramine as the disinfectant. The sample contained 8.6 ng L^{-1} NDMA whilst the corresponding distribution samples contained 13.5 and 26.0 ng L^{-1} NDMA. These levels were significantly higher than those reported during a recent UK wide survey.

FORMATION POTENTIAL

Formation potential (FP) tests were conducted with chlorine and monochloramine to allow us to investigate the levels of DBP precursors in the raw water as well as the effectiveness comparison between the formation of DBPs with chlorine and chloramine disinfectants. As expected the formation of THMs and HAAs was significantly reduced in the presence of chloramines when compared to formation in the presence of chlorine. For example the precursors in the raw water at works 1

were consistently more reactive with chlorine (66.6 μg THM mg C^{-1}) than with chloramines (14.2 μg THM mg C^{-1}). The same trend was also true for HAA where works 1 had the highest formation potential (25.5 and 2.0 μg HAA mg C^{-1}) with chlorine and chloramines, respectively.

The precursors for HAN_4 and CP were a lot less impacted by disinfectant choice and more by season. Tests were also conducted to determine the potential of the waters to form cyanogen chloride (CNCl) and cyanogen bromide (CNBr) and neither CNCl nor CNBr was positively identified in any of the samples with the sensitivity of the method used.

No strong correlations were found between water quality parameters and formation potential of any of the DBPs measured and further investigations are suggested into NPOC removal at a number of the works.

ASSESSMENT OF RISKS

In this phase of the study, IEH scientists considered the hazard profiles – including consideration of the basis for any acceptable daily intake (ADI), tolerable daily intake (TDI) or reference dose (RefD) established by any authoritative bodies – for each of the DBP categories or, where appropriate, individual compounds, using information obtained from a structured search of published and, where possible, 'grey' literature. The maximum measured concentration and the median measured concentration for each group of considered DBPs were used to calculate the total predicted daily (drinking water) intake values for an average consumer (adults and toddlers). These were then compared with the relevant authoritative standard or a derived SSPADI.

A number of compounds and groups were found to have predicted daily intakes in excess of 10% of the relevant standard. For adults, exceedence of 10% of TDI or SPPADI was noted for TCM (44.0%), BDCM (14.7%), THM4 (198.9%), DCAA (12.0%) and HAA9 (87.4%) when the highest measured values of chloraminated samples were used in the calculation. In the case of toddlers, six compounds or groups were found to exceed 10% of standard value when the highest measured values of chloraminated samples were considered, as follows: TCM (93.5%), BDCM (31.3%), THM4 (198.7%), MCAA (14.1%), DCAA (25.5%), and HAA9 (87.5%). In general, the concentrations of halogenated DBPs in chloraminated samples were at lower levels than chlorinated samples which suggests that chloramination of water samples generally reduces exposure to these DBPs when compared to chlorination of water samples.

CONCLUSIONS

The research undertaken during this project has identified that:

- A literature review identified that the DBPs most likely to be found in chloraminated waters are from the group THMs, HAAs, HANs, HNMs, cyanogen halides and nitrosamines. 27 compounds were selected from these groups and were analysed for in three seasonal occurrence surveys of 7 water treatment works.

- In general, the concentrations of halogenated DBPs in chloraminated samples were at lower levels than chlorinated samples. This is especially true for THMs and HAAs. Therefore, this suggests that chloramination of water samples generally reduces exposure to these DBPs when compared to chlorination of water samples.

- NDMA was identified at significant levels (26.0 ng L^{-1}) in chloraminated water but only at one works for one season and hence the significance of this is not clear without further sampling. More information on the occurrence of this DBP of health concern is needed. However, any risk assessment of the occurrence of NDMA must also consider the significant reduction in halogenated DBP formation that accompanies chloramination.

- Consideration of risk management must be undertaken for the DBPs that exceed 100% of standards and this was true for THM4 in both chlorinated and chloraminated samples. Although work is underway in Scotland to reduce THM formation, for a number of the works there is a need to increase precursor removal as chloramination alone is not enough to minimise the risks.

Acronyms and abbreviations

ADI	Acceptable daily intake
APHA	American Public Health Association
BCAA	Bromochloroacetic acid
BCAN	Bromochloroacetonitrile
BCIM	Bromochloroiodomethane
BDCAA	Bromodichloroacetic acid
BDCM	Bromodichloromethane
Cl_2	Chlorine
CP	Chloropicrin (trihalonitromethane)
CNBr	Cyanogen bromide
CNCl	Cyanogen chloride
CNX	Cyanogen halide
DBPs	Disinfection by-products
DBAA	Dibromoacetic acid
DBAN	Dibromoacetonitrile
DBCAA	Dibromochloroacetic acid
DBCM	Dibromochloromethane
DCAA	Dichloroacetic acid
DCAN	Dichloroacetonitrile
DCIM	Dichloroiodomethane
DMC	Dimethyl cyanamide
DOC	Dissolved organic carbon
DWI	Drinking Water Inspectorate
DXAA	Dihalogenated acetic acids
ECD	Electron Capture Device
FP	Formation potential
GC	Gas chromatography
HAAs	Haloacetic acids
HAN	Haloacetonitrile
HNM	Halonitromethane
HOCl	Hypochlorous acid
HOBr	Hypobromous acid
HOI	Hypoiodous acid
HPLC	High performance liquid chromatography
HPSEC	High performance size exclusion chromatography
ICP-MS	Inductively coupled plasma mass spectrometry
IEH	Institute of Environmental Health, Cranfield University
IGHRC	Interdepartmental Group on Health Risks from Chemicals
I-THMs	Iodinated trihalomethanes
LOAEL	Low-adverse-effect level
MCAA	Monochloroacetic acid
MBAA	Monobromoacetic acid
MCL	Maximum contaminant level
MS	Mass spectrometry

N	Nitrogen
NDBA	N nitrosodibutylamine
N-DBPs	Nitrogenous disinfection by-products
NDEA	N nitrosodiethylamine
NDMA	N-nitrosodimethylamine
NDPA	N nitrosodipropylamine
NH_2Cl	Monochloramine
$NHCl_2$	Dichloramine
$NHCl_3$	Trichloramine
NMEA	N-nitroso-methylethylamine
NMOR	N nitrosomorpholine
NOAEL	No-adverse-effect level
NOM	Natural organic matter
NPIP	N nitrosopiperidine
NPOC	Non purgable organic carbon
NPYR	N nitrosopyrrolidine
OFWAT	Office of water services
RefD	Reference dose
SEC	Size exclusion chromatography
SSPADI	Study-specific provisional acceptable daily intake
SUVA	Specific ultraviolet absorbance
TDI	Tolerable daily intake
TBAA	Tribromoacetic acid
TBNM	Tribromonitromethane
TBAN	Tribromoacetonitrile
TBM	Tribromomethane (bromoform)
TCAA	Trichloroacetic acid
TCAN	Trichloroacetonitrile
TCM	Trichloromethane (chloroform)
TCNM	Trichloronitromethane (chloropicrin)
THMs	Trihalomethanes
THM-FP	Trihalomethane formation potential
TOC	Total organic carbon
TXAA	Trihalogenated acetic acids
UCMR2	Unregulated Contaminant Monitoring Regulation 2
USEPA	United States Environmental Protection Agency
UV	Ultraviolet
UV_{254}	Ultraviolet absorbance at 254 nm
WHO	World Health Organisation

1 INTRODUCTION

1.1 Objectives

The aim of this research project was to investigate the formation of disinfection by-products during chloramination and to review potential health implications and techniques for minimising generation of these by-products

The research objectives for this project are to provide:

a) Evaluate and summarise the extent of previous work undertaken in the UK and abroad to quantify the extent of disinfection by-product formation due to chloramination and identify the compounds formed;

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1.2 Background

Drinking water disinfection by-products (DBPs) are formed when a disinfectant reacts with natural organic matter and/or bromide/iodide present in a raw water source. In the UK only one group of DBPs are regulated, the trihalomethanes (THMs). A maximum concentration value of 100 μg L^{-1} at a consumers tap has been set for the sum of the concentrations of the four THMs (trichloromethane (also known as chloroform), dichlorobromomethane, dibromochloromethane and tribromomethane). Details of other guideline or regulations are shown in Table 1.1 below.

In order to comply with the THM target an increasing number of water utilities are switching from chlorine to a chloramine disinfectant to replace free chlorine as a residual disinfectant in distribution. Chloramination is a well understood and widely applied disinfection processes. It can be summarised by the reaction between ammonia and hypochlorous acid (HOCl) to form chloramines. Depending on the ratio of chlorine to ammonia and pH, you can favour the formation of different chloramine species. Chloramine chemistry is well understood and widely practised

and recent research has investigated the role natural organic matter plays in its decomposition as well as the formation of halogenated by-products. When we talk of chloramination as a disinfectant we primarily mean monochloramine (NH_2Cl) but there is also the potential to form dichloramine ($NHCl_2$) and trichloramine (NCl_3) according to the reactions shown below:

$$NH_3 + HOCl \leftrightarrow NH_2Cl + H_2O \quad (1)$$

$$NH_2Cl + HOCl \leftrightarrow NHCl_2 + H_2O \quad (2)$$

$$NHCl_2 + HOCl \leftrightarrow NCl_3 + H_2O \quad (3)$$

Using chloramination in practice though does not always involve adding monochloramine as a chemical but often involves adding ammonia salts to a water containing chlorine. The period when there is free chlorination is key to achieve disinfection and the time before ammonia salts addition can be significant (hours). There is clearly the opportunity during this period of contact with free chlorine to form significant levels of DBPs and a good example was shown by Pope et al. (2006) who showed a significant increase in THMs from 20 $\mu g\ L^{-1}$ to 45 $\mu g\ L^{-1}$ as a result of increasing the chlorination contact time from 5 to 20 minutes.

Table 1-1. International guidelines or regulations for disinfection by-products (adapted from WHO, 2006)

	EU Directive (2004)	WHO (2004)	USEPA Stage 2 DBP Rule (2003)	
			MCL	MCLG
Bromate	10	10	10	0
Bromodichloromethane		60		0
Bromoform		100		0
Chloral hydrate		10		
Chlorate		700		
Chlorite		700	1000	800
Chloroform		300		70
Cyanogen chloride		70		
Dibromoacetonitrile		70		
Dibromodichloromethane		100		60
Dichloroacetic acid		50		0
Dichloromoacetonitrile		20		
Monochloroacetic acid		20		70
NDMA		(0.1)*		
Trichloroacetic acid		200		20
Total THM[a]	100		80	
HAA_5[a]			60	

MCL – Maximum concentration level; MCLG Maximum concentration level goal.
*Guideline from rolling revision of WHO guidelines
[a]these regulations refer to average values

THMs are often the major DBPs we find in chlorinated water but well over 500 other DBPs have been reported in the literature (Richardson, 1998). The second most abundant group of DBPs found in chloraminated supplies are the haloacetic acids (HAAs). There are nine HAAs in total (classified as mono- (monochloroacetic acid (MCAA) and monobromoacetic acid (MBAA)), di- (dichloroacetic acid (DCAA), dibromoacetic acid (DBAA) and bromochloroacetic acid (BCAA)) and tri- (trichloroacetic acid (TCAA), tribromoacetic acid (TBAA), dibromochloroacetic acid (DBCAA) and bromodichloroacetic acid (BDCAA)) and whilst there is no current UK regulatory limit for haloacetic acids, the US Environmental Protection Agency (USEPA) have set a MCL of 60 μg L^{-1} for HAA_5 (mono-, di-, trichloroacetic acid, mono-, dibromoacetic acid) and the WHO have suggested that guideline values for MCAA, DCAA and TCAA are provisionally established as 20 μg L^{-1}, 50 μg L^{-1} and 200 μg L^{-1} respectively.

It has been reported that switching from chlorine to monochloramine can increase the concentration of certain nitrogenous disinfection by-products (N-DBPs) such as dihalogenated haloacetronitriles (HAN) and halonitromethanes (HNM). These two groups of by-products have been shown to be considerably more cytotoxic and genotoxic than THMs and HAAs (Plewa et al., 2004; Muellner et al., 2007). There are no UK regulatory guidelines for these by-products, but the WHO have suggested guideline values of 20 μg L^{-1} for dichloracetonitrile (DCAN) and 70 μg L^{-1} for dibromoacetronitrile (DBAN) based on limited toxicological studies. One other group of N-DBPs that has been identified in chloraminated waters are the nitrosamines and, in particular, N-nitrosodimethylamine (NDMA) (Mitch et al., 2003; Valentine et al., 2005). NDMA has been classified as a probable human carcinogen and WHO have set a guideline value at 100 ng L^{-1}. The California Department of Health Services has notification levels (at 10 ng L^{-1} each) for the following nitrosamines: NDMA, N-nitrosodiethylamine (NDEA), and N-nitrosodi-n-propylamine (NDPA). Moreover, the USEPA will be requiring large drinking water utilities in the United States to monitor for six nitrosamines as part of the unregulated contaminant monitoring regulation 2 (UCMR2): NDEA, NDMA, N-nitroso-di-n-butylamine (NDBA), NDPA, N-nitroso-methylethylamine (NMEA), and N-nitroso-pyrrolidine (NPYR). The UCMR2 will provide occurrence data for possible future regulations on nitrosamines in the United States.

2 METHODOLOGY

2.1 Selection of DBPs for survey

Using an initial literature review it is clear that the DBPs most likely to be found in chloraminated waters are THMs, HAAs, HANs, HNMs, cyanogen halides and nitrosamines (Table 2.1). Alongside the main 4 THMs we have also analysed for the two main iodinated THMs, dichloroiodomethane and bromochloroiodomethane. There is no published data available in the UK for levels of HANs and HNMs although a number of studies have been published in the USA. Typically, HANs and HNMs are detected at low μg L^{-1} levels (Krasner et al., 2006). NDMA has been detected in chloraminated waters in the United States and Canada, with concentrations usually below 20 ng L^{-1} levels (Valentine et al., 2005) and recently at concentrations of up to 5.8 ng L^{-1} in UK potable waters (DWI, 2008). The only other significant DBPs identified during chloramination are cyanogen chloride and bromide, but issues regarding the availability of standards means whilst we have attempted to identify their presence we have been unable to quantify the concentrations found. The full list of DBPs selected for this occurrence survey is given below (Table 2.2).

Table 2-1. Summary of DBP levels found in recent major surveys and chloramination studies.

				Reported concentrations (μg L^{-1})			
Group	Acronym	DBP	Acronym	USEPA (2006)	Canada (1995)	Other	References
Trihalomethanes	THM	Trichloromethane (chloroform)	TCM	-		-	-
		Bromodichloromethane	BDCM	-		-	-
		Dibromochloromethane	DBCM	-		-	-
		Tribromomethane (bromoform)	TBM	-		-	-
		Dichloroiodomethane	DCIM	11		-	-
		Bromochloroiodomethane	BCIM	3		-	-
		Dibromoiodomethane	DBIM	4		-	-
		Chlorodiiodomethane	CDIM	2		-	-
		Bromodiiodomethane	BDIM	0.7		-	-
		Triiodomethane (iodoform)	TIM	2		1	Hanson et al., 1974
Haloacetic acids	HAA	Monochloroacetic acid	MCAA	7.5			
		Monobromoacetic acid	MBAA	1.6		0.1	Lyskins et al., 1994
		Dichloroacetic acid	DCAA	27	24	9.2	
		Trichloroacetic acid	TCAA	18	72	1.7	
		Bromochloroacetic acid	BCAA	18		1.9	
		Dibromoacetic acid	DBAA	43		0.1	
		Bromodichloroacetic acid	BDCAA	15			
		Dibromochloroacetic acid	DBCAA	15			
		Tribromoacetic acid	TBAA	3.6			
		Iodoacetic acid					
		Bromoiodoacetic acid, 3-bromo-3-iodopropenoic acid					
		2-iodo-3-methylbutenedioic acid					
Haloacetonitriles	HAN	Trichloroacetonitrile	TCAN				
		Dichloroacetonitrile	DCAN		10.7		
		Bromochloroacetonitrile	BCAN				
		Dibromoacetonitrile	DBAN				
Halonitromethane	HNM	Chloronitromethane (chloropicrin)		0.8	0.9	1 0.1	Simpson and Hayes, 1998

		Bromonitromethane Dichloronitromethane Bromochloronitromethane Dibromonitromethane Bromodichloronitromethane Dibromochlororonitromethane Trichloronitromethane Tribromonitromethane		0.3 <1 <3 0.6 3 3 9.1 5			Lyskins et al., 1994
Haloketones	HK	Chloropropanone 1,1-Dichloropropanone 1,3-Dichloropropanone 1,1-Dibromopropanone 1,1,1-Trichloropropanone 1,1,3-Trichloropropanone 1-Bromo-1,1-dichloropropanone 1,1,1-Tribromopropanone 1,1,3-Tribromopropanone 1,1,3,3-Tetrachloropropanone 1,1,1,3-Tetrachloropropanone 1,1,3,3-Tetrabromopropanone		2 2 ND 0.4 7 0.3 <3 ND 0.1 0.6 <1 0.6-2	2.1 5.3		
Cyanogen halide	CNX	Cyanogen chloride Cyanogen bromide CNX	CNCl CNBr		5.0 2.8	25 8 2 10-17	Zheng et al., 2004 Simpson and Hayes, 1998. Heller-Grossman et al., 1999 Diehl et al., 2000
Chloral hydrate					13.6	0.1	Lyskins et al., 1994
Haloaldehyde		Monochloroacetaldehyde Dichloroacetaldehyde Bromochloroacetaldehyde Trichloroacetaldehyde Tribromoacetaldehyde		2.4 14 4 16 3			
Nitrosamines		N-nitrosodimethylamine N-nitroso-methylethylamine	NDMA NMEA				

		N nitrosodiethylamine N nitrosomorpholine N nitrosopyrrolidine N nitrosodipropylamine N nitrosopiperidine N nitrosodibutylamine	NDEA NMOR NPYR NDPA NPIP NDBA				
Haloacetamides		Chloroacetamide Bromoacetamide Dicloroacetamide Dibromoacetamide Trichloroacetamide		0.5 1.1 5.6 2.8 1.1			
Dimethylcyanamide	DMC						
Halogenated Furanones		3-chloro-4-(dichloromethyl)-5-hydroxy-2-(5H)-furanone E-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid	MX EX			0.043 0.059	Backlund et al., 1988 Backlund et al., 1988

Table 2-2 DBPs selected for occurrence survey

Halomethanes		
Trichloromethane	Bromodichloromethane	Dibromochloromethane
Tribromomethane	Dichloroiodomethane	Bromochloroiodomethane
Haloacetic acids		
Monochloroacetic acid	Monobromoacetic acid	Dichloroacetic acid
Trichloroacetic acid	Bromochloroacetic acid	Dibromoacetic acid
Bromodichloroacetic acid	Dibromochloroacetic acid	Tribromoacetic acid
Haloacetonitriles		
Trichloroacetonitrile	Dichloroacetonitrile	Bromochloroacetonitrile
Dibromoacetonitrile		
Halonitromethanes		
Chloropicrin		
Cyanogen halides		
Cyanogen chloride	Cyanogen bromide	
	Nitrosamines	
N-Nitrosodimethylamine	N-Nitrosomethylethylamine	N-Nitrosodi-n-propylamine
N-Nitrosopyrollidine	N-Nitrosopiperidine	

2.2 Methods

2.2.1 Water Characterisation

Non purgeable organic carbon (NPOC) was measured using a TOC 5000 Analyser (Shimadzu, Milton Keynes, UK). pH was measured using a Jenway 3520 pH meter (Patterson Scientific UK, Luton, UK). Iodide and Bromide were measured using inductively coupled plasma mass spectrometry (ICP-MS). Conductivity was measured using a Jenway 4010 Conductivity Meter (Patterson Scientific, UK) which compensates for temperature. High performance size exclusion chromatography (HPSEC) with detection at 254 nm (ultraviolet range). HPSEC was carried out using an HPLC (Shimadzu VP Series, Shimadzu, Milton Keynes, UK) with UV detection set to 254 nm. The mobile phase was 0.01 M sodium acetate at a flow rate of 1 ml min^{-1}. The column was a BIOSEP-SEC-S3000 7.8 mm (ID) $\times$ 30 cm and the guard column is a 'Security Guard' fitted with a GFC-3000 disc 4.0 mm (ID) $\times$ 3.0 mm (Phenomenex UK, Cheshire, UK). For each sample a chromatogram of ultraviolet (UV) absorbance (absorbance units) against time (minutes) was produced.

2.2.2 Chlorine Demand and Formation Potential Tests

Chlorine demand was measured by determination of the chlorine residual after exposure to a range of chlorine doses. Measurement of the chlorine residual was carried out using an adaptation of procedure 4500-Cl in '*Standard Methods for the Examination of Water and Wastewater*' (APHA 1992). By product formation potential tests were carried out to determine the potential to form disinfection by-products on exposure to chlorine and chloramines. Tests were carried out over 7 days at pH 7 and at 20 °C (adapted from procedure 5710 in '*Standard Methods for the Examination of Water and Wastewater*' (APHA 1992).

Chlorine formation potential test – samples were chlorinated according to the chlorine demand in order that the residual was ~1 mg L^{-1} as Cl_2 after 7 days contact.
Chloramine formation potential test – samples were chloraminated directly using preformed monochloramines. The dosing level for chloramine was the same as that used in the chlorine formation potential tests.

2.2.3 Disinfection By-Product Analysis

Disinfection by-products were measured after completion of the formation potential tests. Haloacetic acids (HAA) were extracted using an adapted form of USEPA Method 552.3. The extracted methyl esters were measured using gas chromatography (GC) with electron capture device (ECD) detection for quantification. Trihalomethanes (THMs), haloacetonitriles (HANs) and halonitromethanes (HNMs) were extracted using an adapted form of USEPA Method 551.1. The extracts were quantified using GC-ECD. The presence or absence of cyanogen chloride and cyanogen bromide was determined using GC with a Mass Spectrometer (MS) detector. The method of extraction was adapted from Sclimenti et al. (1996). Nitrosamine analysis was carried out by Scottish Water Scientific Services (Edinburgh, UK) using USEPA method 521 which involved solid-phase extraction after which the sample was eluted with dichloromethane. The extract was analysed by GC-MS (in electron impact [EI]+ mode).

3 SAMPLING SURVEY

3.1 Selection of treatment works

Seven water treatment works (works) were selected for the occurrence survey (Table 3.1). The works were selected after discussion with both Scottish Water and the Scottish Government to allow comparison of (i) different water sources, (ii) different treatment processes and (iii) different disinfection practices. Sampling surveys were carried out in January (winter), May (spring) and August (summer) of 2008. One pair of works (3 and 4) offered a direct comparison of the same treatment and source water type but with different disinfection practices. The treatment processes at each works are listed below and these cover a wide range of treatment options including coagulation, lime softening, rapid gravity and pressure filtration, ozonation, chlorination and chloramination. For the sites that use chloramination this was carried out at a Cl_2:N weight ratio of 3:1 to 4:1 and typically involved a period of chlorination (~ 30 minutes) before ammonium salt addition.

Table 3-1. Summary of treatment and disinfection at surveyed works.

Works ID	Source	Treatment	Disinfectant
1	Upland Reservoir	Sand filtration, activated carbon	Chlorine
2	Reservoir	Coagulation, lime softening, pressure filtration	Chloramines
3	River	Coagulation, lime softening, sedimentation, rapid gravity filtration	Chloramines
4	River	Coagulation, lime softening, rapid gravity filtration	Chlorine
5	River	Coagulation, lime softening, rapid gravity filtration	Chloramines
6	Reservoir	Ozonation, rapid gravity filtration	Chloramines
7	Upland Reservoir	Coagulation, lime softening, rapid gravity filtration	Chlorine

Two types of samples were collected from each of the works:

1. Final and distribution samples – the final samples were collected at the works exit and distribution samples were collected from service reservoirs or from designated sampling points.

2. In-works samples – samples of the water entering the works (raw water) and samples of the treated water were collected. These samples had not come into contact with chlorine or chloramines. The in-works samples were subjected to DBP formation potential (FP) tests in the laboratory.

3.1.1 Final and distribution samples overview

An overview of the collected data in terms of the levels of the DBPs found as well as their precursors is presented below (Table 3.2). On a median basis, the raw-water levels of NPOC were 3.6 mg L^{-1} and bromide was 55 μg L^{-1} for the surveyed works, which were lower than for the works selected for the most recent USEPA survey (Krasner et al., 2006). For comparison a US nationwide survey of bromide concentrations showed concentrations ranging from <5 to 429 μg L^{-1} with the mean level being 62 μg L^{-1} (Amy et al., 1995) Here we have measured iodine levels and this will be made up primarily of iodide. A survey of freshwater iodide levels in the US and Europe showed concentrations ranging from 0.5 to 212 μg L^{-1}, with a median level of 10.2 μg L^{-1}. Iodide levels were on average 5% of the bromide levels although this changed seasonally. The median raw water specific UV absorbance (SUVA) was 2.1 m^{-1} L mg^{-1} C which corresponds to a source water of low humic content, whereas the 75th percentile and maximum values corresponded to intermediate and high humic levels (Edzwald and Tobiason, 1999). When comparing the median levels of the DBPs measured during this survey against those for the USEPA survey the THM4 was significantly different. The highest recorded level of THM4 was 419 μg L^{-1}, whereas the highest level in the US survey was 164 μg L^{-1}. The median and maximum sum of two I-THMs was 0.9 and 3.7 μg L^{-1}, respectively, whereas in the US survey the sum of six species was 0.4 and 19 μg L^{-1}, respectively.

Table 3-2. Concentration of selected DBPs and their precursors

Parameter	Unit	Minimum	Median	75th percentile	Maximum	USEPA (2006) Median
NPOC	mg L^{-1}	1.5	3.6	4.5	26.2	5.8
SUVA	m^{-1} .L mg^{-1} C	0.7	2.1	3.4	5.2	2.9
Bromide	µg L^{-1}	17.0	55.1	110	259	120
Iodine	µg L^{-1}	nd	3.0	5.2	12.1	nm
THM4	μg L^{-1}	12	74	119	419	31
Sum of two I-THMs	μg L^{-1}	nd	0.9	1.9	3.7	0.4*
HAA9	μg L^{-1}	11	20	38	134	34
HAN4	μg L^{-1}	0.49	1.36	1.81	4.09	3
DCAN	μg L^{-1}	0.05	0.66	1.07	2.10	1
Chloropicrin	μg L^{-1}	<0.06	0.08	0.14	0.36	0.2
NDMA	ng L^{-1}	nd	-	-	26	nm

nd - not detected
nm – not measured
*sum of six iodinated THMs

3.1.2 Final and distribution samples DBPs

The sections below show the occurrence (using box and whisker plots) of the DBPs measured in the final and distribution samples on both a seasonal and a disinfectant basis (raw data is presented in Appendix C). The median data show some seasonal variations in the levels although this is not as pronounced as previous studies (Goslan et al., 2002). As reported in a number of previous surveys the THMs and HAAs were the two major classes of halogenated DBPs found (Williams et al., 1995; Krasner et al., 1989, Krasner et al., 2006). Each individual group of DBPs is discussed below

THMs: THM4 levels identified during the survey ranged from a low of 12 μg L^{-1} at works 2 to a maximum of 90 μg L^{-1} at the same works. The highest measured level of THM_4 during the survey was 418 μg L^{-1} in the distribution system supplied by works 4 although it was works 7 that had consistently high levels of THM_4 with only one sample being below the 100 μg L^{-1} MCL and the average value being 180 μg L^{-1}. At the chlorinated works the level of THMs typically increases as the water passed through the distribution system. The use of chloramines at four of the surveyed works led to significantly lower levels of THM_4 (Figure 3.1) and these typically did not increase as they went through distribution.

The median THM_4 concentration was 106 μg L^{-1} at the works using chlorine compared to 48 μg L^{-1} at the works that used chloramines. It should be pointed out though even at those works using chloramines as the residual disinfectant THM levels above 100 μg L^{-1} were identified. This happened at two works in winter. In one case (works 5), the majority of the THMs were formed at the works primarily due to the period of chlorination before ammonium salts addition. In distribution, the level of THM_4 was observed to fall. At the other works (works 6), the THM_4 leaving the works was 116 μg L^{-1}. When measuring at two different points in distribution, this was observed to rise for one sample (198 μg L^{-1}) and fall for the other (112 μg L^{-1}).

The concentration of the iodinated THMs was low compared to THM_4 (Table 3.2, Figure 3.2) and the ratio of iodinated THMs to THM_4 was 1.2% on a median basis. This is comparable to the value reported by Krasner et al. (2006) who reported a ratio of 2% on a median basis although this was for six iodinated THMs. In agreement with Krasner et al. (2006), dichloroiodomethane was generally found at higher levels than bromochloroiodomethane. The highest concentration of the two iodinated THMs was at works 2 in spring 2008 (3.7 μg L^{-1}). Levels of iodinated THMs increased in line with increasing iodine levels which increased from a median of 2 μg L^{-1} in winter and spring to 6 μg L^{-1} in summer. A strong linear relationship can be seen between iodide and iodinated THM levels and the only outlier was works 6 which uses ozone (Figure 3.3, outlier circled). Ozone is known to oxidise iodide through to iodate (IO_3^-) and hence minimise any potential for iodinated THM formation (Bischel and Von Gunten, 2000).

Previous research has shown that the formation of iodinated THMs is favoured by chloramination (Hansson et al. 1987; Bischel and von Gunten, 2000; Krasner et al., 2006). Bischel and Von Gunten (2000) investigated the formation of iodinated THMs and found that the mechanism involved the oxidation of iodide to hypoiodous acid (HOI) and the reaction of this species with organic matter. Monochloramine unlike chlorine is unable to oxidise HOI to iodate (IO_3^-) meaning that HOI has a longer lifetime during chloramination and hence more opportunity to react with organic matter to form iodinated THMs. Hua et al. (2006) showed that iodinated THMs could form during chlorination but formation reduced significantly as the concentration of free chlorine increased (above 1 mg L^{-1}). The presence of free chlorine though leads to the formation of mixed chlorine/iodine THMs such as measured during this survey.

The estimated odour threshold concentrations for the iodinated THMs have been reported by Cancho et al. (2000) and Suffet et al. (1995) to be as follows dichloroiodo- (8.0 μg L^{-1}), bromochloroiodo- (8.4 μg L^{-1}), dibromoiodo- (6.4 μg L^{-1}), chlorodiiodo- (1.1 μg L^{-1}), bromodiiodo- (0.8 μg L^{-1}), and triiodomethane (0.3 μg L^{-1}), so it is unlikely that the levels found here are likely to be detected by taste and odour.

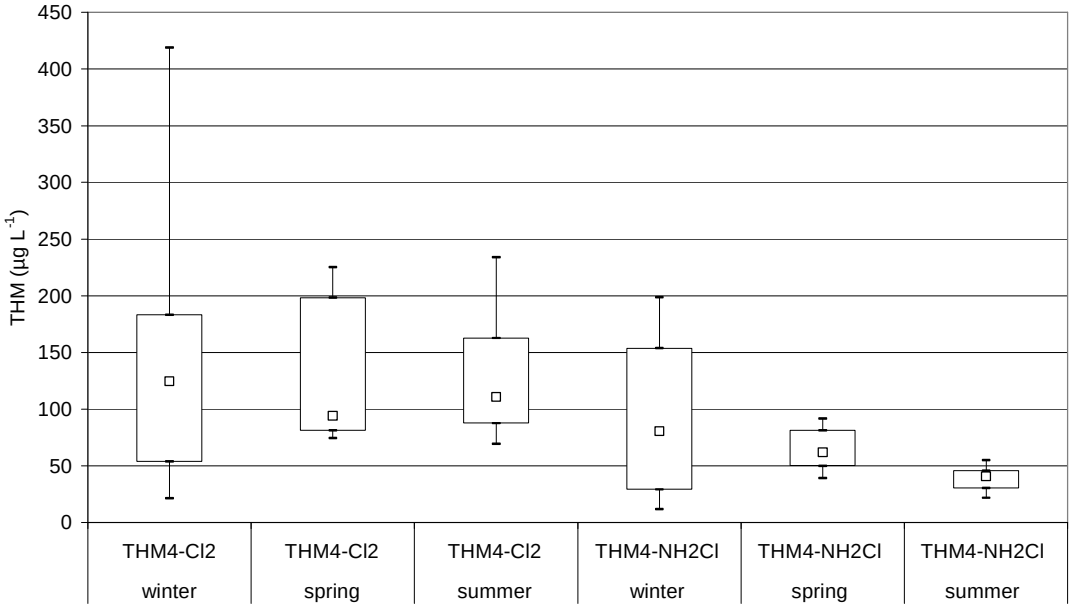

Figure 3-1. Trihalomethanes (THM_4) measured in final and distribution samples: comparison of season and disinfectant

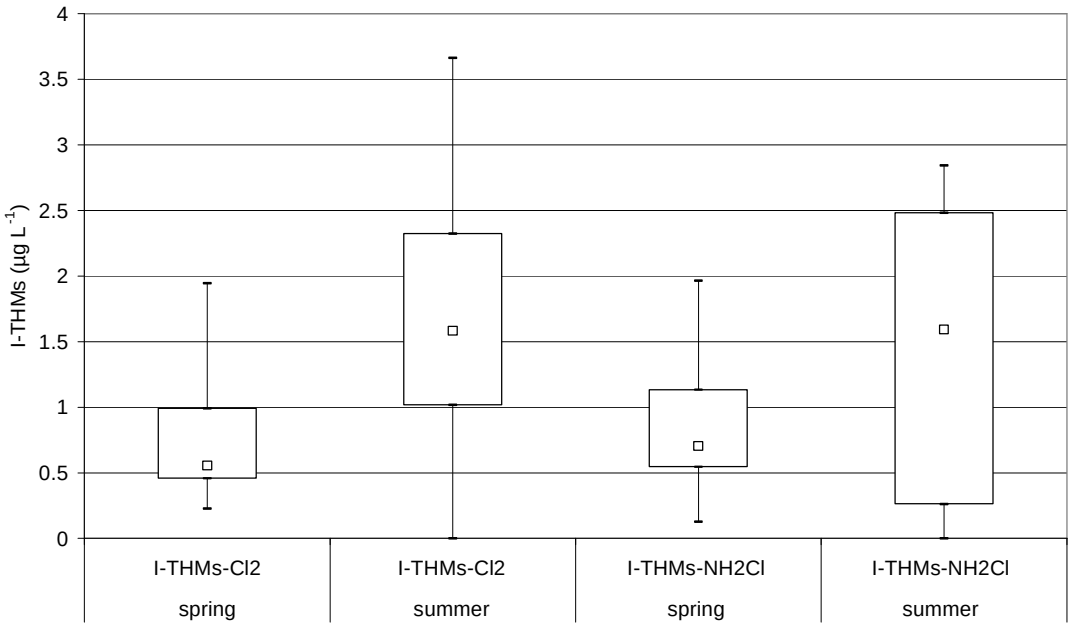

Figure 3-2. Iodinated THMs measured in final and distribution samples: comparison of season and disinfectant

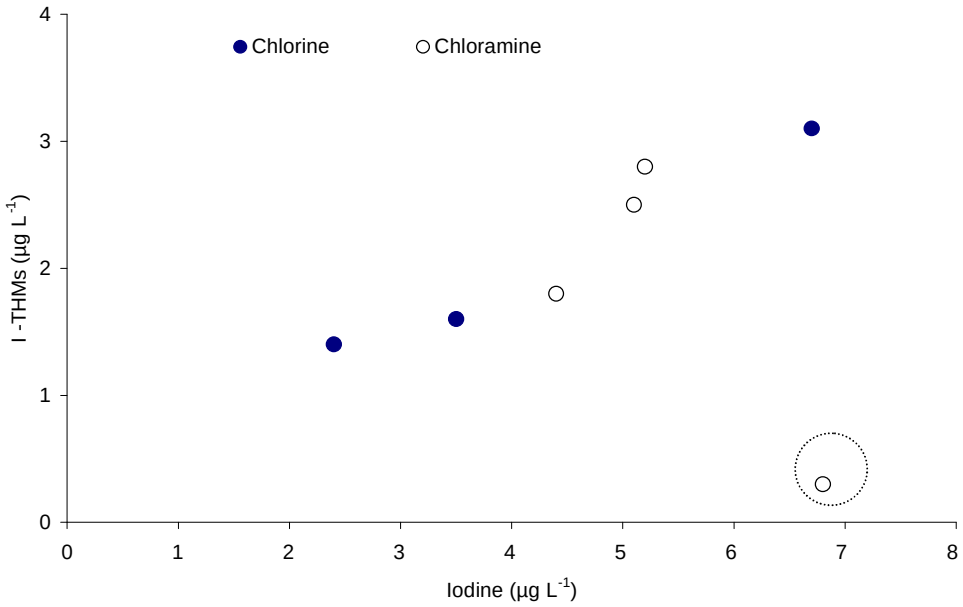

Figure 3-3. Iodide measured against iodinated THMs formed showing the comparison between works using chlorine and chloramines with outlier circled.

HAAs: The median concentration data (Figure 3.4) shows a similar pattern for the HAAs as was observed for THM_4 in that concentrations are higher at the works using chlorine (44 μg L^{-1}) when compared to those works using chloramines (16 μg L^{-1}). As with the THMs there was considerable variation between the individual waters with HAA levels ranging from 11 μg L^{-1} at works 2 to 134 μg L^{-1} at works 7. Overall the median value was 20 μg L^{-1} which is in line with previous studies such as Krasner et al. (2006) and Williams et al. (1997) but

lower than those reported for UK waters by Malliarou et al. (2005) whose regional mean values varied between 35.1 and 94.6 μg L^{-1} for HAA_6 for chlorinated and chloraminated waters. Here only the two upland reservoir works (1 and 7) which were chlorinated had samples with greater concentrations than, the USEPA standard, 60 μg L^{-1}. The annual average for works 1 was 62.8 μg L^{-1} and for works 7 was 71.2 μg L^{-1}.

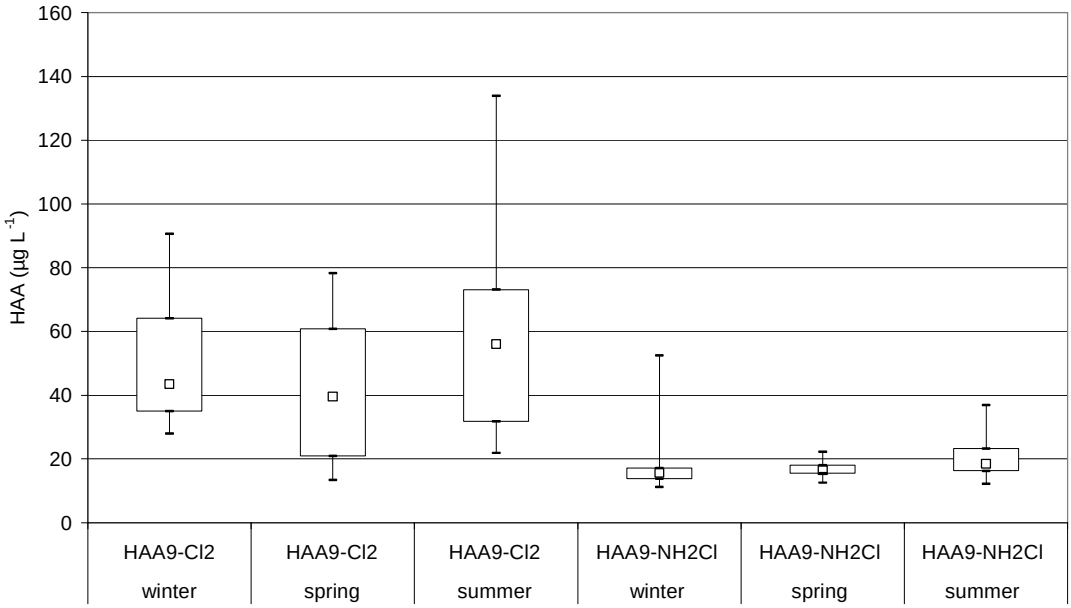

Figure 3-4. HAA_9 measured in final and distribution samples: comparison of season and disinfectant

The impact of chloramination on speciation of HAAs has also been widely reported and we would expect to observe a change in the speciation towards dihalogenated HAAs. Diehl et al. (2000) reported that during chloramination 90% of the total HAAs would be dihalogenated (DXAA) whilst chlorination produced a mixture of mono-, di- and trihalogenated (TXAA) HAAs. The data obtained in this survey (Figure 3.5) agrees with the literature in that there are generally equal levels of DXAA and TXAA in the chlorinated samples but DXAA is always the major group found in the chloraminated sample (Figure 3.5). The findings are in general agreement with the only published UK survey reported by Malliarou et al. (2005) who also found TCAA and DCAA were the major species. Krasner et al. (2008) showed that the dihalogenated HAAs (DCAA, BCAA and DBAA) were the major species formed during their survey (where many of the works used chloramines) whilst Ates et al. (2008) in their survey of 29 water treatment works across Turkey (which used chlorine) reported similar trends to those reported here with the major HAA species reported as TCAA (47.6%) and DCAA (31.3%). Karanfil et al. (2007) have recently studied DXAA vs TXAA formation during chloramination and shown evidence of a direct reaction between NH_2Cl and NOM to form DXAAs.

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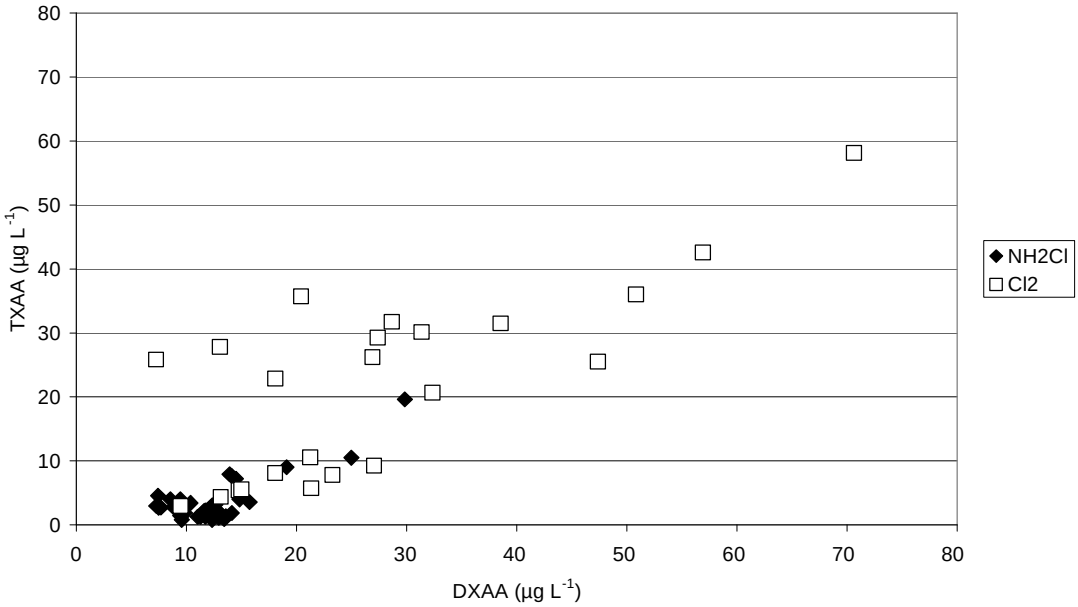

Figure 3-5. Impact of disinfectant choice on the speciation of HAAs.

HAN and HNM: The effect of using chloramines as a disinfectant was less pronounced for HANs (Figure 3.6) and CP (Figure 3.7) where the median concentration of HAN_4 changed from 1.7 μg L^{-1} for chlorinated water to 1.3 μg L^{-1} when using chloramines. For CP, there was no change with median values of 0.1 μg L^{-1} when using chlorine and chloramines. The maximum concentration found was 4.1 μg L^{-1} of HAN_4 at works 4 and 0.36 μg L^{-1} of CP at works 7. Here it must be noted that the concentration of CP measured was almost always at or below the limit of detection. Overall the data are comparable to the USEPA occurrence survey where median values of 3 μg L^{-1} for HAN_4 and 0.2 μg L^{-1} for CP were reported (Krasner et al., 2006). Williams et al. (1996) reported median values of DCAN ranging from 1.4 to 3.1 μg L^{-1} and CP of 0.2 to 1.1 μg L^{-1}. A previous investigation into CP formation during chloramination showed that changing the conditions did not have an effect on CP levels measured (Yang et al., 2007).

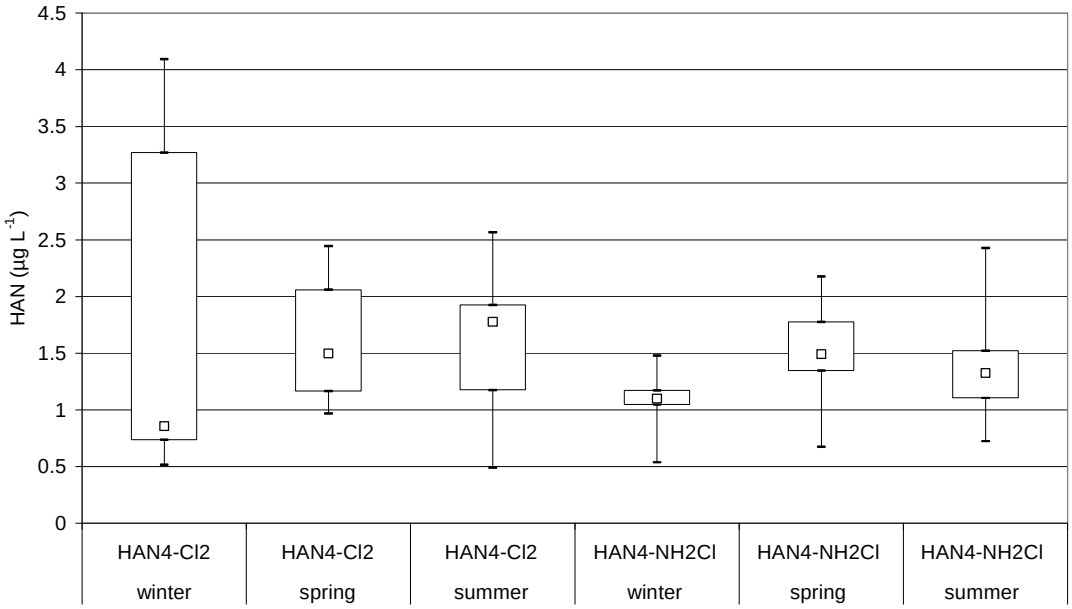

Figure 3-6. HAN_4 measured in final and distribution samples: comparison of season and disinfectant

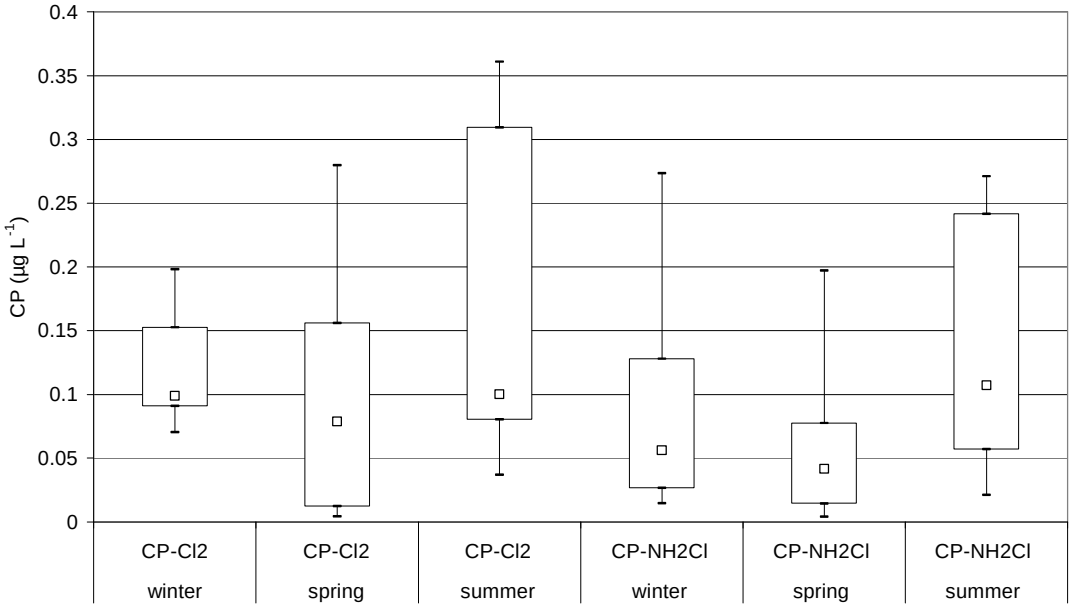

Figure 3-7. Halonitromethane (CP) measured in final and distribution samples: comparison of season and disinfectant

Nitrosamines: Samples were analysed for nitrosamines during the spring and summer surveys. NDMA was only found at one works (works 3) in spring which uses chloramine as the residual disinfectant. The sample contained 8.6 ng L^{-1} NDMA whilst the corresponding distribution samples contained 13.5 and 26.0 ng L^{-1} NDMA. No other nitrosamines were found. These are significant levels and it is recommended that further sampling is carried out to determine whether NDMA occurs at works 3 at other times during the year. Due to the

unpredictable occurrence of NDMA, it was not possible to determine its source (precursors may be present in the raw water and the use of certain polymers at treatment works may contribute NDMA precursors). A recent survey carried out by the DWI (DWI, 2008) reported levels up to 6.8 ng L^{-1} in distribution samples. However, higher levels (39.1 ng L^{-1}) were found in the recycled supernatant from magnetite regeneration at one works and this was attributed to the ferric coagulant used at that works. The State of California has a notification level of 10 ng L^{-1} for NDMA and the province of Ontatio has a drinking water standard of 9 ng L^{-1} for NDMA.

3.1.2.1 Bromine incorporation

The formation of bromine-containing DBPs is of particular interest as they are though to be more harmful than chlorine-containing compounds (Plewa et al., 2006). Here we have use the bromine incorporation factor (BIF) to show the proportion of the DBPs that are partially or totally brominated. The BIF describes the molar contribution of all brominated species (Koudjonou et al., 2008) and for THMs, the BIF can be calculated by the expanded equation below (Hinkley et al., 2005, Gould et al., 1983):

$$\text{BIF (THMs)} = \frac{0\times[CHCl_3]+1\times[CHBrCl_2]+2\times[CHClBr_2]+3\times[CHBr_3]}{[CHCl_3]+[CHBrCl_2]+[CHClBr_2]+[CHBr_3]}$$

where the THM concentrations are on a molar basis

For THMs, the BIF can range from 0 (no brominated species) to 3 (pure tribromomethane) depending on the degree of bromine substitution. A BIF of 1.0 means that the "average" species is bromodichloromethane. For HAAs, separate BIF values are calculated for trihalogenated species and dihalogenated species (Krasner et al., 2008). The equations are as follows:

$$\text{BIF (DXAAs)} = \frac{0\times[DCAA]+1\times[BCAA]+2\times[DBAA]}{[DCAA]+[BCAA]+[DBAA]}$$

$$\text{BIF (TXAAs)} = \frac{0\times[TCAA]+1\times[BDCAA]+2\times[DBCAA]+3\times[TBAA]}{[TCAA]+[BDCAA]+[DBCAA]+[TBAA]}$$

For the dihalogenated HAAs, the BIF ranges from 0 (no brominated species) to 2 (pure DBAA) and for the trihalogenated HAAs, the range is from 0 (no brominated species) to 3 (purely TBAA).

Values have been calculated here for THMs, DXAAs and TXAAs. These have been plotted against the bromide present in the 'filtered' sample collected after treatment but before exposure to disinfectant (Figures 3.8-3.9). For THMs, the BIF is mainly below 0.2 with some higher values reaching ~0.7. The two highest values are from works 4 which had the highest measured levels of bromide. However, the highest bromide level did not correspond with the

highest BIF. In previous research, bromine incorporation was found to be impacted by the bromide to NPOC ratio and the free available chlorine to bromide ratio (Symons et al., 1993). In agreement with Symons et al. (1993), the BIF for both THMs and HAAs typically increased as the bromide to NPOC ratio increased (Figures 3.10-3.11). The low degree of BIF for all the other works indicates that $CHCl_3$ was the main species formed at all the works. There were no clear trends between works that used chlorine and those that used chloramines. This may have been primarily due to the formation of most of the THMs at chloramine works during the pre-chlorine contact time (with free chlorine before ammonia addition). BIF values from 0.32 to 2.05 have been reported for the same system with lower values found in winter when bromide concentration was lowest (Koudjonou et al., 2008). Generally with higher values of bromide, higher BIF values are observed (Krasner et al., 1994; Health Canada, 1995; Williams et al., 1997) and this can been seen here where we have found an R^2 value of 0.70 for all chlorinated and chloraminated data (Figure 3.8, line not shown).

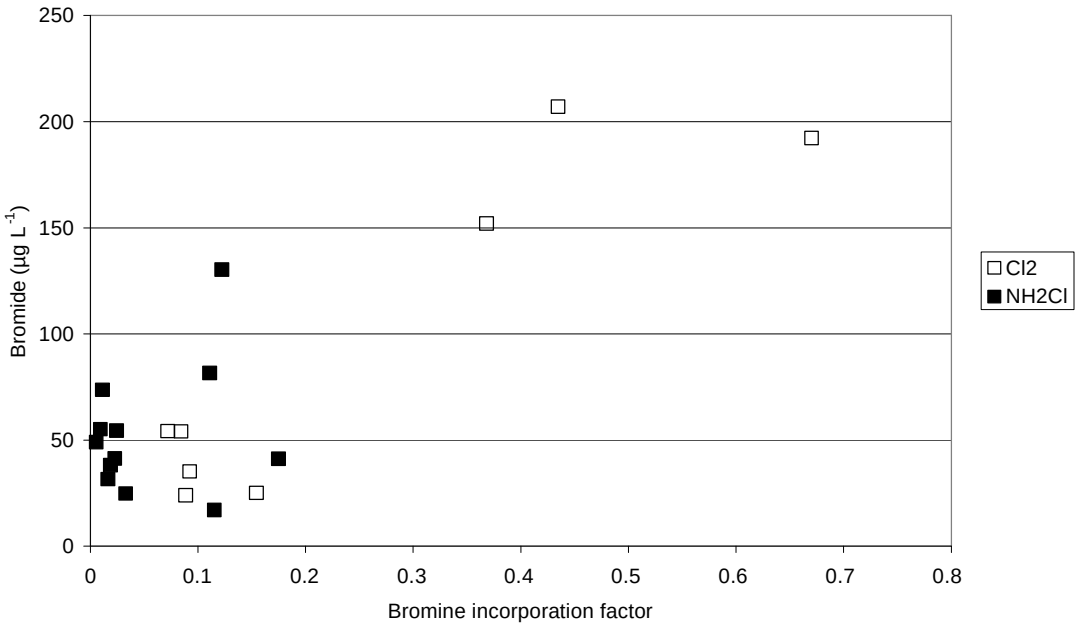

Figure 3-8. THM bromine incorporation factor against bromide concentration in filtered samples

The DXAAs and TXAAs show a similar range of BIF values bearing in mind that the maximum value for DXAAs is 2 and for TXAAs is 3. The highest values for BIF were for works 2 for TXAA and works 4 for DXAA. There was no clear difference for the TXAAs between chlorination and chloramination which we may have expected to see. Cowman and Singer (1996) observed less bromine incorporation in HAAs in their study comparing chlorination and chloramination of humic substances. However, Cowman and Singer (1996) employed direct chloramination whereas the works reported here had a period of chlorination before ammonia salts addition. For the DXAAs, all values for samples that had been chloraminated were less than 0.7 indicating a low degree of bromine

incorporation regardless of bromide concentration in the water. Overall, the TXAA BIF values were higher than the THM BIF values.

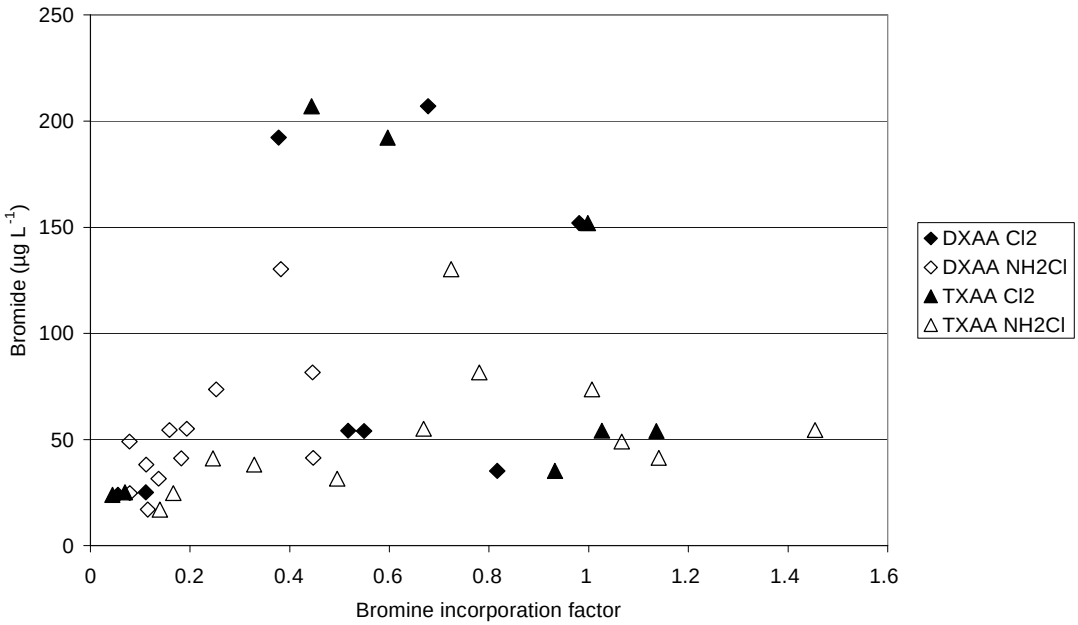

Figure 3-9. HAA bromine incorporation factor against bromide concentration in filtered samples

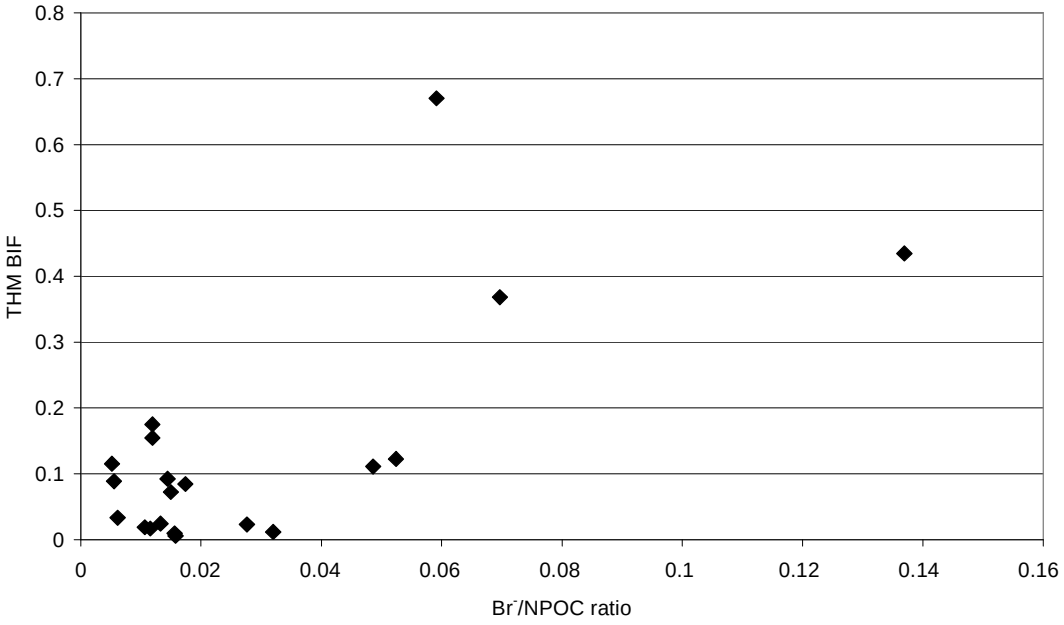

Figure 3-10. THM BIF against bromide:NPOC ratio in filtered samples

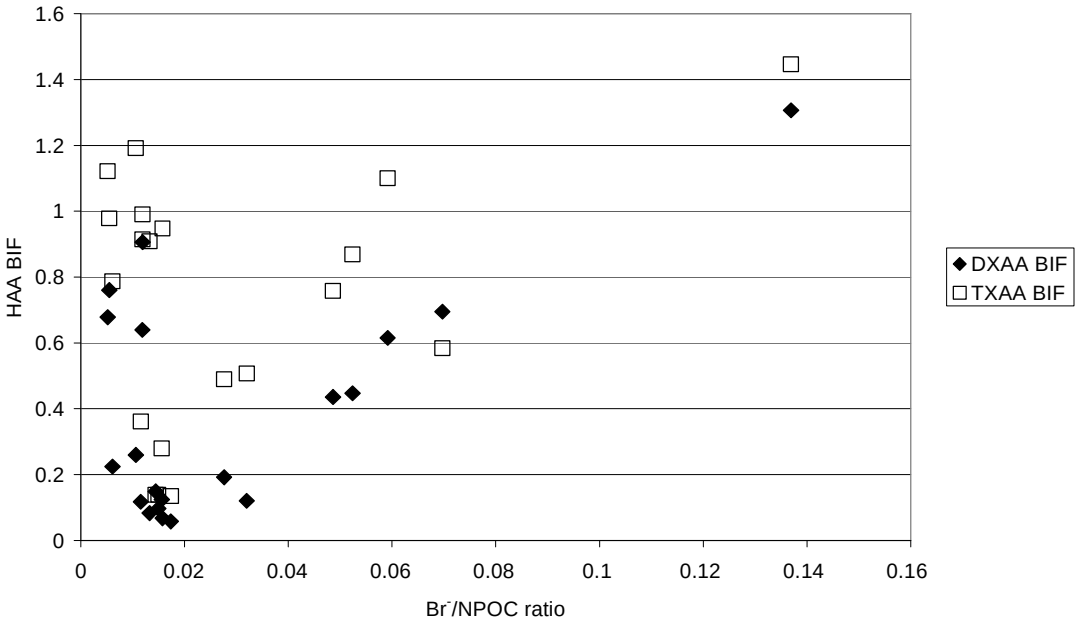

Figure 3-11. HAA BIF against bromide:NPOC ratio in filtered samples

3.1.3 Summary

- The levels of THMs were significantly lower in those works that used chloramines compared to chlorine.
- Levels of THMs were consistently high at a number of works and often above the 100 μg L^{-1} MCL.
- Low μg/L or sub μg/L levels of iodinated THMs were identified and a strong relationship was seen with iodide levels. The use of ozone significantly decreased the potential for iodinated THM formation.
- Levels of HAA were lower in those works that use chloramines when compared to those that used chlorine. Dihalogenated haloacetic acids were the major species found at works using chloramines.
- The median for HAN_4 changed somewhat from 1.7 μg L^{-1} for chlorinated waters to 1.3 μg L^{-1} for works using chloramines. There was no significant change in the levels of CP when using chlorine or chloramines and the levels were low compared to other surveys.
- NDMA was found only at works 3 which used chloramines. The levels found increased from the works into the distribution system and were significantly higher than those reported during a recent UK wide survey.

3.2 In-works samples

This section of the report looks at samples collected from various locations in the treatment works and returned to Cranfield University to assess the potential for disinfection by-product formation. Formation potential (FP) tests were conducted with chlorine and monochloramine to allow us to investigate the levels of DBP precursors in the raw water as well as the effectiveness of the treatment processes in removing them. It also allows a direct comparison between the formation of DBPs with chlorine and chloramine disinfectants.

A summary of water quality data for each works during each season is shown below (Tables 3.3-3.5). The data have been separated into raw and treated water and for two of the works (3 & 6), two treated samples were collected. The treated samples are referred to as 'filtered', 'settled' and 'ozonated' depending on the point of collection.

Table 3-3. Water quality data at works surveyed – Winter

Works ID	Sample	NPOC	UV	SUVA	Bromide	Iodide
		mg L^{-1}	m^{-1}	m^{-1} .L mg^{-1} C	μg L^{-1}	μg L^{-1}
1	Raw	1.48	5.53	3.73	248	1.95
	Filtered	Ns	Ns	Ns	Ns	Ns
2	Raw	4.48	23.4	5.21	63.9	1.62
	Filtered	4.10	9.15	2.23	54.4	0.65
3	Raw	6.80	26.9	3.95	140	2.95
	Settled	2.80	5.63	2.01	149	1.06
	Filtered	2.49	3.15	1.27	130	0.97
4	Raw	12.5	40.2	3.22	224	6.84
	Filtered	3.25	4.43	1.36	192	2.53
5	Raw	5.19	21.2	4.08	71.3	1.80
	Filtered	2.30	3.12	1.36	73.6	0.35
6	Raw	4.31	15.1	3.49	54.2	2.87
	Ozonated	3.90	7.58	1.94	52.3	2.97
	Filtered	3.11	6.45	2.08	49.0	2.92
7	Raw	17.7	52.6	2.96	69.7	3.88
	Filtered	3.11	4.80	1.55	54.0	Nd

Ns – no sample taken
Nd – not detected

Table 3-4. Water quality data at works surveyed – spring

Works ID	Sample	NPOC	UV	SUVA	Bromide	Iodide
		mg L^{-1}	m^{-1}	m^{-1} .L mg^{-1} C	$\mu g\ L^{-1}$	$\mu g\ L^{-1}$
1	Raw	4.07	13.0	3.19	259	1.62
	Filtered	2.44	1.93	0.79	35.2	0.56
2	Raw	5.09	15.8	3.10	95.5	1.53
	Filtered	3.53	6.55	1.86	55.1	1.68
3	Raw	4.43	12.5	2.82	117	3.29
	Settled	2.30	2.70	1.17	85.1	2.41
	Filtered	1.68	2.63	1.56	81.6	1.98
4	Raw	4.23	12.0	2.84	222	8.13
	Filtered	1.51	1.85	1.22	207	4.18
5	Raw	3.01	8.58	2.85	43.8	1.85
	Filtered	1.49	2.33	1.56	41.3	2.17
6	Raw	3.07	12.2	3.97	30.6	2.61
	Ozonated	2.87	5.60	1.95	30.9	3.00
	Filtered	2.73	5.33	1.95	31.6	3.28
7	Raw	11.2	41.8	3.72	64.8	4.21
	Filtered	3.62	5.28	1.46	54.2	1.33

Table 3-5. Water quality data at works surveyed – summer

Works ID	Sample	NPOC	UV	SUVA	Bromide	Iodide
		mg L^{-1}	m^{-1}	m^{-1} .L mg^{-1} C	$\mu g\ L^{-1}$	$\mu g\ L^{-1}$
1	Raw	3.61	14.5	4.00	103	3.61
	Filtered	2.10	3.35	1.59	25.1	3.53
2	Raw	4.81	22.1	4.60	41.4	6.28
	Filtered	3.59	8.30	2.31	38.2	5.24
3	Raw	11.3	42.2	3.74	70.9	7.61
	Settled	3.70	6.30	1.70	43.0	4.68
	Filtered	3.46	5.50	1.59	41.2	5.08
4	Raw	7.81	32.3	4.14	165	12.1
	Filtered	2.18	4.05	1.86	152	6.73
5	Raw	6.23	4.18	0.67	32.8	6.08
	Filtered	3.27	3.83	1.17	17.0	4.36
6	Raw	3.73	15.8	4.22	21.5	6.14
	Ozonated	3.85	9.78	2.54	21.2	6.25
	Filtered	4.04	8.75	2.17	24.8	6.80
7	Raw	26.2	47.1	1.80	56.1	8.99
	Filtered	4.34	8.23	1.89	24.0	2.45

3.2.1 Formation potential data

As expected the formation of THMs and HAAs was significantly reduced in the presence of chloramines when compared to formation in the presence of chlorine (Figures 3.12 and 3.13 respectively). There is considerable variability between works and within works, for example the precursors found in the raw water at works 1 were consistently more reactive with chlorine (66.6 μg THM mg C^{-1}) than all the other works. For comparison Croué et al. (1993) reported values of 46 μg mg C^{-1} for humic acid and 27 μg mg C^{-1} for fulvic acid (both compound are used as models for natural organic matter). The reactivity was reduced significantly in the presence of chloramines (14.2 μg THM mg C^{-1}). Works 4 had the lowest THMFP (1.5 and 4.8 μg THM mg C^{-1} with chlorine and chloramines respectively). The same trend was also true for HAA where works 1 had the highest formation potential (25.5 and 2.0 μg HAA mg C^{-1} with chlorine and chloramines, respectively) and works 4 the lowest levels (11.9 and 1.7 μg HAA mg C^{-1} with chlorine and chloramines respectively). The difference observed between chlorine and chloramines for HAAs is more pronounced when looking at DXAA and TXAA separately (Figure 3.14). The median DXAA:TXAA ratio changes from <1 to >5 when comparing chlorine to chloramines.

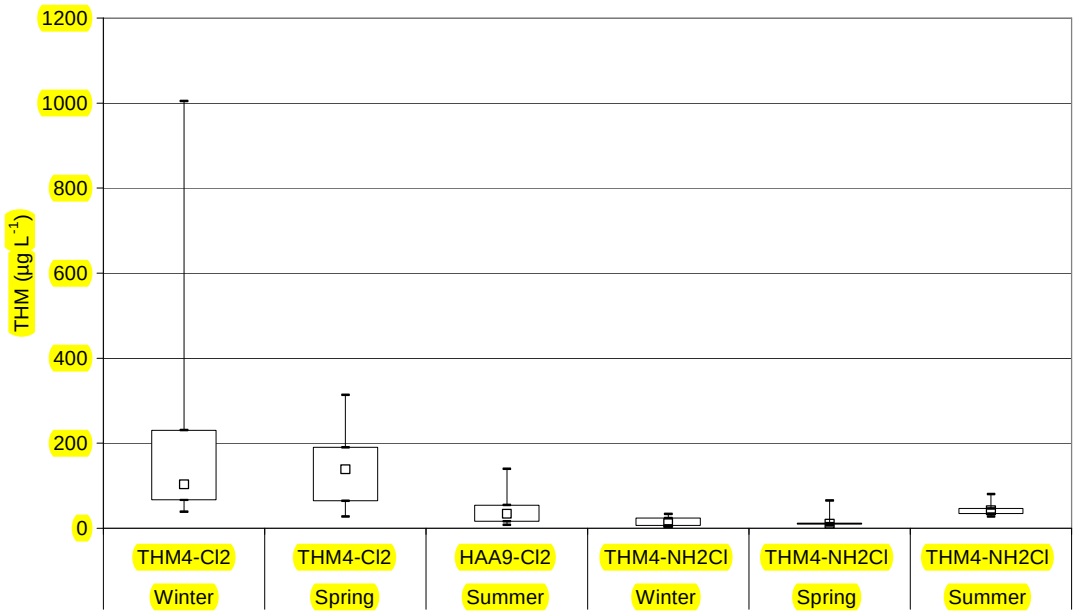

Figure 3-12. Trihalomethane (THM) formation potential for raw and treated waters: comparison of season and disinfectant

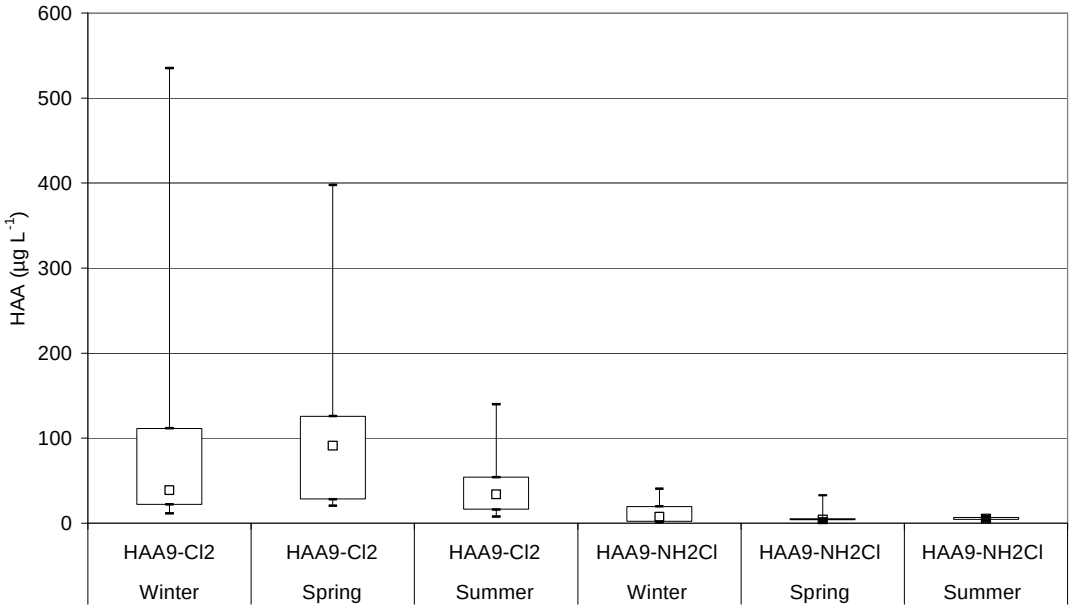

Figure 3-13. Haloacetic acid (HAA) formation potential for raw and treated waters: comparison of season and disinfectant

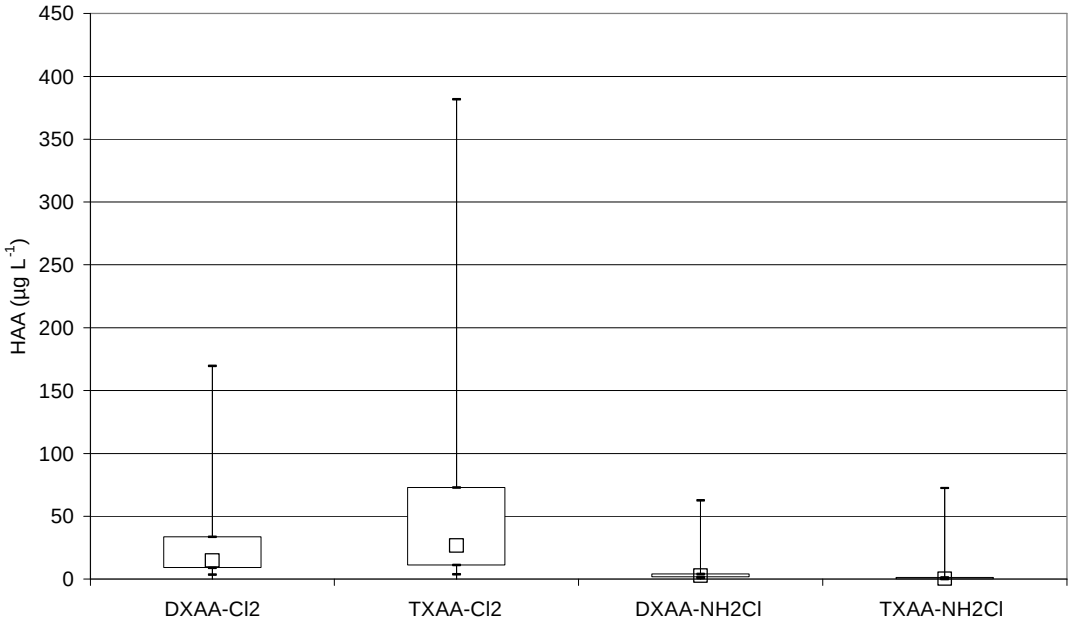

Figure 3-14. DXAA and TXAA formation potential for raw and treated waters: comparison of disinfectant

The precursors for HAN_4 and CP were a lot less impacted by disinfectant choice and more by season (Figures 3.15 and 3.16). This is in general agreement with other researchers who have shown that DCAN is insensitive to pre-chlorination (Yang et al., 2007). They also reported that CP formation was insensitive to bromide concentration, temperature and disinfectant used. Alternatively, other researchers have shown a shift in formation to brominated analogues of CP in high-bromide waters (Thibaud et al., 1988; Krasner et al., 2006).

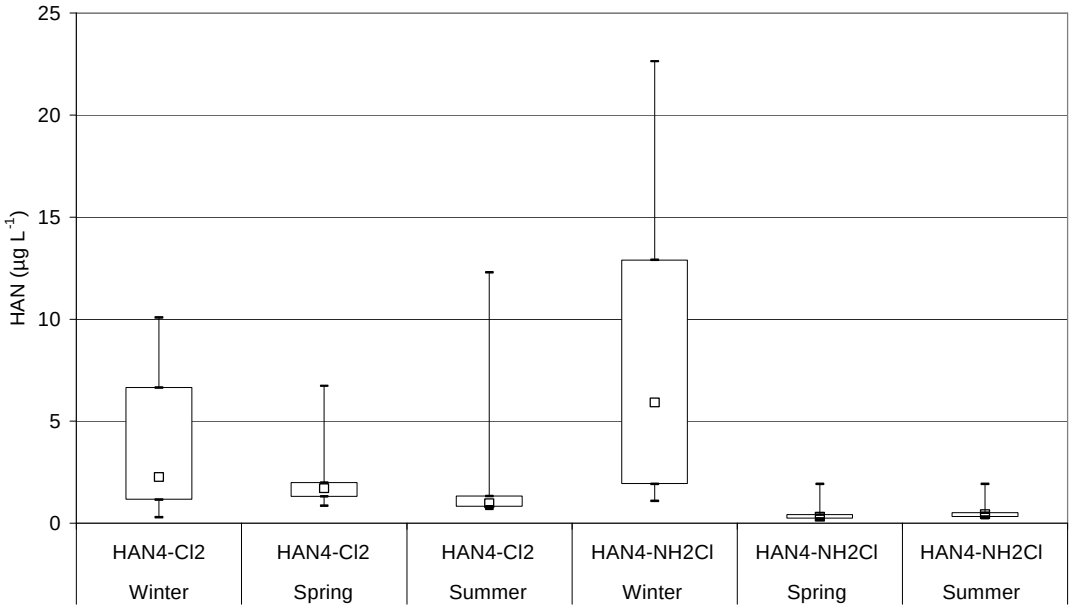

Figure 3-15. Haloacetonitrile (HAN) formation potential for raw and treated waters: comparison of season and disinfectant

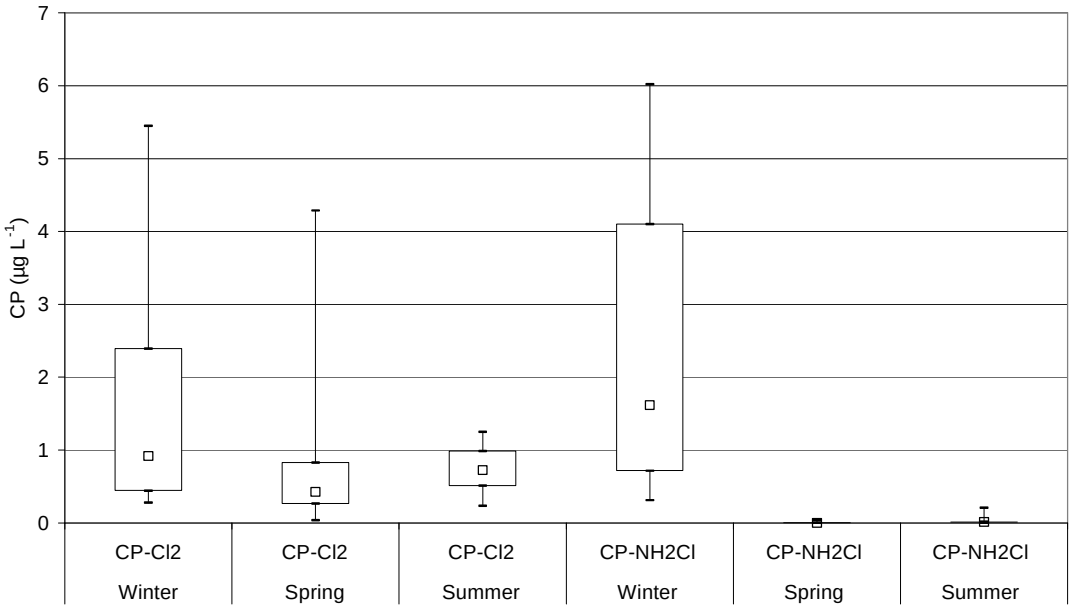

Figure 3-16. Halonitromethane (CP) formation potential for raw and treated waters: comparison of season and disinfectant

Tests to determine the potential of the waters to form CNX were also carried out, although differently than the other FP tests described. To maximise formation of CNX, samples were pre-chlorinated to meet the level of chlorine demand previously determined for other DBPFP tests. After 30 minutes contact time with free chlorine, ammonium sulphate was added to make NH_2Cl at a Cl_2:N weight ratio of between 3:1 and 4:1. After three days, samples were extracted and analysed using GC-MS. This analysis was done without the use of analytical

standards due to the lack of their availability in the UK. Neither CNCl nor CNBr was positively identified in any of the samples with the sensitivity of the method used. In other research in the US where standards were available, CNX precursors were typically found in similar FP tests (Krasner et al., 2007).

As with the final and distribution samples we have investigated the BIF of THMFP samples (Figures 3.17-3.19). The filtered sample at works 4 had the highest BIF in all seasons. When samples were chloraminated, very little bromide was incorporated into the THMs as the bromide was not oxidised to hypobromous acid as there was little or no hypochlorous acid present. When chloramines are used, it is possible to form bromamines in the presence of bromide. However, bromamines are not as strong a halogen substitution agent as hypobromous acid. When samples are chlorinated, generally the more bromide they contain, the more bromide is incorporated into the THMs formed. In summer, where the bromide levels were lower, the BIFs were lower than in winter and spring.

It has been reported that with increasing ozone dose, chlorinated THMs will be reduced and brominated THMs will increase (Amy et al., 1991). Here, the works that used ozone (works 6) showed an increase in BIF when comparing the raw water (6R) BIF to the ozonated water (6O) BIF. Values increased by 79, 154 and 52% in winter, spring and summer, respectively.

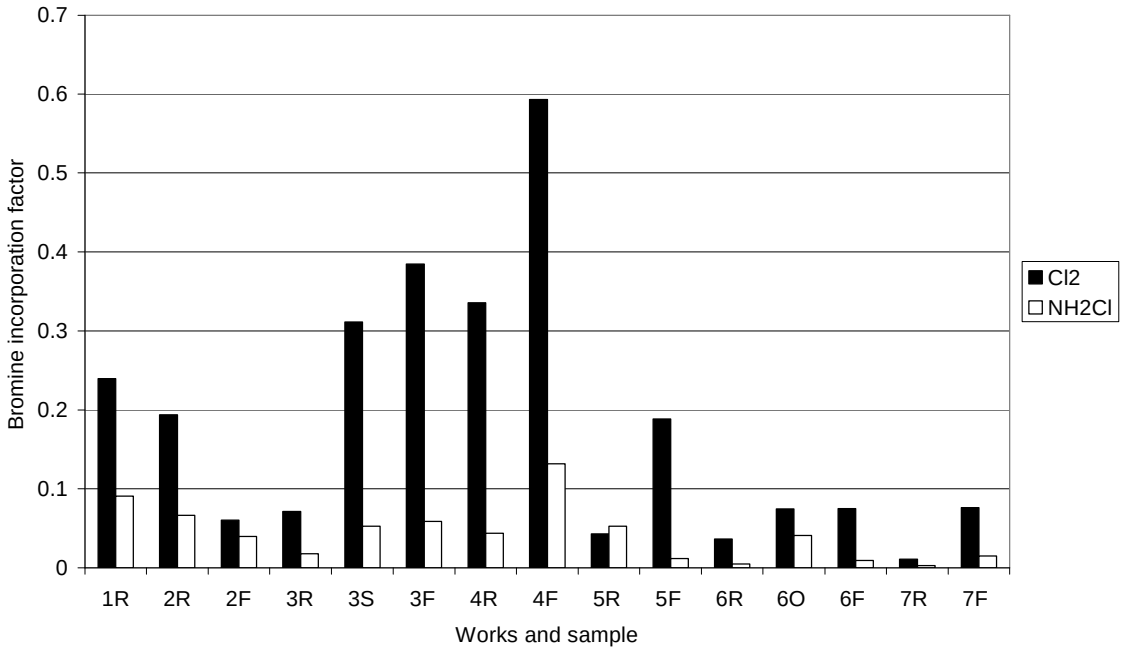

Figure 3-17. Comparison of BIF in chlorination and chloramination THMFP tests (Winter)

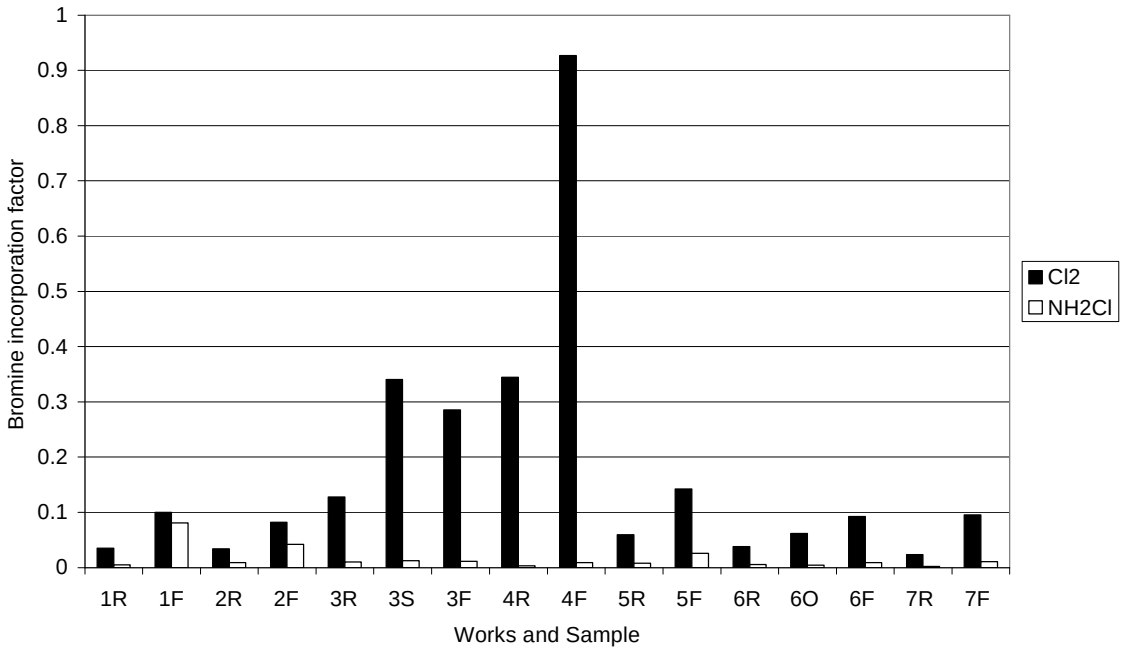

Figure 3-18. Comparison of BIF in chlorination and chloramination THMFP tests (Spring)

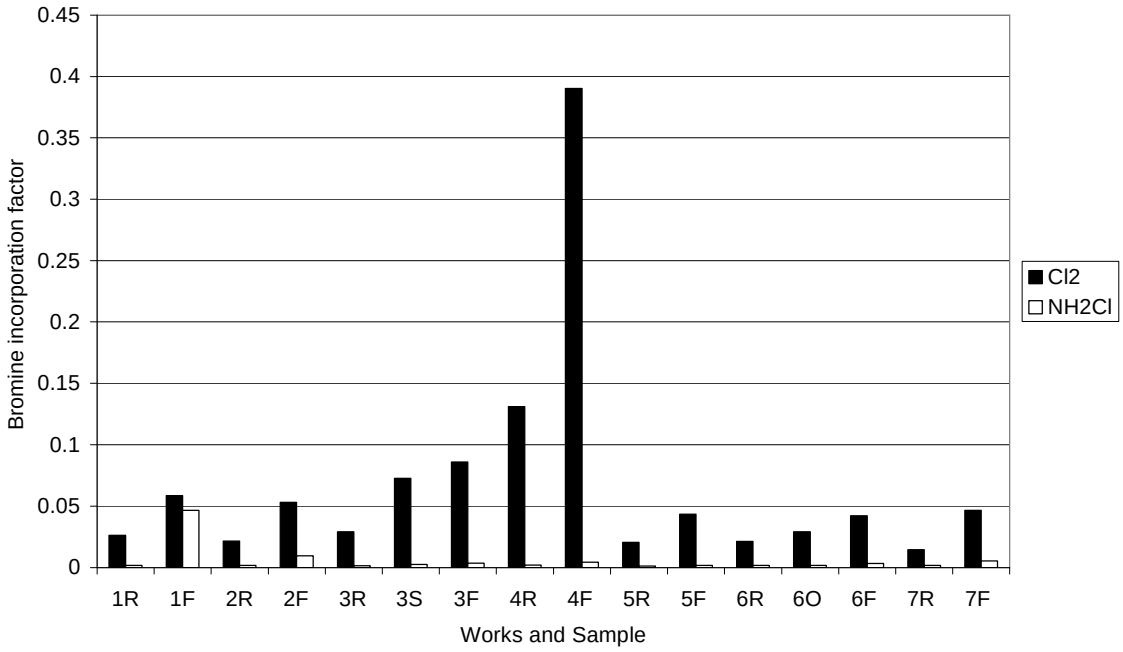

Figure 3-19. Comparison of BIF in chlorination and chloramination THMFP tests (Summer)

3.2.2 Correlation with water quality data.

A number of previous authors have shown strong relationship between water quality parameters such as UV_{254}, SUVA and DOC (Parsons et al., 2005; Yang et

al., 2007) and the formation of disinfection by-products. Here we have looked at the strength of correlations between NPOC, UV, SUVA and bromide and found very weak correlations when all of the data are examined together (Table 3.6). The relationship between SUVA and THMFP and HAAFP is shown as an example of the correlations found (Figures 3.20 and 3.21). However when the data for raw and treated water was segmented and examined for one sample event, better relationships were observed. Figure 3.22 shows the HAAFP and SUVA relationship where the treatment process lowered the levels of SUVA and removed HAA precursors. Note that waters high in humic substances have high SUVA values (e.g. 4 - 5 m^{-1} L mg^{-1} C) (Edzwald and Van Benschoten, 1990). If a works has achieved enhanced coagulation, the treated water SUVA (in the absence of oxidants) should be < 2 m^{-1} L mg^{-1} C, which indicates that the residual natural organic matter is low in humic substances, which coagulation preferentially removes. Figures 3.23 and 3.24 show the THMFP relationship with NPOC or UV, where the relationships were stronger (higher R^2 values) in the treated waters as compared to the raw waters.

Table 3-6. Correlation Table – In-works and FP samples

	THM_4	HAA_9	HAN_4	CP
NPOC	<0.01	0.10	0.18	0.09
UV	<0.01	0.01	0.16	0.03
SUVA	0.01	0.03	0.08	0.01
Bromide	<0.01	0.07	0.05	0.02

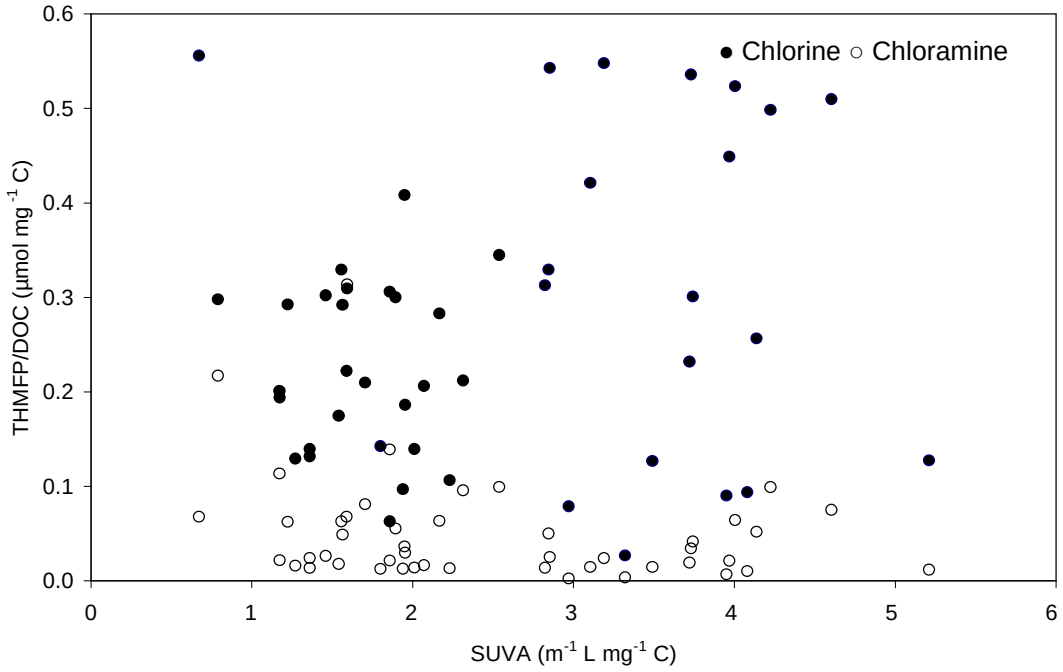

Figure 3-20. The relationship between THMFP yields and SUVA for chlorinated and chloraminated samples.

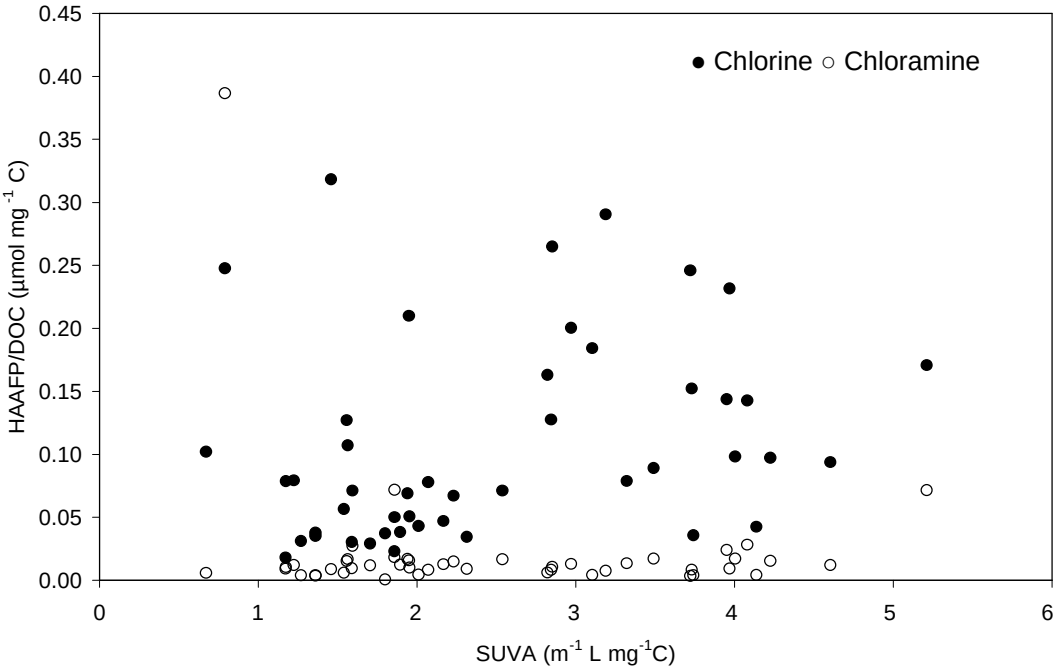

Figure 3-21. The relationship between HAAFP yields and SUVA for chlorinated and chloraminated samples.

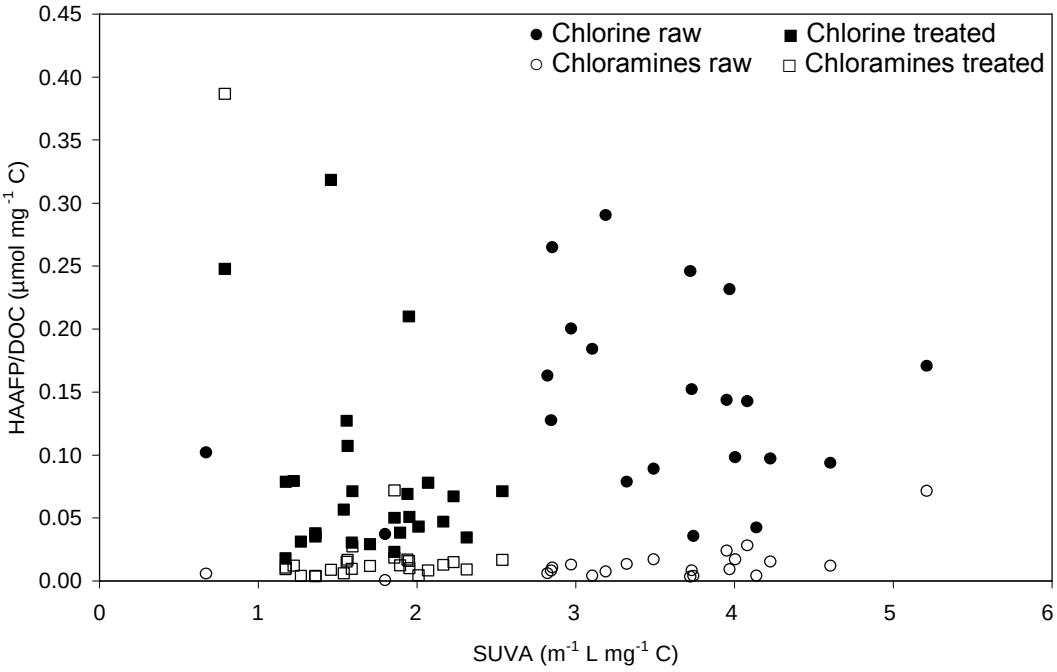

Figure 3-22. The relationship between HAAFP yields and SUVA for chlorinated and chloraminated samples segmented by raw and treated waters.

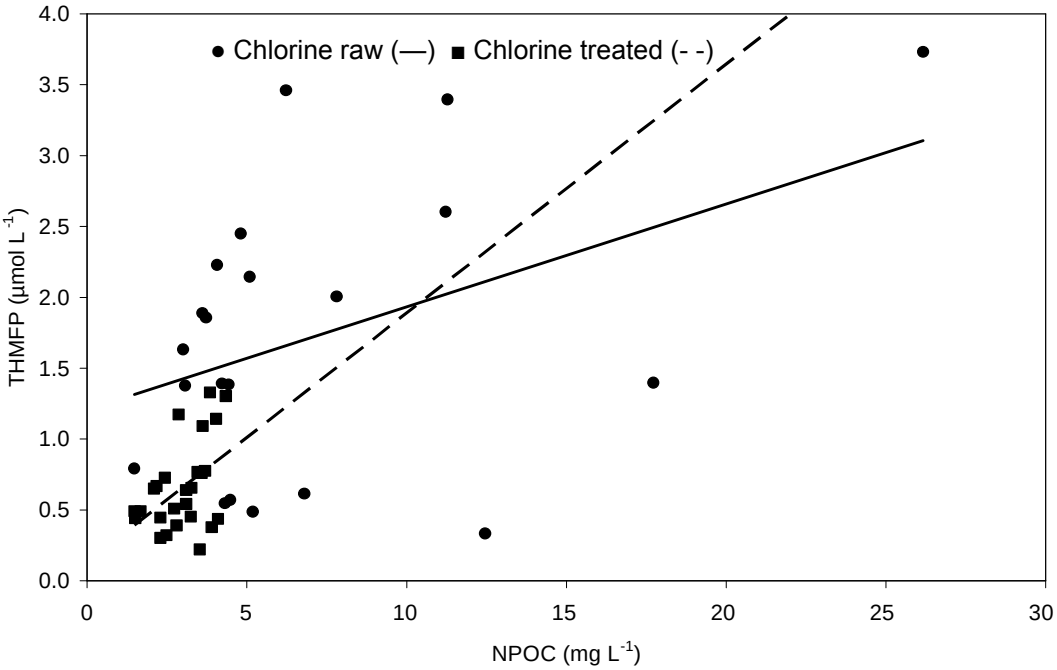

Figure 3-23. The relationship between THMFP and NPOC for chlorinated samples segmented by raw and treated waters (first sample event).

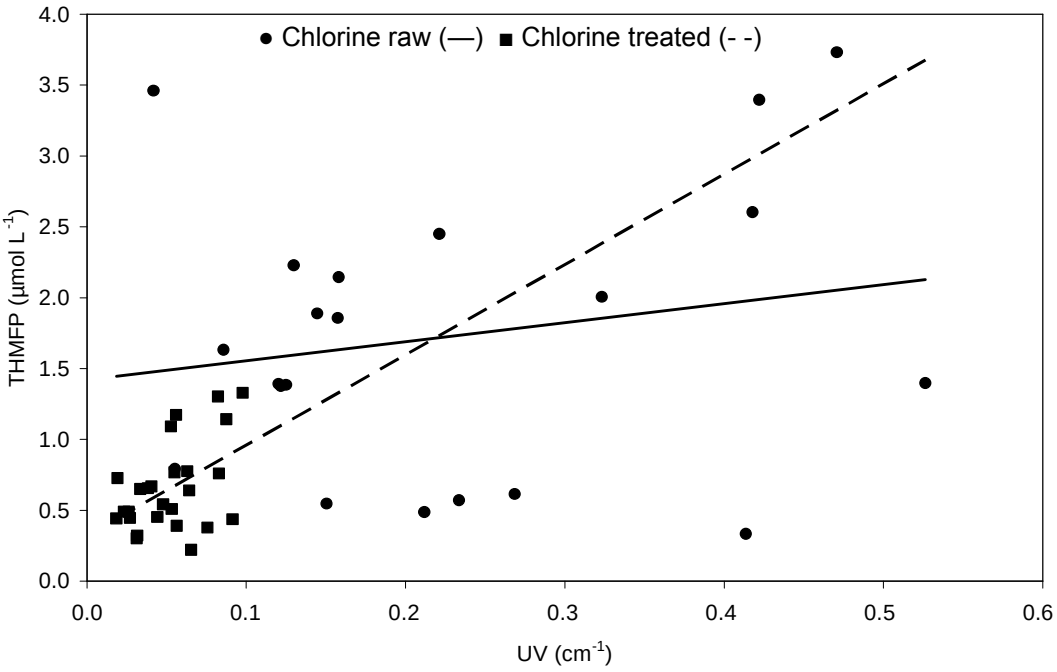

Figure 3-24. The relationship between THMFP and UV for chlorinated samples segmented by raw and treated waters.

3.2.3 Removal of DBP precursors.

This survey has looked at works with a wide range of treatment processes from conventional coagulation/filtration to advanced treatment (activated carbon, ozonation). At all of the works except 6, the treated water SUVA values were from samples that had not seen any oxidant. Most of the treated water SUVA values were < 2 m^{-1} L mg^{-1} C. A summary of % removal is given below (Figure 3.25) and there are some general trends that can be pulled out. The two works (i.e. 2 and 6) with the poorest removal of NPOC were the ones that had the highest treated water SUVA values. Secondly, for all works there is preferential removal of UV adsorbing organic matter over bulk organic matter which would be expected for those works using coagulation or ozonation, which preferentially remove or transform, respectively, humic substances. For all of the works this also equates to preferential removal of THM and for all but works 7 also HAA precursor material. We would have expected to see strong links between UV_{254} and THMFP (Figure 3.24) as a number of studies such as Banks and Wilson (2003) have investigated the use of UV_{254} on a number of water treatment works in the UK and were successful in using it as a surrogate for THM precursors. If we consider all the works we see that there is a strong relationship between the removal of THM and HAA precursors with a slight preference to removing HAA precursors (Figure 3.26). The preference for TXAA and DXAA precursor removal is shown (Figure 3.27) and shows that TXAA precursors are removed in preference to THM whereas THM precursors are removed in preference to DXAA precursors. Reckhow and Singer (1990) found that THM and HAA removal was bracketed by the removal of TOC and UV where the order of precursor removal was TXAA>DXAA>THM. Here, works 3, 4 and 5 follow this pattern and works 1, 2 and 7 have very similar precursor removal for THM and TXAA with DXAA precursor removal lower.

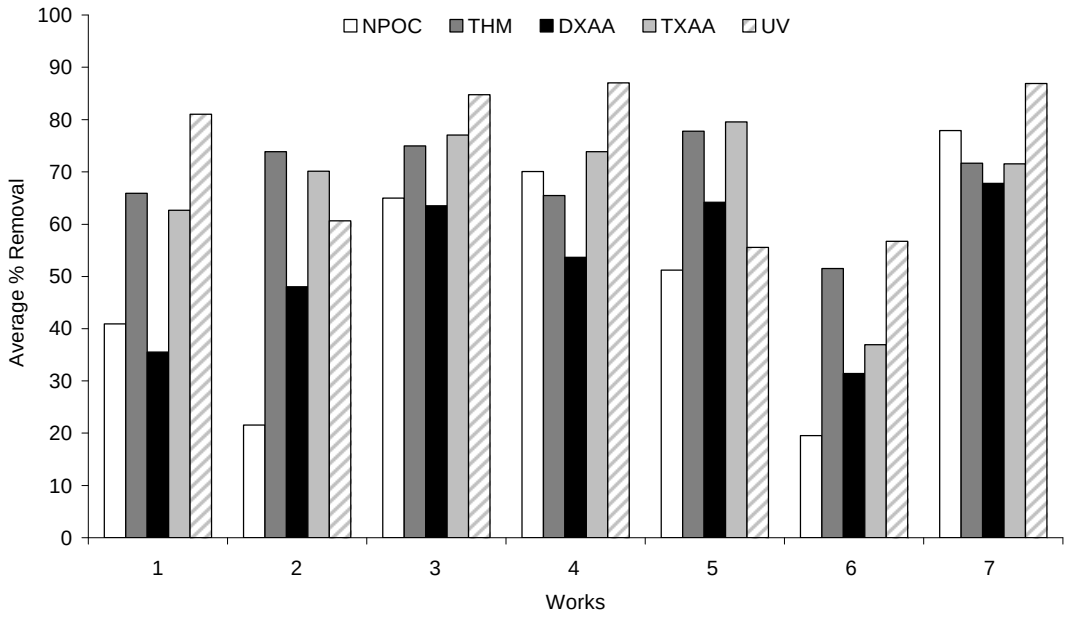

Figure 3-25. Summary of NPOC, THM, DXAA, TXAA and UV_{254} precursor removal observed for the three sampling surveys.

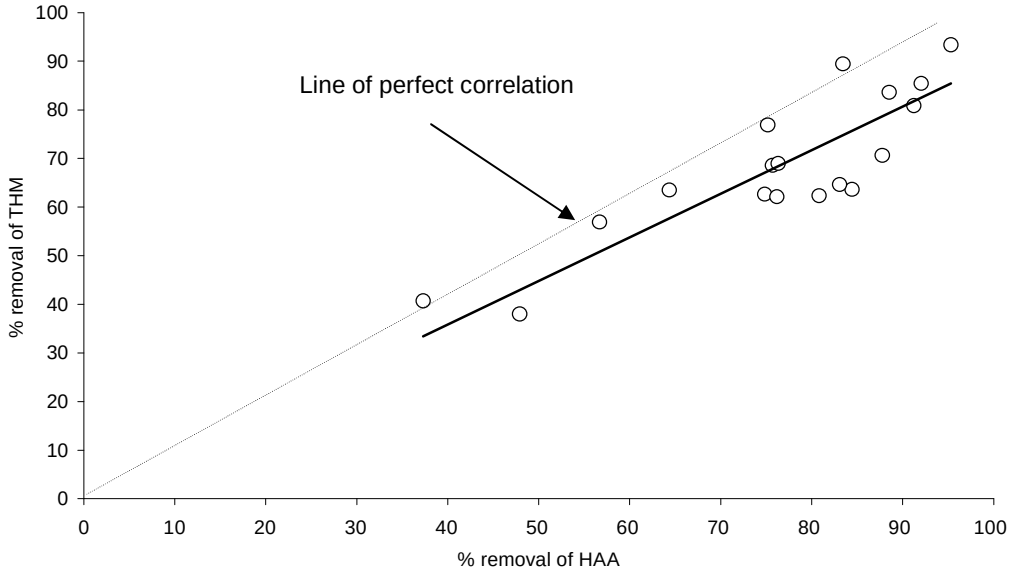

Figure 3-26. Correlation between removal of THM precursors and HAA precursors.

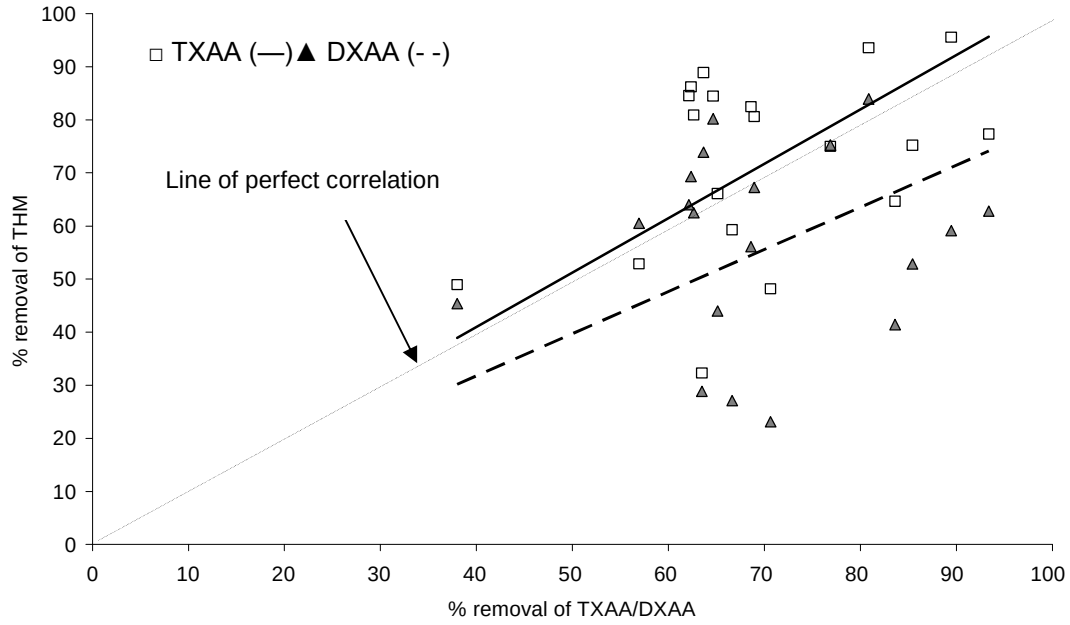

Figure 3-27. Correlation between removal of THM precursors and TXAA/DXAA precursors.

Treatment at works 1 is sand filtration and activated carbon and here we see selective removal of UV, THM and HAA precursors over NPOC. Whilst the formation potential of the natural organic matter (i.e. relatively high yields per unit NPOC) the levels of THM4 and HAA9 found in the final and distribution samples were relatively low for a chlorine works (e.g. all but one THM4 sample was $<100\ \mu g/L$). Thus additional NPOC removal is unlikely to be required.

Works 2 uses coagulation and given that the works has an average SUVA of 4.1 we would have expected to see greater NPOC removal than the 22% observed here. It is clear that the use of chloramines at this works is effective at controlling the formation of THM and HAAs but there may also be potential for further optimisation of coagulation. Works 3 also uses coagulation as the main NPOC removal processes and achieves expected levels of NPOC and UV_{254}. Again the use of chloramines here controls the levels of THM and HAAs effectively but a switch to chlorine would be likely to cause problems given the formation potential of the precursor material. If we compare works 4 and works 3 for example, average levels of removal of NPOC, UV_{254} and THM and HAA precursors were very similar but levels of THMs as high as 418 $\mu g\ L^{-1}$ have been measured in the chlorinated distribution samples of works 4. It is clear that formation of THMs in the distribution system of works 4 is significant here (>8 fold increase between final and distribution sample 2 in the winter sample event) and whilst additional NPOC removal may be beneficial the use of chloramines may be a solution to controlling this formation. In the winter sample event, NPOC removal was 74% (Table 3.2), which is high for conventional treatment. Thus, advanced treatment would be required to remove additional NPOC.

Works 5 and 6 are examples of where additional DOC removal may be periodically required (THMs were >100 μg/L in the winter sample event and they approached 100 μg/L in the spring sample event). Both of these works used chloramines and there was little increase in THM levels into the distribution systems, therefore to control the THM levels something more may be needed in-works. Works 5 has good THM precursor removal (on average 78%) but the reactivity of the precursors is such that more NPOC removal may be required. A first stage would be to optimise removal by coagulation and then consider an alternative DOC removal processes such as ion exchange. Parsons et al. (2004) for example showed that if the residual natural organic matter after coagulation was high and likely to cause a THM or HAA problem then MIEX® as a pre-treatment prior to coagulation should be considered as an alternative option. Works 6 used ozone, which has little effect on NPOC removal, although it does selectively remove UV_{254} and both THM and HAA forming material. Given the SUVA value we would expect significant NPOC removal should be possible using coagulation. Currently the plant uses filtration but not coagulation.

Works 7 had variable and high levels of NPOC in its raw water (11.2 – 26.2 mg NPOC L^{-1}) and on average achieved significant levels of NPOC, $UV_{254,}$ and HAA precursor removal. The removal of THM precursors is variable with 94% removal in spring removal compared to 57% in the summer and this indicates a change in the precursor material and/or treatment process. The former is in agreement with previous work on seasonal variation in natural organic matter released from moorland and upland catchments (Parsons et al., 2004). For this works further investigation of the natural organic matter would be required to show if the coagulation process would be capable of controlling the THM and HAA levels under all seasonal conditions. The raw water SUVA at works 7 was highest in the spring (3.72 m^{-1} L mg^{-1} C) and lowest in the summer (1.80 m^{-1} L mg^{-1} C), which is consistent with the treatability results. Works 7, which used chlorine, produced some of the highest THM and HAA levels among the works studied. Formation potential tests have shown that the formation potential is reduced by over 80% when switching from chlorine to chloramines. So a switch to chloramines at works 7 would help control THM and HAA formation.

3.2.4 Summary

- The formation of THMs and HAAs was significantly reduced in the presence of chloramines when compared to formation in the presence of chlorine.
- The median DXAA:TXAA ratio changed from <1 to >5 when comparing chlorine to chloramines.
- The precursors for HAN4 and CP were much less impacted by disinfectant choice and more by season
- Neither CNCl nor CNBr were identified in any of the samples analysed here, in part due to sensitivity issues.

- For all works there is preferential removal of UV adsorbing organic matter over bulk organic matter and also preferential removal of THM precursors and apart from works 7, HAA precursors.
- For works 4-7 the levels of THM and HAA in the final water and distribution samples warrant further investigation into NPOC removal processes, alternative disinfectants, and/or other optimisation schemes.

4 REVIEW OF TOXICOLOGY AND AESTHETIC DATA AND ASSESSMENT OF RISK

4.1 BACKGROUND

DBPs have been the subject of some concern and have been discussed in a number of published expert workshops and risk assessments. For example, a recent Gordon Research Conference (2006) entitled *Drinking Water Disinfection By-Products* brought together many of the world's experts to examine the most recent health findings with the purpose of integrating knowledge on the occurrence and formation of disinfection by-products, exposure, current toxicity, and epidemiology.

In this task the toxicology data, assessment of risk and aesthetic data were reviewed in order to:

1. Establish, based on published literature, the hazard potential of the chemicals identified as of priority (from Task 2);
2. Develop in the light of toxicological knowledge and available exposure information, an assessment of the risk to human health that may be posed by exposure to any individual chemicals, related group of chemicals or, the DBPs as a whole; and
3. Critically interpret the risk assessment in terms of significance to public health and any aesthetic implications.

In this phase of the study, IEH scientists considered the hazard profiles – including consideration of the basis for any acceptable daily intake (ADI), tolerable daily intake (TDI) or reference dose (RefD) established by any authoritative bodies – for each of the DBP categories or, where appropriate, individual compounds, using information obtained from a structured search of published and, where possible, 'grey' literature. Particular attention was given to the DBPs for which a difference in relative concentration was apparent between the Sewage Treatment Plants (STPs) studied here that used chlorination and those employing chloramination disinfection treatment (as informed by the sampling and analysis strategy undertaken during the course of the task), and also for any compounds that showed particular seasonal concentration peaks.

Supported by the hazard profiles developed, appropriate ADIs, TDIs or RefDs were compared with the drinking water exposure information gathered during the course of the sampling campaign using standard defaults for intakes by particular population subgroups. Where no such value was available or where there was clear concern (because of more recent evidence on toxicity) as to the basis on which such values had been derived, a precautionary study-specific provisional acceptable daily intake (SSPADI) value was estimated using available information on the critical endpoint's no-adverse-effect or low-adverse-effect level (NOAEL and LOAEL, respectively) based on the most informative toxicity studies. It should be noted that these SSPADIs have no regulatory status, they have been derived on similar principles to ADI or RefD produced by international committees. On this basis, the margin of safety for each

compound was calculated so as to inform on the extent and nature of any appreciable risk that might exist.

A more detailed description of the work undertaken, and the findings and recommendations that arise, are presented in Appendix C.

4.2 HAZARD PROFILES FOR DBPs

4.2.1 Literature search

A comprehensive search structure was applied to the published and 'grey' literature using on-line databases. The output of the search was reviewed by experienced scientists and selected material obtained. In addition, the internet was searched to enable on-line access to authoritative reviews and assessments and databanks. Whilst the initial focus of the literature review was original papers, good quality reviews were identified and used to ensure that the appropriate literature was captured.

4.2.2 Derivation of hazard profiles and acceptable exposures

The human and animal toxicity data were subject to critical review by experienced toxicologists and detailed hazard profiles developed for each group of chemicals. In particular, attention was given to determining the following key aspects of toxicity:

- Human evidence of adverse effects;
- Toxicokinetics;
- Acute toxicity;
- Repeat dose toxicity;
- Genetic toxicology and carcinogenicity;
- Reproductive and developmental toxicity;
- Mechanism(s) of action; and
- Authoritative or project specific provisional acceptable levels.

Efforts were made, wherever possible, to identify an established exposure standard or guideline value by an authoritative body for each of the chemicals and/or groups, and to document the basis on which this value had been established.

For some of the potential contaminants considered, no authoritative standard (ADI, TDI or RefD) exists. In these cases, the toxicological datasets were considered to identify the nature and dosimetry of any critical end points of effect. The toxicological profiles were based on a review of the most current review evaluations published by authoritative organisations and extensive literature searches. Where possible, an appropriate '*de novo'* study-specific provisional acceptable daily intake (SSPADI) was derived from the data

available. In such instances, the relevant NOAEL was selected for the chemical, and an uncertainty factor applied that reflected the nature of the endpoint and the degree of uncertainty regarding the dataset; the approach adopted followed the guidance of the UK International Group of Health Risks from Chemicals (IGHRC, 2003).

For a number of chemicals, the toxicity dataset was grossly inadequate or absent. In such cases, read-across from other chemicals with similar properties was attempted to allow derivation of a putative SSPADI. However, despite these efforts in a few instances no suitable SSPADI could be identified and, for these, no hazard-based risk assessment could be derived with any confidence.

4.2.3 Risk assessment

The maximum measured concentration and the median measured concentration for each group of considered DBPs were used to calculate the total predicted daily (drinking water) intake values for an average consumer (adults and toddlers). These were then compared with the relevant authoritative standard or a derived SSPADI. The maximum measured concentration was taken as "worst-case" scenario for both toddler and adult exposures. It is acknowledged that the maximum determined levels include extreme outliers for some chemicals, and that extreme concentrations are unlikely to be experienced by the same population.

The potential worst-case exposure of the various sections of the human population considered were calculated by multiplying the maximum detected concentration of the compounds (from all chlorinated or chloraminated samples) present in drinking water supplies, with the standard default assumptions regarding the average amounts of water consumed per day by adults and children and used to determine estimates of intake for each person (DEFRA/EA, 2002). Where data were available, the intake of each individual substance from drinking water was expressed as a proportion of the "acceptable" intake derived from the authoritative standard or the SSPADI, for adults and toddlers separately.

In these initial assessments, a highly precautionary approach was adopted in which it was assumed that that all of the drinking water consumed would contain residues at the estimated levels, on a long-term basis. Where the total predicted daily intake amounted to less than 5% of the authoritative standard or the SSPADI, there was considered not to be any appreciable risk associated with these sources. Where a potential for exceeding 10% of the selected authoritative standard or the SSPADI was estimated for either adults or toddlers, a more detailed assessment of the extent and character of the risk was undertaken. Any value falling between 5 and 10% was considered on a case by case basis and discussed in the following sections.

4.3 OVERALL ASSESSMENT OF HAZARD PROFILES AND KEY DETERMINANTS OF TOXICITY FOR CHEMCIALS DETECTED IN EXPERIMENTAL INVESTIGATIONS

4.3.1 Chemicals not detected in water samples

The following individual or groups of chemicals were not measured in the chloraminated or chlorinated water samples analysed and, therefore, no risk assessment can be performed in the absence of any evidence of exposure:

- Trihalomethanes: water samples were not analysed for the presence of dibromoiodomethane, chlorodiiodomethane, bromodiiodomethane, or triiodomethane (due to the analytical methods used), whereas other trihalomethanes, including two iodinated species (dichloroiodomethane and bromochloroiodomethane) were analysed for and detected in both chlorinated and chloraminated samples;

- Haloacetic acids: water samples were not analysed for the presence of iodoacetic acid, bromoiodoacetic acid, 3-bromo-3-iodopropenoic acid, or 2-iodo-3-methylbutenedioic acid due to the analytical methods used, however other haloacetic acids were analysed for and detected in both chlorinated and chloraminated samples;

- Haloacetonitriles: water samples were analysed for the presence of four haloacetonitriles (all three dihalogenated species and trichloroacetonitrile), whereas samples were not analysed for the two monohalogenated species or the brominated analogues of trichloroacetonitrile;

- Halonitromethanes: water samples were analysed for the presence of trichloronitromethane (also known as chloropicrin; detected in both chlorinated and chloraminated samples), no other halonitromethanes were included in the analysis;

- Haloketones: samples were not analysed for haloketone concentrations;

- Haloaldehydes: samples were not analysed for haloaldehyde concentrations;

- Cyanogen halides: whilst analytical investigations identified that there was the theoretical potential for the formation of cyanogen halides, this only indicates the possibility of their generation. No evidence was available that this class of DBPs was actually present in any of the water samples tested, and in the absence of any data on exposure occurring at a quantifiable level, quantitative risk assessment is not possible.

- Haloacetamides: samples were not analysed for haloacetamide concentrations;

- Dimethyl cyanamide: samples were not analysed for DMC concentration;

- Halogenated furanones: samples were not analysed for halogenated furanone concentrations.

4.3.2 Chemicals detected in water samples

For the remaining chemicals included in the analysis suite, some evidence of exposure was found during the sampling programme and intake estimates were derived based on the highest level detected obtained in the sampling programme from all three sample collection periods. Intakes were calculated in terms of units per kg bodyweight per day for adults and for children. There is evidence to suggest that there is a significant degree of DBP exposure via inhalation during showering; indeed higher THM4 blood concentrations were noted in individuals after taking a 10 minute shower (n = 11) when compared to THM4 blood concentrations in individuals after drinking 1L of water (n = 10; (Backer et al., 2000). While it is acknowledged that inhalation and dermal exposure to DBPs may constitute an important proportion of the total DBP exposure of some individuals, it is not possible within the constraints of the current study design to estimate the extent of such exposures in the populations considered here. Therefore, the current assessment of risk posed by the various DBPs is restricted solely to consideration of oral exposure through consumption of drinking water.

The intake value of each chemical and/or group, as appropriate, was then compared with the most appropriate reference standard (be it an established guideline or standard) or with the SSPADI, for adults and toddlers separately. This approach is considered highly precautionary since it assumes the worse-case scenario in which all drinking water consumed by relevant individuals would contain residues at the worst-case levels on a long-term basis and, in addition, makes no allowance for only partial absorption of a chemical into the gastrointestinal tract or for volatilisation of compounds from the water during processing prior to consumption (e.g. as would be the case particularly for THMs when water is boiled prior to making a hot drink or preparation of infant milk formula). As a slightly more realistic, though still highly precautionary approach, intakes were also derived using the median detected values obtained from the sampling programmes for chlorination and chloramination plants separately. The values derived for both these scenarios are presented in Tables 4.1 to 4.4. Where the percentage of the derived intake value was greater than 5% of the appropriate reference standard, these are highlighted in the tables.

Table 4-1. Percentage of derived reference standards for highest concentrations (chloraminated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	*6.60*	15	**44.0**
Bromodichloromethane	*0.29*	2	**14.7**
Dibromochloromethane	*0.09*	21.4	**0.4**
Tribromomethane	*0.02*	17.9	**0.1**
THM4obs:THM4guide	*6.99*	56.3	**0.1**
THM4	***6.62***	**3.33**	**198.9**
Trichloroacetonitrile	*0.00*	0.2	**2.2**
Dichloroacetonitrile	*0.07*	0.7	**10.6**
Dibromoacetonitrile	*0.02*	2.3	**0.8**
Monochloroacetic acid	*0.23*	3.5	**6.6**
Dichloroacetic acid	*0.91*	7.6	**12.0**
Bromochloroacetic acid	*0.09*	41	**0.2**
Dibromoacetic acid	*0.33*	20	**1.6**
Trichloroacetic acid	*0.58*	32.5	**1.8**
HAA9obs:HAA9guide	*2.15*	78.6	**0.0**
HAA9 (sum)	***1.75***	**2**	**87.4**
NDMA	**0.00**	**0.0277**	**3.1**

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	*14.03*	15	**93.5**
Bromodichloromethane	*0.63*	2	**31.3**
Dibromochloromethane	*0.19*	21.4	**0.9**
Tribromomethane	*0.03*	17.9	**0.2**
THM4obs:THM4guide	*14.88*	56.3	**0.3**
Sum (trihalomethanes)	***14.09***	**7.09**	**198.7**
Trichloroacetonitrile	*0.01*	0.2	**4.6**
Dichloroacetonitrile	*0.15*	1.4	**10.6**
Dibromoacetonitrile	*0.04*	5	**0.8**
Monochloroacetic acid	*0.49*	3.5	**14.1**
Dichloroacetic acid	*1.94*	7.6	**25.5**
Bromochloroacetic acid	*0.19*	41	**0.5**
Dibromoacetic acid	*0.70*	20	**3.5**
Trichloroacetic acid	*1.24*	32.5	**3.8**
HAA9obs:HAA9guide	*4.57*	104.6	**0.0**
Sum (haloacetic acids	***3.72***	**4.25**	**87.5**
NDMA	**0.00**	**0.0277**	**6.7**

Table 4-2. Percentage of derived reference standards for median concentrations (chloraminated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	*1.41*	15	**9.4**
Bromodichloromethane	*0.06*	2	**2.8**
Dibromochloromethane	*0.01*	21.4	**0.0**
Tribromomethane	*0.002*	17.9	**0.0**
THM4obs:THM4guide	*1.48*	56.3	**0.0**
Sum (trihalomethanes)	***1.60***	**3.33**	**48.0**
Trichloroacetonitrile	*0.00*	0.2	**0.2**
Dichloroacetonitrile	*0.03*	0.7	**4.9**
Dibromoacetonitrile	*0.00*	2.3	**0.0**
Monochloroacetic acid	*0.08*	3.5	**2.2**
Dichloroacetic acid	*0.35*	7.6	**4.7**
Bromochloroacetic acid	*0.05*	15	**0.3**
Dibromoacetic acid	*0.02*	20	**0.1**
Trichloroacetic acid	*0.02*	32.5	**0.1**
HAA9obs:HAA9guide	*0.52*	78.6	**0.0**
Sum (haloacetic acids)	***0.55***	**2**	**27.6**
NDMA	***0.00***	**0.0277**	**1.6**

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	*3.01*	15	**20.0**
Bromodichloromethane	*0.12*	2	**5.9**
Dibromochloromethane	*0.01*	21.4	**0.1**
Tribromomethane	*0.004*	17.9	**0.0**
THM4obs:THM4guide	*3.14*	56.3	**0.1**
Sum (trihalomethanes)	***3.40***	**7.09**	**47.9**
Trichloroacetonitrile	*0.00*	0.2	**0.4**
Dichloroacetonitrile	*0.07*	1.4	**4.9**
Dibromoacetonitrile	*0.00*	5	**0.0**
Monochloroacetic acid	*0.16*	3.5	**4.6**
Dichloroacetic acid	*0.75*	7.6	**9.9**
Bromochloroacetic acid	*0.10*	41	**0.2**
Dibromoacetic acid	*0.04*	20	**0.2**
Trichloroacetic acid	*0.05*	32.5	**0.2**
HAA9obs:HAA9guide	*1.11*	104.6	**0.0**
Sum (haloacetic acids	***1.17***	**4.25**	**27.6**
NDMA	***0.00***	**0.0277**	**3.5**

Table 4-3. Percentage of derived reference standards for highest concentrations (chlorinated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	12.32	15	82.2
Bromodichloromethane	0.84	2	42.1
Dibromochloromethane	0.83	21.4	3.9
Tribromomethane	0.33	17.9	1.8
THM4obs:THM4guide	14.32	56.3	0.3
Sum (trihalomethanes)	13.96	3.33	419.3
Trichloroacetonitrile	0.01	0.2	2.6
Dichloroacetonitrile	0.03	0.7	5.2
Dibromoacetonitrile	0.07	2.3	2.8
Monochloroacetic acid	0.17	3.5	4.9
Dichloroacetic acid	2.20	7.6	28.9
Bromochloroacetic acid	0.27	41	0.7
Dibromoacetic acid	1.85	20	9.2
Trichloroacetic acid	1.08	32.5	3.3
HAA9obs:HAA9guide	5.57	78.6	0.1
Sum (haloacetic acids)	4.46	2	223.1

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	26.21	15	174.8
Bromodichloromethane	1.79	2	89.6
Dibromochloromethane	1.76	21.4	8.2
Tribromomethane	0.69	17.9	3.9
THM4obs:THM4guide	30.46	56.3	0.5
Sum (trihalomethanes)	29.70	7.03	422.5
Trichloroacetonitrile	0.01	0.2	5.5
Dichloroacetonitrile	0.07	1.4	5.2
Dibromoacetonitrile	0.14	5	2.8
Monochloroacetic acid	0.36	3.5	10.4
Dichloroacetic acid	4.68	7.6	61.5
Bromochloroacetic acid	0.57	41	1.4
Dibromoacetic acid	3.93	20	19.6
Trichloroacetic acid	2.30	32.5	7.1
HAA9obs:HAA9guide	11.84	104.6	0.1
Sum (haloacetic acids	9.49	4.25	223.4

Table 4-4. Percentage of derived reference standards for median concentrations (chlorinated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	2.58	15	17.2
Bromodichloromethane	0.40	2	19.9
Dibromochloromethane	0.07	21.4	0.3
Tribromomethane	0.00	17.9	0.0
THM4obs:THM4guide	3.05	56.3	0.0
Sum (trihalomethanes)	3.54	3.33	106.2
Trichloroacetonitrile	0.00	0.2	0.5
Dichloroacetonitrile	0.01	0.7	1.4
Dibromoacetonitrile	0.01	2.3	0.3
Monochloroacetic acid	0.05	3.5	1.5
Dichloroacetic acid	0.57	7.6	7.5
Bromochloroacetic acid	0.14	15	0.9
Dibromoacetic acid	0.11	20	0.6
Trichloroacetic acid	0.19	32.5	0.6
HAA9obs:HAA9guide	1.07	78.6	0.0
Sum (haloacetic acids)	2.11	2	105.6

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	5.49	15	36.6
Bromodichloromethane	0.85	2	42.3
Dibromochloromethane	0.14	21.4	0.7
Tribromomethane	0.00	17.9	0.0
THM4obs:THM4guide	6.49	56.3	0.1
Sum (trihalomethanes)	7.52	7.03	107.0
Trichloroacetonitrile	0.00	0.2	1.1
Dichloroacetonitrile	0.02	1.4	1.4
Dibromoacetonitrile	0.01	5	0.3
Monochloroacetic acid	0.11	3.5	3.2
Dichloroacetic acid	1.21	7.6	15.9
Bromochloroacetic acid	0.30	41	0.7
Dibromoacetic acid	0.24	20	1.2
Trichloroacetic acid	0.41	32.5	1.3
HAA9obs:HAA9guide	2.27	104.6	0.0
Sum (haloacetic acids	4.49	4.25	105.7

4.3.3 Consideration of risk for individual or groups of compounds for which the predicted daily intake from drinking water amounted to less than 5% of the reference standard

The following individual or groups of compounds (Table 4.5) were detected in water samples at amounts below 5% of the reference standard, even on the basis of a worst-case scenario (toddler exposure) using the highest water concentration detected.

Table 4-5. Individual or groups of compounds present in water samples at less than 5% of reference standard for toddlers in a worst-case scenario (using the highest recorded concentration).

Chloraminated samples	Chlorinated samples
Dibromomethane	Tribromomethane
Tribromomethane	Dibromoacetonitrile
Triacetonitrile	Chloropicrin
Dibromoacetonitrile	Bromochloroacetic acid
Chloropicrin	Trichloroacetic acid
Bromochloroacetic acid	THM4 (sum)[1] HAA9 (sum)[1]

[1]THM4 (sum) and HAA9 (sum) have been determined by taking the ratio of the sum of the observed concentrations against the sum of the guideline values.

The presence of these contaminants at such low levels is not considered to represent a significant risk to human health and will not be considered further.

4.3.4 Consideration of risk for individual or groups of compounds for which the predicted daily intake from drinking water amounted to between 5 and 10% of the reference standard

The only compound that was identified as having a predicted daily intake for adults of between 5 and 10% of the relevant reference standard or SSPADI when the highest measured chloraminated sample concentrations were considered was MCAA (6.6%; Table 4.1). When the same criteria were applied to chlorinated water samples, only DBAA (9.2%) and DCAN (5.2%) were identified (Table 4.3). As can be seen, even continuous exposure of humans to these compounds through drinking water at the highest concentrations detected in the sampling programme would represent only a small percentage of the health-based reference standards for these chemicals and is not considered to represent a significant issue with regard to human safety. Furthermore, when the more representative values based on median measured concentrations were used to calculate predicted daily intake, only TCM reached this nominal threshold intake range for chloraminated samples (Table 4.2) whilst DCAA (7.5%) was the only DBP identified for the chlorinated water samples (Table 4.4).

When intakes predicted for toddlers were considered, the highest predicted daily intake of DCAN (5.5%) and NDMA (6.7%) for chloraminated water

marginally exceeded 5% of the SSPADI. NDMA was the only detected species of nitrosamines, and it was only detected in samples at one works and its distribution system; the significance of this single occurrence within the context of a quantitative risk assessment is questionable. While, because of its toxicological properties, any exposure to NDMA is considered undesirable, the frequency of occurrence of this pollutant in the water supply is unclear on the basis of the current limited sampling programme. However, if viewed as an isolated occurrence then this finding is unlikely to represent any quantifiable risk to human health and should, in any case, be viewed in the context of the established major routes of human exposure to nitrosamines which are known to be through use of tobacco products and through some food stuffs (such as cured meats, fish and cheese; (Lijinsky, 1999). Indeed, it has previously been estimated that consumption of drinking water accounts for considerably less than 1% of the total intake of nitrosamines (Fristachi & Rice, 2007).

Comparisons based on the median measured concentrations in chloraminated water (excluding NDMA, for which the median value was not calculated due to a limited dataset) resulted in the predicted daily intake of BDCM (5.9%) and DCAA (9.9%) for toddlers which exceeded 5% but not 10% of the SSPADI, but these were again considered to represent only marginal diminutions of the margin of safety implicit for exposures lower than the reference standard. When the same criteria were applied to chlorinated water samples, the highest measured sample concentration resulted in a predicted daily intake of DBCM (8.2%) for toddlers exceeding 5% but not 10% of SSPADI, but when the median concentration levels were used there were no DBP that fell within this range.

4.3.5 Consideration of extent of risk for compounds or groups for which predicted daily intake from drinking water amounted to 10% or greater of the reference standard

A number of compounds and groups of compounds were found to have predicted daily intakes in excess of 10% of the relevant standard. For adults, exceedence of 10% of TDI or SSPADI was noted for TCM (44.0%), BDCM (14.7%), THM4 (198.9%), DCAN (10.6%), DCAA (12.0%) and HAA9 (87.4%) when the highest measured values of chloraminated samples was used in the calculation. Of these, only the predicted daily intake of THM4 concentration exceeded the reference value and thus represents a slight erosion of the safety margin. However, when the more representative median measured concentrations were used to calculate the predicted daily intake for adults, the percentage was significantly less for each compound or compound group (THM4 and HAA9 at 48.0% and 27.6 % of SSPADI, respectively). When chlorinated water samples were considered for adults, exceedence of 10% of SSPADI (or TDI) was noted for TCM (82.2%), BDCM (42.1%), THM4 (419.3%), DCAA (28.9), DBAA (9.2%), and HAA9 (223.1%). When the median measured concentration was used, the compounds exceeding 10% of TDI or SSPADI were: TCM (17.2%), BDCM (19.9%), THM4 (106.2%), DCAA (7.5%) and HAA9 (105.6%).

In the case of toddlers, six compounds or groups were found to exceed 10% of standard value when the highest measured values of chloraminated samples were considered, as follows: TCM (93.5%), BDCM (31.3%), THM4 (198.7%), MCAA (14.1%), DCAA (25.5%), and HAA9 (87.5%). However, when median measured concentrations were considered, only the predicted daily intake for TCM (20.0%), THM4 (47.9%), and HAA9 (27.6%) exceeded 10% of SSPADI. When maximum values for chlorinated water samples were evaluated, seven compounds or groups were found to exceed the 10% of SSPADI for toddlers: TCM (174.8%), BDCM (89.6%), THM4 (422.5%), DCAN (10.6%), MCAA (10.4%), DCAA (61.5%), DBAA (19.6%), and HAA9 (223.4%). When median measured concentrations were considered, only the predicted daily intake for TCM (at 36.6%), BDCM (42.3%), THM4 (107.0%), DCAA (15.9%), and HAA9 (105.7%) exceeded 10% of the SSPADI.

Thus, the two groups of compounds that exceeded 10% of the SSPADI were THMs and HAAs. For both groups, the chlorinated and brominated compounds have been shown to have different potencies with regards to mutagenicity, cytotoxicity and genotoxicity. In these cases it may not be appropriate to consider the concentrations of the sums of the brominated and chlorinated compounds in each group for use as the risk assessment but instead to consider the individual compounds separately.

If individual compounds are considered for chloraminated water samples, the relevance of the predicted highest intakes of TCM (93.6%), BDCM (31.3%), MCAA (14.1%) and DCAA (25.5%) to human health are considered questionable and of limited concern given that there is still a significant margin between these calculated intakes and the reference standard which is itself highly precautionary and designed to ensure the safety of the general population. If THM4 (198.7%) and HAA9 (87.5%) are considered, this safety margin is somewhat eroded. However, when median concentrations for chloraminated samples are used, no compound or compound group exceeds the relevant reference standard. When chlorinated water samples are considered using the same criteria for individual compounds, the relevance of the predicted highest intakes of BDCM (89.6%), DCAA (61.5%), DBAA (19.6%), and MCAA (10.4%) to human health are considered questionable and of limited concern given that there is still a margin between these calculated intakes and the reference standards, although this is eroded in the case of TCM (174.8%). When the predicted intake is calculated using the median measured concentration, the reference standard is exceeded only by THM4 (107.0%) and HAA9 (105.7%); this represents a slight erosion of the margin of safety.

If individual compounds are considered for chloraminated water samples, the relevance of the predicted highest intakes of TCM, BDCM, and DCA to human health are considered questionable and of limited concern given that there is still a significant margin between these calculated intakes and the reference standard which is itself highly precautionary and designed to ensure the safety of the general population. If THM4 and HAA9 are considered, this safety margin is somewhat eroded. However, when median concentrations are used, no compound or compound group exceeds the reference standard. When

chlorinated water samples are considered using the same criteria, the relevance of the predicted highest intakes of TCM, BDCM, DCA, and MCA to human health are considered questionable and of limited concern given that there is still a margin between these calculated intakes and the reference standard. When the predicted intake is calculated using the median measured concentration, the reference standard is exceeded only by THM4 and HAA9; this represents a slight erosion of the margin of safety. It should be noted, however, that when a modified approach is used to comparing $THM4_{obs}$:$THM4_{guide}$ and $HAA9_{obs}$:$HAA9_{guide}$ (see Section 3.4), neither ratio exceeded 1 suggesting that, in practice, there is little cause for concern across the whole population considered. However, it is noted that the ratio method takes into account the health-based guideline values for the individual chemical species but may not take into account chemical mixtures.

4.3.6 Consideration of potential for mixture interactions influencing overall toxic outcome

Investigation of exposures to, and risks posed by, DBPs is a rapidly evolving research area and as individual chemicals are identified and toxicity data become available, various component-based and whole-mixture techniques are being developed which will allow risk assessments to be further refined (Simmons et al., 2004). In addition, other models may allow cumulative risk assessment models for DBPs to take account of toxicokinetics and dose addition integrated over time (Teuschler et al., 2004).

4.4 CONCLUSIONS AND RECOMMENDATIONS

Most known DBPs are present at levels markedly below the levels of concern in the water samples tested.

In general, the concentrations of halogenated DBPs in chloraminated samples were at lower levels than chlorinated samples. Therefore, this suggests that chloramination of water samples generally reduces exposure to these DBPs when compared to chlorination of water samples.

NDMA was found at one works in one sample event that used chloramines. More information on the occurrence of this DBP of health concern is needed in order to allow a judgement to be reached as to the significance of this observation.

Certain DBPs were present in samples at levels (based on median values) which exceeded 10% of the reference standard for toddlers, namely TCM, THM4 and HAA9 in chloraminated samples and TCM, BDCM, THM4, DCAA, and HAA9 in chlorinated samples.

Risk assessment of DBPs is a rapidly evolving research area and as individual chemicals are identified and toxicity data become available, various component-based and whole-mixture techniques are being developed which will allow risk assessments to be further refined and cumulative risk assessment models to be developed. In this current investigation, the risk assessment of individual DBPs and groups of related DBPs has been done based on current toxicological knowledge and good practice.

5 OVERALL CONCLUSIONS

The research undertaken during this project has identified that:

- A literature review identified that the DBPs most likely to be found in chloraminated waters are from the group THMs, HAAs, HANs, HNMs, cyanogen halides and nitrosamines. 27 compounds were selected from these groups and were analysed for in three seasonal occurrence surveys of 7 water treatment works.
- In general, the concentrations of halogenated DBPs in chloraminated samples were at lower levels than chlorinated samples for samples exiting the works and in distribution. This is especially true for THMs and HAAs. Therefore, this suggests that chloramination of water samples generally reduces exposure to these DBPs when compared to chlorination of water samples.
- NDMA was identified at significant levels (26.0 ng L^{-1}) in chloraminated water but only at one works for one season and hence the significance of this is not clear without further sampling. More information on the occurrence of this DBP of health concern is needed. However, any risk assessment of the occurrence of NDMA must also consider the significant reduction in halogenated DBP formation that accompanies chloramination.
- Consideration of risk management must be undertaken for the DBPs that exceed 100% of standards and this was true for THM4 in both chlorinated and chloraminated samples. For a number of the works there is a need to increase precursor removal as chloramination alone is not enough to minimise the risks.

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APPENDIX A METHOD STATEMENTS

Table A.1 Methods of Analysis

ID	Analysis method	Method name
A.1.1	Dissolved organic carbon (DOC)	n/a
A.1.2	pH	n/a
A.1.3	Iodide and Bromide	n/a
A.1.4	Conductivity	Standard Method 2510 A, APHA 1998
A.1.5	High performance size exclusion chromatography (HPSEC)	n/a
A.1.6	Chlorine/chloramine demand	Standard Method 2350 B, APHA 1998
A.1.7	Formation potential test	Adapted from Standard Method 5710, APHA 1992
A.1.8	Determination of Haloacetic acids (HAA) in drinking water	Adapted from USEPA Method 552.3
A.1.9	Trihalomethanes (THMs), Haloacetonitriles (HANs) and Halonitromethanes (HNMs)	Adapted from USEPA Method 551.1
A.1.10	Cyanogen chloride and cyanogen bromide	Taken from Sclimenti et al. 1996

A.1 Method Statements

A.1.1 Non purgeable organic carbon (NPOC) measurement by high-temperature combustion method

Method Statement: The non purgeable organic carbon concentration of each sample is determined. As samples are filtered before analysis, the terms dissolved non purgeavle organic carbon and total non purgeable organic carbon are used interchangeably. The organic content of a sample is often an indication of its propensity to form disinfection by-products when exposed to a disinfectant. Generally higher NPOC values give rise to higher levels of DBPs.

Standard Operating Procedure

Before analysis, samples are filtered to 1.2 μm using Whatman glass fibre filter paper; grade GF/C (Fisher Scientific UK).

Principle: NPOC was measured using a Shimadzu TOC-5000A analyser (Shimadzu, Milton Keynes, UK). Samples were acidified and purged with air to convert the inorganic carbon to CO_2. The total carbon (TC) of the sample was then measured and was referred to as NPOC.
To measure the total carbon, the sample is diluted as necessary and a microportion is injected into a heated reaction chamber packed with an oxidative catalyst such as platinum. The water is vaporised and the organic carbon is oxidised to CO_2 and H_2O. The CO_2 from oxidation of organic and inorganic carbon is transported into the carrier gas system and measured by means of a non-dispersive infrared (NDIR) analyser.

Calibration: The TC standard was made by dissolving 2.125 g potassium hydrogen phthalate in 1 L RO water. The standard had a concentration of 1000 mg L^{-1} and working standards were diluted to the appropriate concentration with deionised water. The machine was calibrated before each use.

Measurement: The analyser took up to five replicates and reported an average of three given that the coefficient of variance was not greater than 2%.

Quality Control: In addition to calibrating the machine before each use, after every tenth analysis, a blank and laboratory control sample prepared from a source other than the calibration standards and at a similar level to the samples will be run. The laboratory control sample will be a solution of commercial humic acid at 5 mg/L.

Precision: Interlaboratory studies conducted in the range above 2 mg/L have been carried out (Standard Methods 5310B, APHA 1998). The resulting equation for single-operator precision on matrix water is:

$S_o = 0.027x + 0.29$

Overall precision is:

$S_t = 0.044x + 1.49$

Where S_o = single-operator precision, S_t = overall precision and x = TOC concentration in mg/L

A.1.2 pH

Method Statement: The measurement of pH will be carried out during certain analyses to ensure pH values are uniform as DBP analyses can be affected by pH. For example, more THMs are formed at high pH than at low pH values.

Standard Operating Procedure

Measurement: pH measurements are undertaken using an electrode that is specific for the measurement of hydrogen ions. The pH of a solution is equivalent to the negative log of the activity of the hydrogen ions (pH = –log $[H^+]$). Temperature is compensated for by using a temperature probe which is put into the sample alongside the electrode. A Jenway 3520 pH meter will be used for all measurements.

Calibration: Calibration will be carried out before each use. Commercially available pH buffers at pH 4, 7 and 10 will be used for calibration.

Precision and bias: The careful use of a laboratory pH meter with good electrodes results in a precision of ± 0.02 pH units with a bias of ± 0.05 pH units. However, ± 0.1 pH units represents the limit of bias under normal conditions especially for the measurement of water and poorly buffered solutions. Values should be reported to the nearest 0.1 pH unit.

A.1.3 Iodide and Bromide

Method Statement: Samples are analysed to determine their levels of bromide and iodide. This will give an indication of the sample's likelihood to form brominated and iodated disinfection by-products.

Standard Operating Procedure

Principle: Samples are analysed using inductively coupled plasma mass spectrometry (ICP-MS). The ICP-MS can measure most of the elements in the periodic table at or below the parts per trillion (ppt) range. At the extremely high temperature of the plasma ion source, the molecules are completely broken down. As a result the ICP-MS detects only elemental ions. ICP-MS can also determine the individual isotopes if each element which allows isotope ratio and isotope dilution measurements.

Quantification and calibration: The ICP-MS (Elan 9000, Perkin Elmer, UK) accurately determines how much of a specific element is in the material analysed. The concentration of each element is determined by comparing the counts for a selected isotope to an external calibration curve generated for that element. For bromide, a calibration curve will be set up from 10 – 250 μg/L and for iodide, 0.5 – 15 μg/L. Samples that are outside the calibration range will be diluted volumetrically.

Operation: Liquid samples are introduced to the ICP-MS by a peristaltic pump whereupon samples are nebulised and sprayed into the instrument to meet the high temperature plasma. For each samples, 3 replicates are analysed at a rate of 60 sweeps per reading. The integration time is set at 3000 ms and the dwell time 50 ms per atomic mass unit. The scan mode is peak hopping. The carrier gas is argon set at 1 mL/minute.

Quality assurance: Samples will be run in triplicate. Every 15 samples a calibration standard and a blank will be run.

A.1.4 Conductivity (Standard Method 2510 A, APHA 1998)

Method Statement: Samples are analysed to determine their conductivity. This will give an indication of the hardness and alkalinity of the sample.

Standard Operating Procedure

Chemistry: Conductivity is the measure of the ability of an aqueous solution to carry an electric current. This ability depends on the presence of ions: on their total concentration, mobility and valence; and on the temperature of measurement. Solutions of most inorganic compounds are relatively good conductors. Conversely, molecules of organic compounds that do not dissociate in aqueous solution conduct a current very poorly, if at all.

Definitions and units of expression: Conductance of a solution is measured between two spatially fixed and chemically inert electrodes. To avoid polarisation at the electrode surfaces the conductance measurement is made with an alternating current signal. The conductance of a solution, G, is directly proportional to the surface area, A (cm^2) and inversely proportional to the distance between the electrodes, L (cm). The constant of proportionality, k, such that:

$$G = k\,(A/L)$$

is called 'conductivity'. It is a characteristic property of the solution between the electrodes. The SI units of conductivity are siemens (S) and conductivity is reported in millisiemens per metre (mS/m).

Measurement: In the laboratory, conductance (G_s) of a standard KCl solution is measured and from the corresponding conductivity, k_s (from table), a cell constant, C (cm^{-1}) is calculated:

$$C = (k_s/G_s)$$

Equivalent Conductivity, Λ, and conductivity, k, of potassium chloride at 25 °C

KCl concentration (M/L)	Equivalent conductivity Λ (mS/cm^2)	Conductivity k_s (mS/cm)
0	14.99	
0.0001	14.89	1.49
0.0005	14.77	7.39
0.001	14.69	14.69
0.005	14.36	71.75
0.01	14.12	141.2

0.02	13.82	276.5
0.05	13.33	666.7
0.1	12.89	1289
0.2	12.40	2480
0.5	11.73	5867
1	11.19	11190

Once the cell constant has been determined, the conductivity of an unknown solution can be calculated

$k_u = CG_u$

The conductivity meter is a Jenway 4010 Conductivity Meter (Patterson Scientific, UK) which compensates for temperature.

Precision and bias: the precision of commercial conductivity meters is commonly between 0.1 and 1.0 %. Reproducibility of 1 to 2 % is expected after an instrument has been calibrated with data from the table above.

A.1.5 High performance size exclusion chromatography (HPSEC)

Method Statement: Samples are analysed to determine their molecular weight profile. The analysis is comparative and gives information on the molecules removed during treatment processes.

Standard Operating Procedure

Principle: Samples are analysed to determine their molecular weight profile. Chromatographic separation by size is used with detection at 254 nm (ultraviolet range). At this wavelength aromatic molecules will give a response whereas molecules with single bonds will not be detected.

Measurement: The samples will be analysed at their natural DOC concentration and filtered to 1.2 μm before analysis. HPSEC will be carried out using an HPLC (Shimadzu VP Series, Shimadzu, Milton Keynes, UK) with UV detection set to 254 nm. The mobile phase will be 0.01 M sodium acetate at a flow rate of 1 ml min^{-1}. The column is a BIOSEP-SEC-S3000 7.8 mm (ID) × 30 cm and the guard column is a 'Security Guard' fitted with a GFC-3000 disc 4.0 mm (ID) × 3.0 mm (Phenomenex UK, Cheshire, UK). For each sample a chromatogram of ultraviolet (UV) absorbance (absorbance units) against time (minutes) will be produced.

Quality Control: A solution of humic acid (10 mg/L) is run alongside each batch of samples. The peak heights and areas are measured to determine that they are within 10 % of the expected values.

Precision: The analysis is purely comparative and does not involve quantification. Therefore precision is not calculable.

A.1.6 Chlorine/chloramine demand (Standard Method 2350 B, APHA 1998)

Method Statement: The intention is to expose samples to chlorine or chloramines for a specified period of time in order to determine the sample's potential to form disinfection by-products. Here, samples are exposed to differing concentrations of chlorine or chloramines to determine the appropriate dose. The aim is to achieve a chlorine residual of $\geq$ 1 mg/L Cl_2.

Standard Operating Procedure

Chemistry: The fate of oxidants in water and wastewater is complex. For example, chlorine reacts with sample constituents by three general pathways: oxidation, addition and substitution. First chlorine can oxidise reduced species such as Fe^{2+}, Mn^{2+} and sulphide. In these reactions chlorine is reduced to inorganic chloride (Cl^-). Second, chlorine can add to olefins and other double-bond-containing organic compounds to produce chlorinated organic compounds. Third, chlorine can substitute onto chemical substrates. Oxidant demand is influenced by temperature, pH, contact time and oxidant dose. As a result, oxidant demand should always be reported alongside pH, time and temperature conditions.

Principle: The sample is divided into subsamples and each is dosed with the standardised oxidant (chlorine/chloramine) solution to yield a series of increasing doses. After the appropriate contact time, oxidant residual, pH and temperature are measured and the demand/requirement determined by difference between initial and final concentrations.

Sampling: Most reliable results are obtained on fresh samples that contain low amount of suspended solids. If samples will be analysed within 24 hours of collection, refrigerate unacidified at 4 °C immediately after collection. To preserve for up to 28 days, freeze unacidified samples at -20 °C. Warm chilled samples to desired test conditions before analysis.

Reagents: Deionised, chlorine demand free water, acetic acid (glacial), potassium iodide crystals, standard sodium thiosulphate titrant (0.025N), starch indicator solution, standard chlorine solution.

Procedure: Measure three equal sample portions of 75 mL into 100 mL bottles with PTFE lined screw caps. Buffer samples including blank with 2 mL pH7 buffer. Add increasing amounts of a standard chlorine solution to successive portions in the series. Increase dosage by 0.1 mL increments for low demands and increase by 1.0 mL increments for high demands.

Determination of the chlorine residual was carried out using an adaptation of procedure 4500-Cl in 'Standard Methods for the Examination of Water and Wastewater' (American Public Health Association 1992) and is described below.
After the bottles were stored during the contact time required, the chlorine residual was measured as follows:
Titration is carried out away from direct sunlight. The burette is filled up with 0.01N of sodium thiosulphate ($Na_2S_2O_3$). 5 mL of acetic acid and about 1 g of potassium iodide (KI) are placed in a conical flask. Then a volume sample of 100 mL is added. Titration is carried out until the yellow colour of the liberated iodine is almost discharged. Starch solution is added and titrated until the blue/black colour is discharged.

Blank titration: This is carried out to correct the result of sample titration by determining the blank contribution by oxidising or reducing reagent impurities. The blank also compensates for the concentration of iodine bound to starch at the end point. A volume of deionised water corresponding to the volume sample used for titration is placed in a conical flask followed by 5 mL of acetic acid, plus 1 g of KI. The titration is performed as follows:
Before calculating the chlorine concentration, the blank titration is subtracted from the sample titration; or, if necessary, the net equivalent value is added to the blank titration.

The chlorine residual was calculating using the equation:

$$\text{Chlorine Residual (mg Cl as } Cl_2\text{/L)} = Co - \frac{(A \pm B) \times N \times 35450}{mLsample}$$

Where:

C_o = initial concentration of chlorine (mg Cl as Cl_2/L)
A = mL titration for sample
B = mL titration for blank (positive or negative) and
N = normality of $Na_2S_2O_3$

Precision and bias: Because demand is calculated by difference, the uncertainty associated with the demand value will be greater than the uncertainty of the individual residual measurements. If the standard deviation of the dose measurement and residual measurements are the same, then the standard deviation and minimum detection limit of the oxidant demand will be $\sqrt{2}$ times the standard deviation and minimum detection limit of the measurement technique respectively.
The chlorine dose and amount consumed affect the precision in two ways. First, the amount consumed must be sufficiently large, relative to the dose, to minimise errors associated with a value calculated from the difference of two numbers of approximately equal value. Second, the amount consumed must be small enough, relative to the dose to prevent the residual concentration from being too small.

A.1.7 Formation potential test (adapted from procedure 5710 in 'Standard Methods for the Examination of Water and Wastewater' (American Public Health Association 1992)).

Method Statement: Samples are exposed to chlorine or chloramines for a specific period of time under specified conditions. Following this, the potential for water samples to from disinfection by-products can be assessed.

NOTE: samples were chlorinated according to the chlorine demand calculated to give a chlorine residual of 1 mg L^{-1}. Samples were chloraminated using preformed monochloramines at the same level as chlorine in order to have a direct comparison of chlorine vs chloramines.

Standard Operating Procedure

Principle: Under standard conditions, samples are buffered at pH 7.0 ± 0.2, chlorinated with an excess of free chlorine (or monochloramine) and stored at 20 ± 2 °C for 7 days to allow the reaction to continue to completion. At the end of the reaction period, ≥ 1 mg/L free chlorine should remain so as not to limit the reaction. After the 7 day period, the chlorine is quenched to prevent the reaction from proceeding further and samples analysed for the disinfection by-products formed.

Reagents:

Hypochlorite solution

Determination of strength of hypochlorite (HOCl) solution – sodium hypochlorite (8%), 3 mL solution was diluted to 600 mL in a glass bottle with deionised water and mixed well. The diluted solution (100 mL) was placed in a conical flask containing acetic acid glacial (5 mL) and potassium iodide (~ 1 g). The contents of the flask were mixed and titrated with standard sodium thiosulphate (0.1M) until the yellow colour of the liberated iodine was almost discharged. Starch indicator powder (~0.5 g) was added and the titration continued until the blue/black colour was discharged. The volume was recorded. The chlorine concentration of the sodium hypochlorite was calculated using the following equation:

$$Hypochlorite\ concentration\ (mg\ L^{-1}\ Cl_2) = \frac{(M \times 35450 \times titrant\ volume\ (mL))}{hypochlorite\ added\ (mL)}$$

Where M is the molarity of the titrant (sodium thiosulphate).

The strength of the hypochlorite solution was measured every week. The sodium hypochlorite solution was discarded when the concentration fell below 20 mg L^{-1} Cl_2 (every two weeks).

Buffer

Stock solutions of sodium phosphate dibasic (Na_2HPO_4) at 1/15 M and potassium acid phosphate (KH_2PO_4) at 1/15 M were prepared respectively by dissolving 4.733g in 0.5 L deionised water and 4.540g in 0.5 L deionised water. The buffer at pH 7.2 was made up by adding 27 mL of the KH_2PO_4 stock solution to 73 mL of Na_2HPO_4. The buffer was made fresh when the pH fell below 0.2 pH unit of the expected value.

Sodium sulphite solution

10 g sodium sulphite was dissolved in 100 mL deionised water. It was used for dechlorination. 0.1 mL destroyed about 5 mg residual chlorine. This solution was discarded after 2 weeks.

Sample chlorination: The appropriate volume of chlorine dosing solution (so that the final concentration was 5 mg/L) was put in a 100 mL glass bottle with PTFE-lined screw cap with 2 mL of buffer. Then the bottle was filled completely with sample. Bottles were stored at 20 ± 2^{o}C for 7 days.

Quality control samples: 5 mg/L chlorine dosing solution was put into 100 mL glass bottle with PTFE-lined screw cap with deionised water. 2 mL of buffer was added. Then the bottle was filled with deionised water and stored with the samples at 20 ± 2 ^{o}C for 7 days.

Precision and bias: The precision and bias of this method is determined by the analytical precision and bias for the method used for measuring the disinfection by-products formed as well as the control of variables such as pH, chlorine residual, temperature and sample homogeneity.

A.1.8 Determination of Haloacetic acids (HAA) in drinking water (adapted from USEPA Method 552.3)

Method Statement: Samples that have been exposed to chlorine or chloramines are analysed for disinfection by-products (DBPs) formed. One specific group of compounds is determined: HAAs. The HAAs are acidified and extracted by liquid-liquid extraction into the solvent phase. The HAAs are then converted to their more volatile methyl esters and the solvent extract neutralised. The solvent extract is injected into a Gas Chromatograph with Electron Capture Device detection for quantification.

Standard Operating Procedure

Summary of Method: A 30 mL sample is adjusted to a pH of 0.5 or less and extracted with 3 mL of methyl tert-butyl ether (MTBE) containing an internal standard (1,2,3-trichloropropane). The HAAs that have been partitioned into the organic phase are then converted to their methyl esters by the addition of acidic methanol followed by heating for 2 hours. The solvent phase containing the methylated acids is separated from the acidic methanol by adding 3 mL of a concentrated sodium sulphate solution. The aqueous phase is discarded. The

extract is neutralised by further addition of the sodium sulphate solution (1 mL) and the solvent layer removed for analysis. The target analytes are identified and quantified using capillary gas chromatography using an electron capture device detector. Analytes are quantified relative to the internal standard.

Sample collection: Samples are collected using glass vials with PTFE screw lined caps and capacities of at least 50 mL. Prior to collection, sample vials are prepared with either ammonium chloride or sodium sulphite granules. Fill sample vials but take care not to flush out the granules. After collecting the sample, screw the cap on and agitate by hand for 15 seconds. Samples must be chilled during transport and storage ($\leq$ 10 °C) and extracted/derived within 14 days.

Method detail:
HAA derivatisation

1. Remove samples from storage and allow them to equilibrate to room temperature.
2. Measure exactly 30 mL sample into a 60 mL glass vial with PTFE septum lid by weight.
3. Add approximately 1.5 mL sulphuric acid (to achieve pH 1.5)
4. Add 3 mL MTBE with internal standard using a dispenser (internal standard is 1, 2, 3 – trichloropropane at 300 μg/L)
5. Add approximately 12 g sodium sulphate into vial, replace cap and shake for approx. 3 minutes (put vial on side if not shaking immediately to prevent clumping).
6. All layers to separate for 5 minutes
7. Transfer ~1 mL upper layer to a test tube.
8. Add approx 1 mL of freshly made 10% sulphuric acid/methanol solution (add methanol first, hood down, double gloves on while making solution).
9. Cap tubes tightly and place in 50°C water/sand bath for exactly 2 hours. Ensure the temperature is 50°C by using a thermometer.
10. After 2 hours, take out tubes and let tubes cool to room temperature (at least 5 minutes)
11. Add approximately 1 mL MTBE (no internal standard) to each tube.
12. Add 3 mL of 10% sodium sulphate into each tube and vortex for 30 seconds
13. Remove water from bottom phase.
14. Add 1 mL of 10% sodium sulphate into each tube and vortex for 30 seconds
15. Tranfer approximately 1 mL of MTBE top layer to a GC vial and analyse using the method below.

Notes: sodium sulphite should be muffled by heating overnight in an oven at just over 100 °C. MTBE is methyl tert butyl ether.

HAAs were then measured on a gas chromatograph with a micro electron capture detector (Agilent 6890 GC-ECD). A capillary column (Rtx-1MS – 15 m $\times$

0.25 mm id × 0.25 μm) was used with helium carrier gas at a constant rate of 1.1 mL min^{-1}. The split ratio was set at 10:1. A volume of 1 μL was injected. The initial oven temperature was 35°C held for 8 minutes followed by an 8°C per minute temperature ramp to 200°C and hold for 1 minute. The temperature of the injector was set at 200°C and the detector at 270°C. The rate of data collection was 20 Hz.

Calibration: At least 5 calibration standards are required to prepare the calibration curve. Standards are treated in exactly the same way as samples. To create a calibration curve plot (peak area/IS area) against the standard concentration. Quantify by dividing the peak area of the sample by the IS area for that sample. That is, all peak areas are normalised with respect to the internal standard area for each sample.

Quality Assurance: Samples will be analysed in batches of 30. Standards will be run first followed by samples. After 15 samples and at the end of the batch, a laboratory blank (deionised water) will be run followed by a standard at 20 μg/L to check the calibration. Each blank should have a response less than the detection limit for each HAA. The calibration check should be within ± 30% of the expected value.
The response of the internal standard (IS) in each standard sample and quality control sample will be monitored. The area of the IS peak should not deviate by more than ± 50% from the average area measured during the initial calibration.
A fortified sample matrix will also be produced for each batch to determine that the sample matrix does not adversely affect method performance. This will consist of one non-chlorinated field sample being spiked with the 9 HAAs at a known concentration (50 μg/L). The value should not deviate from the expected value by more than ± 30%.

Limit of Detection: The limit of detection is determined by preparing at least seven replicates of deionised water spiked with low levels of each HAA (~1 μg/L). The prepared samples are extracted as detailed above. The detection limit is calculated using the formula:

$$\text{Detection limit} = \text{STDEV} \times t_{(n-1,\ 1-\alpha = 0.99)}$$

Where STDEV is the standard deviation of the replicate analyses, n is the number of replicates and t is the Students t value for 99 % confidence level with n-1 degrees of freedom.

A.1.9 Trihalomethanes (THMs), Haloacetonitriles (HANs) and Halonitromethanes (HNMs) (adapted from USEPA Method 551.1)

Method Statement: Samples that have been exposed to chlorine or chloramines are analysed for disinfection by-products (DBPs) formed. Three specific groups of compounds are determined: THMs, HANs and a HNM. The DBPs are extracted by liquid-liquid extraction into the solvent phase. The solvent extract is

injected into a Gas Chromatograph with Electron Capture Device detection for quantification.

Standard Operating Procedure

Summary of Method: A 50 mL sample aliquot is extracted with 3 mL of MTBE or 5 mL of pentane. Two μL of the extract is then injected into a GC equipped with a fused silica capillary column and linearised electron capture device for separation and analysis.

Sample collection: Samples are collected using glass vials with PTFE screw lined caps and capacities of at least 50 mL. Prior to collection, sample vials are prepared with either ammonium chloride or sodium sulphite granules. Vials will also contain a buffer (granular) to adjust the pH to 4.5-5.5. Fill sample vials completely but take care not to flush out the granules. After collecting the sample, screw the cap on and agitate by hand for 15 seconds. Samples must be chilled during transport and storage ($\leq$ 4 °C) and extracted/derived within 14 days.

Buffer preparation: used to lower sample matrix pH to 4.8-5.5 in order to inhibit base catalysed degradation of the HANs and to standardise the pH of all of the samples. Prepare by homogenously mixing 1% sodium phosphate dibasic (Na_2HPO_4) with 99% potassium phosphate monobasic (KH_2PO_4) by weight. Both salts should be in granular form and be ACS grade or better.

Note: the dechlorinating agent can be combined with the buffer as a homogenous mixture. For example, if 200 g of buffer is prepared, 1.2 g of ammonium chloride or sodium sulphite can be added to the buffer mixture. Then 1 g of the buffer/dechlorinating mixture can be added to a 60 mL vial for sample collection. This gives a concentration of 100 mg/L of the dechlorinating agent.

Method detail:
DBP derivatisation

1. Remove samples from storage and allow them to equilibrate to room temperature.
2. Remove the vial caps and remove a 10 mL aliquot for pH measurement. Check the pH to verify it is within the range 4.5-5.5. If the pH is not within range, a new sample must be collected.
3. Replace the vial caps and weigh the containers with contents to the nearest 0.1 g and record these weights for subsequent volume determination.
4. Add 3 mL MTBE with internal standard using a dispenser (internal standard is bromoflurobenzene at 1 μg/mL)
5. Add approximately 10 g sodium chloride or 20 g sodium sulphate into vial, replace cap and shake for approx. 4 minutes (put vial on side if not shaking immediately to prevent clumping).
6. All layers to separate for 2 minutes

7. Tranfer approximately 1 mL of MTBE top layer to a GC vial and analyse using the method below.

Notes: sodium sulphite and sodium chloride should be muffled by heating overnight in an oven at just over 100 °C. MTBE is methyl tert butyl ether. The use of NaCl should be avoided with preference given to Na_2SO_4 as the extraction salt. This is due to the presence of bromide in the NaCl which can give rise to an increase in brominated DBPs measured.

DBPs (trichloromethane, dichlorobromomethane, dibromochloromethane, tribromomethane, bromochloroacetonitrile, dibromoacetonitrile, dichloroacetonitrile, trichloroacetonitrile and chloropicrin) were then measured on a gas chromatograph with a micro electron capture detector (Agilent 6890 GC-ECD). A capillary column (Rtx-1MS – 15 m $\times$ 0.25 mm id $\times$ 0.25 μm) was used with helium carrier gas at a constant linear velocity of 25 cm/second. The split ratio was set at 10:1. A volume of 1 μL was injected. The initial oven temperature was 35 °C held for 0 minutes followed by a 2 °C per minute temperature ramp to 50 °C and held for 10 minutes. The temperature was increased to 225 °C at a rate of 10 °C/minute and held for 15 minutes followed by an increase to 260 °C at a rate of 10 °C/minute and held for 30 minutes. The temperature of the injector was set at 200°C and the detector at 290°C. The rate of data collection was 20 Hz.

Calibration: At least 5 calibration standards are required to prepare the calibration curve. Standards are treated in exactly the same way as samples. To create a calibration curve plot (peak area/IS area) against the standard concentration. Quantify by dividing the peak area of the sample by the IS area for that sample. That is, all peak areas are normalised with respect to the internal standard area for each sample. Standards should not be prepared in a volumetric flask and weighed into glass vials due to the volatility of the analytes. Standards should be prepared using a prepared aliquot of deionised water followed by syringe injection of the appropriate amount of standard into the middle of the water volume. Aqueous standards should be prepared daily and extracted immediately after preparation.

Quality Assurance: Samples will be analysed in batches of 30. Standards will be run first followed by samples. After 15 samples and at the end of the batch, a laboratory blank (deionised water) will be run followed by a standard at 20 μg/L to check the calibration. Each blank should have a response less than the detection limit for each analyte. The calibration check should be within $\pm$ 25% of the expected value.
The response of the internal standard (IS) in each standard sample and quality control sample will be monitored. The area of the IS peak should not deviate by more than $\pm$ 20% from the average area measured during the initial calibration.
A fortified sample matrix will also be produced for each batch to determine that the sample matrix does not adversely affect method performance. This will consist of one non-chlorinated field sample being spiked with the 9 DBPs at a

known concentration (50 μg/L). The value should not deviate from the expected value by more than $\pm$ 30%.

Limit of Detection: The limit of detection is determined by preparing at least seven replicates of deionised water spiked with low levels of each DBP (~1 μg/L). The prepared samples are extracted as detailed above. The detection limit is calculated using the formula:

$$\text{Detection limit} = \text{STDEV} \times t_{(n-1,\ 1-\alpha = 0.99)}$$

Where STDEV is the standard deviation of the replicate analyses, n is the number of replicates and t is the Students t value for 99 % confidence level with n-1 degrees of freedom.

A.1.10 Analysis of Nitrosamines (USEPA method 521)

Nitrosamine analysis was carried out by Scottish Water Solutions (Edinburgh, UK) using USEPA method 521 which involves a solid-phase cartridge that is conditioned with dichloromethane, methanol, and high-performance liquid chromatography (HPLC)-grade water. 500 mL of the potable or raw water sample is then passed through the cartridge. After drying the sample lines using a vacuum and the cartridges using a centrifuge, the sample is eluted with dichloromethane. An internal standard is added to the extract, which is then evaporated to 0.5 mL. This mixture is then transferred to a sealed gas chromatography (GC) vial, and it is then stored in a refrigerator until required for analysis by GC-mass spectrometry (MS) (electron impact [EI]+). Analysis is performed using selected ion recording. A spiked sample is also put through the process to allow for extraction recovery correction.

The specific nitrosamines analysed, the method calibration range, and the limits of detection are listed in the table below.

Compound	Code	Range (ng/L)	Limit of detection (ng/L)
N-Nitrosodimethylamine	NDMA	1.0 to 50.0	1.0
N-Nitrosomethylethylamine	NMEA	1.0 to 50.0	1.0
N-Nitrosodi-n-propylamine	NDPA	2.0 to 50.0	2.0
N-Nitrosopyrollidine	NPYR	2.0 to 50.0	2.0
N-Nitrosopiperidine	NPIP	2.0 to 50.0	2.0

Throughout the project the samples will be collected in 500-mL glass Duran bottles with red Teflon (PTFE) caps and liners and where required the bottles will contain 0.12 mL of 10% sodium thiosulphate solution to neutralise (quench) any chlorine or chloramines residuals in the samples. Samples will be transported from between sample sites, Cranfield, and Scottish Water Scientific Services under temperature-controlled conditions. Details of the rigorous quality control procedures to ensure quality are listed below. For each batch of samples the analysis includes:

1. A recovery sample – 500 mL of a similar matrix spiked with a known amount, put through the procedure to check % recovery for the batch of samples, taking into account a matrix blank (samples are corrected for this).
2. A blank control sample is run to ensure no process effects (samples are corrected for this).
3. A quality control sample – put through the procedure and the results entered into a Shewhart chart to check statistical controls. This allows one to compare results to statistically defined control limits.
4. System suitability injection to ensure sufficient sensitivity and system stability.
5. 5-point calibration curve with drift checks at least every 10 samples.

A.1.10 Analysis of Cyanogen Chloride and Cyanogen Bromide (adapted from Sclimenti et al. 1996)

Method Statement: Samples that have been exposed to chlorine followed by exposure to chloramines are analysed for CNCl and CNBr formed. The cyanogen halides are extracted by liquid-liquid extraction into the solvent phase. The solvent extract is injected into a Gas Chromatograph with Mass Spectrometric detection for qualification.

Standard Operating Procedure

Summary of Method: A 30 mL sample is extracted by addition of 10g of sodium sulfate (Na_2SO_4) and 4 mL of methyl tert-butyl ether. The sample is then shaken in a mechnical shaker for 10 minutes. The methyl tert-butyl ether layer is transferred between two 1.5-mL autosampler vials. The analysis is conducted on a gas chromatograph (GC) with temperature programming and a fused silica capillary column to obtain baseline resolution of all the analytes. Detection is with a mass spectrometer detector.

Sample collection: Samples are collected using glass vials with PTFE screw lined caps and capacities of at least 40 mL. Prior to collection, sample vials are prepared with ascorbic acid (0.1 mL of a 0.142M freshly prepared solution) as a quenching agent. Fill sample vials completely but take care not to flush out the ascorbic acid. Sulphuric acid should also be added to the samples to bring the pH to 2-3 thereby stabilising the CNBr from degradations. Samples must be chilled during transport and storage ($\leq$ 4 °C). Samples should not be kept for longer than 48 hours.

Due to the danger of preparing CNCl and CNBr standards and the unavailability of standards from industry, CNCl and CNBr will be determined qualitatively but not quantitatively.

Method detail:
CNCl and CNBr derivatisation

1. Remove samples from storage and allow them to equilibrate to room temperature.
2. A 30 mL aliquot is withdrawn from the sample container and placed in a 60 mL glass vial.
3. Add approximately 10 g sodium sulphate into vial followed by 4 mL MTBE with internal standard using a dispenser (internal standard is bromoflurobenzene at 1 μg/mL).
4. The vials are then capped and shaken for 3 minutes manually.
5. Stand upright and allow layers to separate for 5 minutes
6. Tranfer approximately 1 mL of MTBE top layer to a GC vial and analyse using the method below.

Notes: sodium sulphite should be muffled by heating overnight in an oven at just over 100 °C. MTBE is methyl tert butyl ether.

CNCl and CNBr were then measured on a gas chromatograph with a mass spectrometer detector (Perkin Elmer Turbo Mass Gold). A capillary column (Rtx-624 – 30 m × 0.25 mm id × 1.25 μm) was used with helium carrier gas at a constant linear velocity of 1.25 mL/miute. The injection was split-less with the split valve opening after 2.5 minutes. A volume of 1.5 μL was injected. The initial oven temperature was 30 °C held for 0 minutes followed by a 10°C per minute temperature ramp to 120 °C then ramped up to 190°C at 35°C per minute and held for 1 minute. The temperature of the injector was initially set at 35°C and ramped to 200 °C at a rate of 180 °C per minute.
The mass spectrometer conditions were as follows:
0.5 minute solvent delay TIC scan m/z 20-150 amu
SIR Masses 61 and 63 for CNCl
SIR Masses 105 and 107 for CNBr
Transfer line temperature – 190 ˚C
Source temperature – 190 ˚C
Electron Energy – 70 eV
Multiplier Voltage – 500 V

A.2 Method Limits of Detection and Minimum Reporting Limits (MRL)

Method 551.1

Analyte	Fortification Level (μg/L)	Observed Concentration (μg/L)	Detection Limit (μg/L)*	MRL (μg/L)**
Trichloromethane	0.1	0.114	0.028	0.084
Trichloroacetonitrile	0.1	0.064	0.022	0.066
Dichlorobromomethane	0.1	0.106	0.028	0.083
Dichloroacteonitrile	0.1	0.106	0.023	0.069
Chloropicrin	0.1	0.097	0.020	0.060
Dibromochloromethane	0.1	0.098	0.030	0.090
Bromochloroacetonitrile	0.1	0.141	0.030	0.089
Tribromomethane	0.1	0.124	0.052	0.157
Dibromoacetonitrile	0.10	0.076	0.014	0.041

Method 552.3

Analyte	Fortification Level (μg/L)	Observed Concentration (μg/L)	Detection Limit (μg/L)*	MRL (μg/L)**
Monochloroacetic acid	1	1.324	0.783	2.349
Monobromoacetic acid	0.1	0.087	0.086	0.258
Dichloroacetic acid	1	1.918	0.317	0.951
Trichloroacetic acid	0.1	0.175	0.026	0.078
Bromochloroacetic acid	1	1.228	0.064	0.192
Dibromoacetic acid	0.1	0.158	0.022	0.066
Bromodichloroacetic acid	0.1	0.083	0.037	0.111
Dibromochloroacetic acid	0.1	0.081	0.055	0.165
Tribromoacetic acid	0.1	0.046	0.045	0.135

*Fortified deionised water samples were extracted and analysed over three days for 8 replicates. Fortification was at three different concentrations (0.1, 0.5 and 1μg/L).
**MRL is at least three times the LOD for each analyte.

Note: The LOD value is a statistical determination of precision only. If the LOD replicates are fortified at a low enough concentration, it is likely that they will not meet the precision and bias criteria, and may result in a calculated LOD that is higher than the fortified concentration. Therefore no precision and bias criteria are specified for the LOD.

Compound	Code	Range (ng/L)	Limit of detection (ng/L)
N-Nitrosodimethylamine	NDMA	1.0 to 50.0	1.0
N-Nitrosomethylethylamine	NMEA	1.0 to 50.0	1.0
N-Nitrosodi-n-propylamine	NDPA	2.0 to 50.0	2.0
N-Nitrosopyrollidine	NPYR	2.0 to 50.0	2.0
N-Nitrosopiperidine	NPIP	2.0 to 50.0	2.0

A.3 Precision and Bias in fortified sample matrices

Method 551.1

	Organic rich reservoir water fortified at 5 μg/L		
Analytes	Mean recovery	Standard deviation	RSD (%)
Trichloromethane	86	1.6	9.2
Trichloroacetonitrile	55	1.2	13.0
Dichlorobromomethane	93	1.7	9.3
Dichloroacteonitrile	95	1.5	9.5
Chloropicrin	71	1.3	11.1
Dibromochloromethane	120	0.7	3.1
Bromochloroacetonitrile	76	1.1	9.0
Tribromomethane	141	0.4	8.1
Dibromoacetonitrile	83	1.2	8.7

	Organic rich reservoir water fortified at 25 μg/L		
Analytes	Mean recovery	Standard deviation	RSD (%)
Trichloromethane	98	8.4	8.6
Trichloroacetonitrile	86	1.1	5.3
Dichlorobromomethane	96	1.1	4.6
Dichloroacteonitrile	111	1.5	5.3
Chloropicrin	90	0.9	4.1
Dibromochloromethane	101	1.1	4.2
Bromochloroacetonitrile	89	0.6	2.8
Tribromomethane	90	0.8	3.6
Dibromoacetonitrile	91	0.9	4.1

	Organic rich reservoir water fortified at 75 μg/L		
Analytes	Mean recovery	Standard deviation	RSD (%)
Trichloromethane	110	8.0	7.3
Trichloroacetonitrile	88	15.5	23.4
Dichlorobromomethane	95	11.2	15.7
Dichloroacteonitrile	110	7.0	8.4
Chloropicrin	89	10.4	15.5
Dibromochloromethane	104	8.9	11.4
Bromochloroacetonitrile	97	7.2	9.8
Tribromomethane	85	3.5	5.5
Dibromoacetonitrile	101	7.5	9.9

The relative standard deviation (RSD) of the replicate analyses must be less than 20%. It is recommended in the method that recovery should be range between 70 and 130%, except for the low-level fortification near or at the MRL where 50 to 150% recoveries are acceptable.

Method 552.3

	Organic rich reservoir water fortified at 5 μg/L		
Analytes	Mean recovery (%)	Standard deviation	RSD (%)
Monochloroacetic acid	122	4.3	3.6
Monobromoacetic acid	132	4.6	3.5
Dichloroacetic acid	153	5.7	3.7
Dichloroacetic acid	145	2.0	1.4
Trichloroacetic acid	119	3.8	3.2
Bromochloroacetic acid	146	3.3	2.3
Bromodichloroacetic acid	100	6.1	6.0
Dibromochloroacetic acid	96	7.1	7.4
Tribromoacetic acid	88	9.0	10.3

	Organic rich reservoir water fortified at 25 μg/L		
Analytes	Mean recovery (%)	Standard deviation	RSD (%)
Monochloroacetic acid	119	6.1	5.2
Monobromoacetic acid	117	2.6	2.2
Dichloroacetic acid	131	1.4	1.1
Dichloroacetic acid	136	1.6	1.1
Trichloroacetic acid	115	3.5	3.1
Bromochloroacetic acid	142	2.1	1.5
Bromodichloroacetic acid	103	5.3	5.1
Dibromochloroacetic acid	93	6.3	6.7
Tribromoacetic acid	81	6.9	8.5

	Organic rich reservoir water fortified at 75 μg/L		
Analytes	Mean recovery (%)	Standard deviation	RSD (%)
Monochloroacetic acid	117	2.2	1.9
Monobromoacetic acid	109	1.2	1.1
Dichloroacetic acid	121	1.7	1.4
Dichloroacetic acid	133	1.5	1.1
Trichloroacetic acid	117	2.5	2.1
Bromochloroacetic acid	141	2.1	1.5
Bromodichloroacetic acid	114	5.4	4.8
Dibromochloroacetic acid	103	6.7	6.5
Tribromoacetic acid	86	8.2	9.6

The relative standard deviation (RSD) of the replicate analyses must be less than 20%. It is recommended in the method that recovery should be range between 70 and 130%, except for the low-level fortification near or at the MRL where 50 to 150% recoveries are acceptable.

Method 551.1

	Lowland water fortified at 5 μg/L		
Analytes	Mean recovery	Standard deviation	RSD (%)
Trichloromethane	134	1.4	21.3
Trichloroacetonitrile	50	0.5	21.5
Dichlorobromomethane	82	0.6	14.0
Dichloroacteonitrile	92	1.0	22.6
Chloropicrin	63	0.6	20.5
Dibromochloromethane	75	0.7	17.3
Bromochloroacetonitrile	66	0.6	17.8
Tribromomethane	80	0.7	17.9
Dibromoacetonitrile	73	0.6	16.8

	Lowland water fortified at 25 μg/L		
Analytes	Mean recovery	Standard deviation	RSD (%)
Trichloromethane	111	1.4	5.0
Trichloroacetonitrile	89	1.4	6.2
Dichlorobromomethane	102	0.9	3.5
Dichloroacteonitrile	121	1.3	4.2
Chloropicrin	97	0.7	2.7
Dibromochloromethane	111	0.1	0.5
Bromochloroacetonitrile	97	0.2	0.8
Tribromomethane	105	1.3	5.1
Dibromoacetonitrile	101	0.4	1.6

	Lowland water fortified at 75 μg/L		
Analytes	Mean recovery	Standard deviation	RSD (%)
Trichloromethane	109	16.9	20.7
Trichloroacetonitrile	88	5.6	8.5
Dichlorobromomethane	94	6.5	9.2
Dichloroacteonitrile	119	2.9	3.2
Chloropicrin	100	7.0	9.3
Dibromochloromethane	116	4.6	5.3
Bromochloroacetonitrile	97	1.5	2.1
Tribromomethane	103	6.9	8.9
Dibromoacetonitrile	107	1.8	2.2

The relative standard deviation (RSD) of the replicate analyses must be less than 20%. It is recommended in the method that recovery should be range between 70 and 130%, except for the low-level fortification near or at the MRL where 50 to 150% recoveries are acceptable.

Method 552.3

	Lowland water fortified at 5 μg/L		
Analytes	Mean recovery (%)	Standard deviation	RSD (%)
Monochloroacetic acid	132	12.2	9.3
Monobromoacetic acid	121	6.7	5.5
Dichloroacetic acid	150	4.2	2.8
Dichloroacetic acid	143	2.7	1.9
Trichloroacetic acid	111	5.8	5.2
Bromochloroacetic acid	143	4.3	3.0
Bromodichloroacetic acid	90	7.1	7.9
Dibromochloroacetic acid	84	9.3	11.0
Tribromoacetic acid	76	12.4	16.4

	Lowland water fortified at 25 μg/L		
Analytes	Mean recovery (%)	Standard deviation	RSD (%)
Monochloroacetic acid	120	14.4	12.0
Monobromoacetic acid	106	5.4	5.1
Dichloroacetic acid	130	1.5	1.1
Dichloroacetic acid	138	1.9	1.3
Trichloroacetic acid	113	6.5	5.7
Bromochloroacetic acid	150	3.1	2.1
Bromodichloroacetic acid	103	9.6	9.3
Dibromochloroacetic acid	90	10.1	11.2
Tribromoacetic acid	71	9.4	13.1

	Lowland water fortified at 75 μg/L		
Analytes	Mean recovery (%)	Standard deviation	RSD (%)
Monochloroacetic acid	112	1.3	1.1
Monobromoacetic acid	102	1.5	1.5
Dichloroacetic acid	123	1.7	1.4
Dichloroacetic acid	136	2.5	1.8
Trichloroacetic acid	115	7.1	6.1
Bromochloroacetic acid	148	4.2	2.9
Bromodichloroacetic acid	111	9.7	8.7
Dibromochloroacetic acid	98	11.3	11.5
Tribromoacetic acid	77	10.9	14.1

The relative standard deviation (RSD) of the replicate analyses must be less than 20%.

It is recommended in the method that recovery should be range between 70 and 130%, except for the low-level fortification near or at the MRL where 50 to 150% recoveries are acceptable.

APPENDIX B RESULTS OF SURVEYS AND LABORATORY TESTS

Works 1

Table B-1.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	19.7	1.5	0.1	<MRL	21.4
	Dist 1	Ns	Ns	Ns	Ns	Ns
Spring	Final	73.1	7.9	1.3	<MRL	82.2
	Dist 1	66.0	7.1	1.2	<MRL	74.3
Summer	Final	56.2	11.9	1.2	<MRL	69.3
	Dist 1	109.5	11.0	1.1	0.1	121.7

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	<MRL	<MRL	35.9	2.3	29.1	0.3	2.2	<MRL	0.1	72.3
	Dist 1	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns
Spring	Final	2.9	<MRL	23.9	4.3	27.7	0.5	3.5	0.5	0.1	63.5
	Dist 1	3.1	<MRL	22.7	4.2	25.7	0.5	3.2	0.3	<MRL	60.0
Summer	Final	<MRL	<MRL	23.2	3.3	24.0	0.4	2.0	<MRL	<MRL	54.7
	Dist 1	<MRL	<MRL	27.5	3.6	27.6	0.3	2.4	<MRL	0.2	63.3

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	0.4	<MRL	<MRL	0.5
	Dist 1	Ns	Ns	Ns	Ns	Ns
Spring	Final	<MRL	0.3	0.2	0.9	1.4
	Dist 1	<MRL	0.2	0.3	1.0	1.5
Summer	Final	<MRL	0.2	0.2	0.1	0.5
	Dist 1	<MRL	0.2	0.2	0.1	0.5

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	0.1
	Dist 1	Ns
Spring	Final	<MRL
	Dist 1	<MRL
Summer	Final	0.1
	Dist 1	0.1

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Ns	Ns	Ns
Spring	Final	2.0	<MRL	2.0
	Dist 1	1.9	<MRL	1.9
Summer	Final	1.6	<MRL	1.6
	Dist 1	<MRL	<MRL	<MRL

Nm – not measured
Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Ns	Ns	Ns	Ns	Ns	Ns
Spring	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

Nm – not measured
Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	1.5	5.5	3.7	248.4	1.9	78.9
	Filtered	Ns	Ns	Ns	Ns	Ns	Ns
Spring	Raw	4.1	13.0	3.2	259.0	1.6	37.1
	Filtered	2.4	1.9	0.8	35.2	0.6	53.7
Summer	Raw	3.6	14.5	4.0	103.0	3.6	36.8
	Filtered	2.1	3.4	1.6	25.1	3.5	50.4

Ns – no sample taken

Table B-1.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	79.6	10.4	13.1	<MRL	103.1
	Filtered	Chlorine	Ns	Ns	Ns	Ns	Ns
	Raw	Chloramine	5.6	0.7	0.1	<MRL	6.3
	Filtered	Chloramine	Ns	Ns	Ns	Ns	Ns
Spring	Raw	Chlorine	256.9	12.4	0.3	<MRL	269.5
	Filtered	Chlorine	78.6	10.2	1.0	<MRL	89.9
	Raw	Chloramine	58.6	5.7	0.6	0.1	65.1
	Filtered	Chloramine	11.6	<MRL	<MRL	<MRL	11.7
Summer	Raw	Chlorine	219.8	7.7	0.2	<MRL	227.8
	Filtered	Chlorine	73.4	5.6	0.4	<MRL	79.4
	Raw	Chloramine	75.4	4.3	0.4	<MRL	80.1
	Filtered	Chloramine	27.7	<MRL	<MRL	<MRL	27.8

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	<MRL	<MRL	12.3	0.7	17.7	<MRL	0.8	<MRL	<MRL	32.8
	Filtered	Chlorine	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns
	Raw	Chloramine	<MRL	<MRL	1.2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL	1.4
	Filtered	Chloramine	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns	Ns
Spring	Raw	Chlorine	<MRL	<MRL	47.4	1.7	125.8	<MRL	3.4	<MRL	<MRL	180.0
	Filtered	Chlorine	<MRL	<MRL	31.7	3.8	46.9	0.2	5.4	0.3	<MRL	90.3
	Raw	Chloramine	2.6	0.4	54.9	7.3	71.2	0.6	0.3	0.5	0.5	138.2
	Filtered	Chloramine	<MRL	<MRL	2.7	<MRL	0.1	<MRL	<MRL	<MRL	1.1	4.0
Summer	Raw	Chlorine	<MRL	<MRL	15.4	0.4	36.3	<MRL	0.7	<MRL	<MRL	52.7
	Filtered	Chlorine	<MRL	<MRL	8.1	0.6	11.8	<MRL	0.7	<MRL	<MRL	21.3
	Raw	Chloramine	2.5	0.4	4.0	<MRL	0.3	<MRL	<MRL	<MRL	<MRL	7.3
	Filtered	Chloramine	<MRL	<MRL	3.6	0.4	3.4	<MRL	0.2	<MRL	<MRL	7.6

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	<MRL	0.1	0.1	<MRL	0.3
	Filtered	Chlorine	Ns	Ns	Ns	Ns	Ns
	Raw	Chloramine	<MRL	0.8	0.3	0.1	1.2
	Filtered	Chloramine	Ns	Ns	Ns	Ns	Ns
Spring	Raw	Chlorine	<MRL	0.4	0.2	0.6	1.3
	Filtered	Chlorine	<MRL	0.3	0.2	0.5	1.0
	Raw	Chloramine	<MRL	0.4	<MRL	<MRL	0.4
	Filtered	Chloramine	<MRL	1.6	0.2	0.2	1.9
Summer	Raw	Chlorine	<MRL	0.7	0.1	<MRL	0.9
	Filtered	Chlorine	<MRL	0.6	0.2	<MRL	0.8
	Raw	Chloramine	<MRL	0.4	<MRL	<MRL	0.5
	Filtered	Chloramine	<MRL	0.7	0.1	<MRL	0.8

Ns – no sample taken
<MRL – below the minimum reporting limit

Table B-1.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	0.3
	Filtered	Chlorine	Ns
	Raw	Chloramine	0.3
	Filtered	Chloramine	Ns
Spring	Raw	Chlorine	4.3
	Filtered	Chlorine	0.2
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	0.5
	Filtered	Chlorine	1.0
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL

Ns – no sample taken
<MRL – below the minimum reporting limit

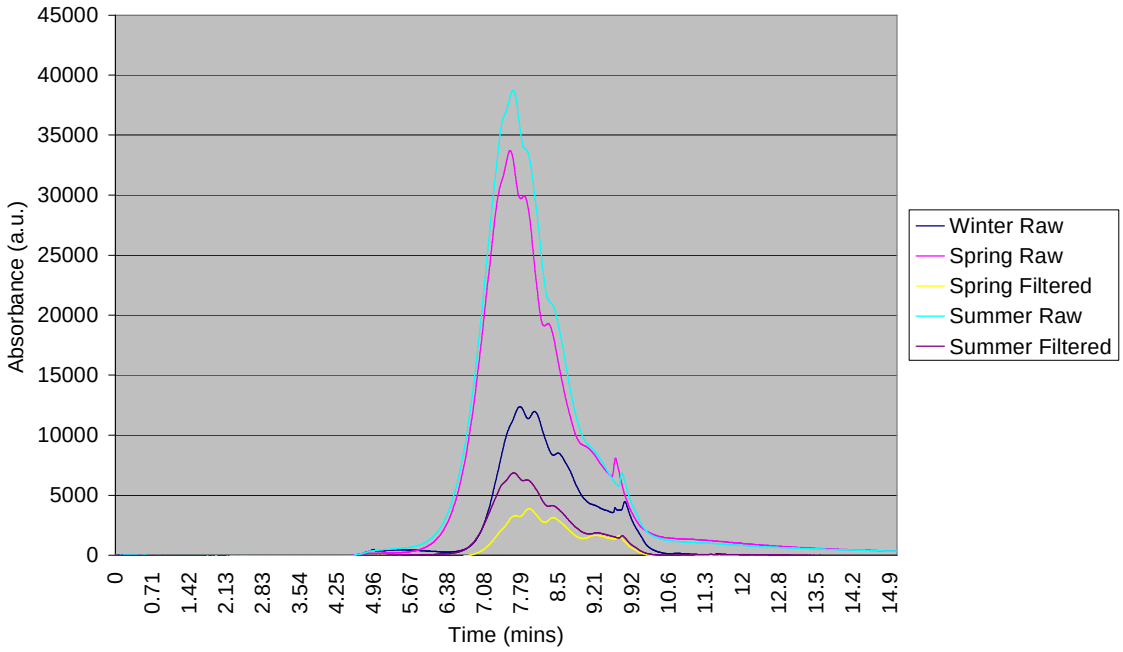

Figure B-1 HPSEC chromatogram of raw and treated waters

Works 2

Table C-2.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	11.4	0.3	<MRL	<MRL	11.8
	Dist 1	30.2	0.7	0.1	<MRL	30.9
	Dist 2	22.7	0.6	0.1	<MRL	23.4
Spring	Final	67.9	0.7	0.1	<MRL	68.7
	Dist 1	54.4	0.6	0.1	<MRL	55.1
	Dist 2	89.2	0.8	0.1	<MRL	90.2
Summer	Final	53.7	1.2	0.1	<MRL	55.0
	Dist 1	52.5	1.4	0.1	<MRL	54.1
	Dist 2	25.4	1.1	0.1	<MRL	26.7

<MRL – below the minimum reporting limit

Table B-2.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	<MRL	<MRL	8.9	0.8	0.9	0.1	0.5	0.4	0.2	14.0
	Dist 1	<MRL	<MRL	10.4	0.9	1.4	0.1	0.6	0.5	0.3	16.0
	Dist 2	<MRL	<MRL	10.6	0.9	1.0	0.1	0.6	0.4	0.3	15.6
Spring	Final	2.7	<MRL	10.1	0.2	1.4	1.0	0.2	<MRL	<MRL	15.8
	Dist 1	2.9	<MRL	11.7	0.2	1.6	1.1	0.2	<MRL	<MRL	18.0
	Dist 2	2.8	<MRL	10.6	0.2	1.5	1.0	0.2	<MRL	<MRL	16.6
Summer	Final	<MRL	<MRL	8.2	1.1	1.1	0.2	0.1	<MRL	<MRL	12.1
	Dist 1	<MRL	<MRL	10.4	1.3	1.2	0.1	0.1	<MRL	0.9	15.7
	Dist 2	<MRL	<MRL	11.1	1.3	1.3	0.1	0.1	<MRL	0.2	16.4

<MRL – below the minimum reporting limit

Table B-2.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	1.3	<MRL	<MRL	1.3
	Dist 1	<MRL	1.1	<MRL	<MRL	1.1
	Dist 2	<MRL	1.1	<MRL	<MRL	1.1
Spring	Final	<MRL	1.4	<MRL	0.2	1.6
	Dist 1	<MRL	1.3	<MRL	<MRL	1.3
	Dist 2	<MRL	1.4	<MRL	0.2	1.6
Summer	Final	<MRL	1.2	<MRL	<MRL	1.2
	Dist 1	0.1	0.9	<MRL	<MRL	1.0
	Dist 2	<MRL	0.9	<MRL	<MRL	0.9

<MRL – below the minimum reporting limit

Table B-2.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	<MRL
	Dist 1	<MRL
	Dist 2	<MRL
Spring	Final	<MRL
	Dist 1	<MRL
	Dist 2	<MRL
Summer	Final	<MRL
	Dist 1	<MRL
	Dist 2	<MRL

<MRL – below the minimum reporting limit

Table B-2.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm
Spring	Final	0.3	<MRL	0.3
	Dist 1	<MRL	0.4	0.6
	Dist 2	<MRL	0.6	0.7
Summer	Final	1.4	<MRL	1.4
	Dist 1	2.6	<MRL	2.6
	Dist 2	2.8	<MRL	2.8

Nm – not measured
<MRL – below the minimum reporting limit

Table B-2.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm	Nm	Nm	Nm
Spring	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

Nm – not measured
<MRL – below the minimum reporting limit

Table B-2.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	4.5	23.4	5.2	63.9	1.6	35.2
	Filtered	4.1	9.2	2.2	54.4	0.6	36.2
Spring	Raw	5.1	15.8	3.1	95.5	1.5	35.8
	Filtered	3.5	6.6	1.9	55.1	1.7	58.5
Summer	Raw	4.8	22.1	4.6	41.4	6.3	34.6
	Filtered	3.6	8.3	2.3	38.2	5.2	53.1

Table B-2.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	242.7	10.3	39.5	<MRL	292.5
	Filtered	Chlorine	98.3	8.2	0.3	<MRL	106.8
	Raw	Chloramine	24.5	0.9	0.5	0.4	26.2
	Filtered	Chloramine	12.7	0.3	0.1	<MRL	13.2
Spring	Raw	Chlorine	247.4	11.6	0.3	<MRL	259.3
	Filtered	Chlorine	24.5	2.6	0.2	<MRL	27.3
	Raw	Chloramine	8.9	<MRL	<MRL	<MRL	9.0
	Filtered	Chloramine	8.7	0.4	<MRL	<MRL	9.2
Summer	Raw	Chlorine	286.4	8.1	0.1	0.1	294.8
	Filtered	Chlorine	86.2	5.9	0.4	<MRL	92.5
	Raw	Chloramine	43.0	<MRL	<MRL	<MRL	43.1
	Filtered	Chloramine	40.7	0.4	<MRL	<MRL	41.1

<MRL – below the minimum reporting limit

Table B-2.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	3.4	<MRL	33.6	0.8	75.5	<MRL	0.4	<MRL	<MRL	113.7
	Filtered	Chlorine	<MRL	<MRL	11.8	0.5	25.0	<MRL	1.0	<MRL	<MRL	40.5
	Raw	Chloramine	4.0	<MRL	34.2	0.9	1.3	<MRL	<MRL	<MRL	0.2	40.5
	Filtered	Chloramine	<MRL	<MRL	5.9	0.3	0.4	<MRL	<MRL	<MRL	<MRL	7.6
Spring	Raw	Chlorine	<MRL	<MRL	39.9	1.5	96.1	<MRL	2.6	<MRL	0.8	142.3
	Filtered	Chlorine	<MRL	0.3	15.5	1.3	3.9	0.1	0.2	<MRL	0.3	23.6
	Raw	Chloramine	3.3	0.8	24.8	1.6	1.2	0.1	<MRL	<MRL	0.9	32.8
	Filtered	Chloramine	<MRL	<MRL	1.5	<MRL	0.1	<MRL	<MRL	<MRL	1.1	2.8
Summer	Raw	Chlorine	<MRL	<MRL	16.9	0.4	49.2	<MRL	0.7	<MRL	<MRL	68.3
	Filtered	Chlorine	<MRL	<MRL	7.1	0.4	8.4	<MRL	0.4	<MRL	<MRL	17.5
	Raw	Chloramine	2.9	0.3	2.9	<MRL	0.5	<MRL	<MRL	<MRL	<MRL	6.7
	Filtered	Chloramine	<MRL	<MRL	2.8	<MRL	0.1	<MRL	<MRL	<MRL	<MRL	3.0

<MRL – below the minimum reporting limit

Table B-2.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	<MRL	9.4	0.3	0.4	10.1
	Filtered	Chlorine	<MRL	1.3	0.1	0.6	2.0
	Raw	Chloramine	<MRL	16.6	5.0	2.9	24.5
	Filtered	Chloramine	<MRL	4.6	1.6	0.6	6.7
Spring	Raw	Chlorine	<MRL	1.4	0.1	0.4	2.0
	Filtered	Chlorine	<MRL	2.1	0.4	<MRL	2.5
	Raw	Chloramine	<MRL	0.3	<MRL	<MRL	0.3
	Filtered	Chloramine	<MRL	0.6	<MRL	<MRL	0.6
Summer	Raw	Chlorine	<MRL	0.5	0.1	<MRL	0.7
	Filtered	Chlorine	0.1	0.8	0.5	<MRL	1.4
	Raw	Chloramine	<MRL	0.4	<MRL	<MRL	0.5
	Filtered	Chloramine	<MRL	1.8	<MRL	<MRL	1.9

<MRL – below the minimum reporting limit

Table B-2.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	1.1
	Filtered	Chlorine	0.4
	Raw	Chloramine	5.0
	Filtered	Chloramine	1.6
Spring	Raw	Chlorine	0.3
	Filtered	Chlorine	0.5
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	0.6
	Filtered	Chlorine	0.4
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL

<MRL – below the minimum reporting limit

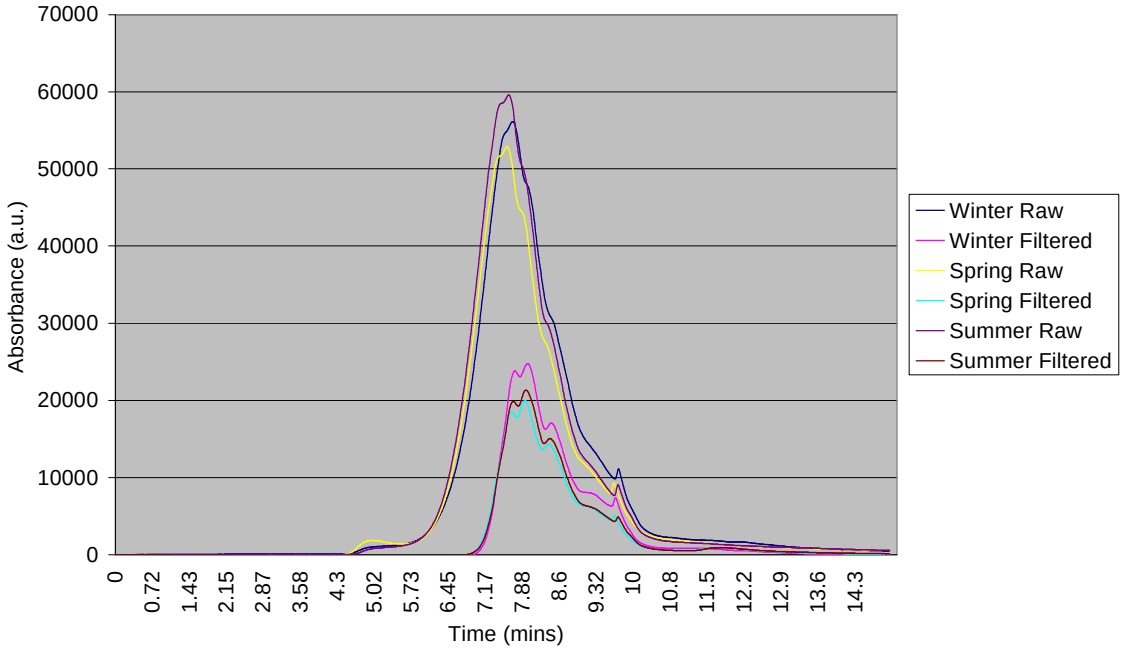

Figure B-2 HPSEC chromatogram of raw and treated waters

Works 3

Table B-3.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	31.3	2.8	1.6	0.2	36.0
	Dist 1	16.9	3.7	2.0	0.5	23.1
	Dist 2	41.9	3.8	2.1	0.5	48.4
Spring	Final	34.6	2.7	1.6	0.3	39.1
	Dist 1	42.8	2.4	1.4	0.2	46.9
	Dist 2	43.3	4.6	2.6	0.4	51.0
Summer	Final	37.7	8.4	1.3	0.1	47.5
	Dist 1	38.2	5.5	1.0	0.1	44.7
	Dist 2	31.2	8.8	1.6	0.1	41.7

Table B-3.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	<MRL	<MRL	5.3	1.0	2.4	1.1	1.2	0.3	0.2	12.8
	Dist 1	<MRL	<MRL	4.1	0.9	2.5	0.7	1.3	0.4	0.4	11.5
	Dist 2	<MRL	<MRL	4.1	0.9	2.5	0.8	1.2	0.4	0.2	11.2
Spring	Final	<MRL	<MRL	4.6	0.9	2.2	1.2	0.9	0.5	<MRL	12.6
	Dist 1	2.7	<MRL	13.0	0.9	1.8	1.8	1.1	0.5	0.2	22.2
	Dist 2	<MRL	<MRL	9.1	0.9	2.6	1.5	1.0	0.5	0.2	18.1
Summer	Final	<MRL	<MRL	10.9	2.6	5.8	0.4	1.7	0.3	<MRL	22.8
	Dist 1	<MRL	<MRL	11.1	2.7	5.7	0.3	1.7	0.2	<MRL	23.2
	Dist 2	<MRL	<MRL	11.4	2.7	5.4	0.4	1.6	0.1	<MRL	23.5

<MRL – below the minimum reporting limit

Table B-3.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	0.3	0.5	0.2	0.9
	Dist 1	<MRL	0.3	0.5	0.2	1.1
	Dist 2	<MRL	0.4	0.6	0.2	1.1
Spring	Final	<MRL	0.5	0.5	0.2	1.2
	Dist 1	<MRL	0.5	0.5	0.2	1.2
	Dist 2	<MRL	0.5	0.3	0.1	1.0
Summer	Final	<MRL	0.9	0.3	0.1	1.4
	Dist 1	<MRL	0.9	0.4	0.0	1.3
	Dist 2	<MRL	1.0	0.3	0.0	1.3

<MRL – below the minimum reporting limit

Table B-3.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	0.1
	Dist 1	0.1
	Dist 2	0.1
Spring	Final	0.1
	Dist 1	0.2
	Dist 2	0.1
Summer	Final	0.2
	Dist 1	0.3
	Dist 2	0.3

Table B-3.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm
Spring	Final	<MRL	0.5	0.6
	Dist 1	<MRL	<MRL	0.4
	Dist 2	<MRL	<MRL	0.2
Summer	Final	2.6	<MRL	2.6
	Dist 1	2.4	<MRL	2.4
	Dist 2	2.3	<MRL	2.5

Nm – not measured

Table B-3.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm	Nm	Nm	Nm
Spring	Final	8.6	<MRL	<MRL	<MRL	<MRL	8.6
	Dist 1	13.5	<MRL	<MRL	<MRL	<MRL	13.5
	Dist 2	26.0	<MRL	<MRL	<MRL	<MRL	26.0
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

Nm – not measured

<MRL – below the minimum reporting limit

Table B-3.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	6.8	26.9	4.0	139.9	2.9	175.9
	Settled	2.8	5.6	2.0	149.2	1.1	191.2
	Filtered	2.5	3.2	1.3	130.2	1.0	184.8
Spring	Raw	4.4	12.5	2.8	117.0	3.3	185.3
	Settled	2.3	2.7	1.2	85.1	2.4	198.1
	Filtered	1.7	2.6	1.6	81.6	2.0	197.5
Summer	Raw	11.3	42.2	3.7	70.9	7.6	156.5
	Settled	3.7	6.3	1.7	43.0	4.7	177.4
	Filtered	3.5	5.5	1.6	41.2	5.1	174.9

Table B-3.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	273.2	26.9	1.1	<MRL	301.2
	Settled	Chlorine	34.0	15.1	2.9	0.2	52.1
	Filtered	Chlorine	25.8	14.4	3.4	0.3	43.9
	Raw	Chloramine	22.1	0.5	<MRL	<MRL	22.6
	Settled	Chloramine	4.6	0.2	<MRL	<MRL	4.9
	Filtered	Chloramine	4.6	0.2	0.1	<MRL	4.9
Spring	Raw	Chlorine	145.5	25.8	1.9	<MRL	173.3
	Settled	Chlorine	38.0	17.4	4.4	0.3	60.1
	Filtered	Chlorine	44.2	16.4	3.8	0.3	64.7
	Raw	Chloramine	7.3	<MRL	<MRL	<MRL	7.3
	Settled	Chloramine	6.0	<MRL	<MRL	<MRL	6.0
	Filtered	Chloramine	9.8	<MRL	<MRL	<MRL	9.8
Summer	Raw	Chlorine	393.7	15.8	0.2	<MRL	409.7
	Settled	Chlorine	86.5	7.8	0.6	0.3	95.1
	Filtered	Chlorine	84.5	9.2	0.7	0.3	94.7
	Raw	Chloramine	55.9	<MRL	<MRL	<MRL	56.0
	Settled	Chloramine	35.7	<MRL	<MRL	<MRL	35.8
	Filtered	Chloramine	28.0	<MRL	<MRL	<MRL	28.0

<MRL – below the minimum reporting limit

Table B-3.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	3.6	<MRL	45.3	1.9	91.8	<MRL	2.6	<MRL	0.1	145.3
	Settled	Chlorine	<MRL	<MRL	6.1	1.1	7.1	1.4	2.1	0.3	<MRL	18.0
	Filtered	Chlorine	<MRL	<MRL	4.1	1.0	3.7	0.1	1.6	0.3	<MRL	10.8
	Raw	Chloramine	3.0	<MRL	15.7	0.7	0.9	<MRL	<MRL	<MRL	<MRL	20.5
	Settled	Chloramine	<MRL	<MRL	1.1	<MRL	0.2	<MRL	<MRL	<MRL	<MRL	1.5
	Filtered	Chloramine	<MRL	<MRL	<MRL	<MRL	0.2	<MRL	<MRL	<MRL	<MRL	1.1
Spring	Raw	Chlorine	<MRL	0.3	30.9	4.0	65.8	0.2	7.5	0.3	0.1	110.6
	Settled	Chlorine	<MRL	0.3	9.2	2.8	10.1	0.5	4.3	0.8	0.2	28.1
	Filtered	Chlorine	<MRL	0.3	10.1	2.7	9.3	0.4	4.0	0.8	<MRL	27.5
	Raw	Chloramine	<MRL	<MRL	1.6	<MRL	0.1	<MRL	<MRL	<MRL	2.3	4.4
	Settled	Chloramine	<MRL	<MRL	1.3	0.2	0.1	<MRL	<MRL	<MRL	1.2	2.7
	Filtered	Chloramine	<MRL	<MRL	1.9	0.3	0.1	<MRL	<MRL	<MRL	1.2	3.7
Summer	Raw	Chlorine	<MRL	<MRL	23.8	0.6	31.6	<MRL	1.1	<MRL	<MRL	58.8
	Settled	Chlorine	<MRL	<MRL	5.5	0.5	8.6	<MRL	0.8	<MRL	<MRL	15.4
	Filtered	Chlorine	<MRL	<MRL	5.6	0.5	7.3	<MRL	0.8	<MRL	<MRL	15.1
	Raw	Chloramine	<MRL	0.3	2.8	<MRL	0.2	<MRL	<MRL	<MRL	<MRL	5.1
	Settled	Chloramine	<MRL	<MRL	2.6	0.2	0.2	<MRL	<MRL	<MRL	<MRL	4.1
	Filtered	Chloramine	<MRL	<MRL	2.3	0.4	0.1	<MRL	<MRL	<MRL	<MRL	4.0

<MRL – below the minimum reporting limit

Table B-3.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	<MRL	0.5	1.0	1.5	3.1
	Settled	Chlorine	<MRL	0.5	0.7	3.1	4.3
	Filtered	Chlorine	<MRL	0.6	0.9	0.7	2.3
	Raw	Chloramine	<MRL	8.5	5.1	1.9	15.5
	Settled	Chloramine	<MRL	0.9	0.5	0.3	1.7
	Filtered	Chloramine	<MRL	1.0	0.4	0.2	1.6
Spring	Raw	Chlorine	<MRL	0.8	0.9	0.4	2.1
	Settled	Chlorine	<MRL	0.4	1.0	0.4	1.8
	Filtered	Chlorine	<MRL	0.5	0.7	0.5	1.8
	Raw	Chloramine	<MRL	0.2	<MRL	<MRL	0.2
	Settled	Chloramine	<MRL	0.2	<MRL	<MRL	0.2
	Filtered	Chloramine	<MRL	0.3	<MRL	<MRL	0.3
Summer	Raw	Chlorine	0.2	4.2	0.2	<MRL	4.7
	Settled	Chlorine	<MRL	0.6	0.5	<MRL	1.1
	Filtered	Chlorine	<MRL	0.8	0.1	<MRL	0.9
	Raw	Chloramine	<MRL	0.5	<MRL	<MRL	0.5
	Settled	Chloramine	<MRL	0.3	<MRL	<MRL	0.3
	Filtered	Chloramine	<MRL	0.3	<MRL	<MRL	0.4

<MRL – below the minimum reporting limit

Table B-3.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	3.2
	Settled	Chlorine	0.5
	Filtered	Chlorine	0.4
	Raw	Chloramine	5.1
	Settled	Chloramine	0.5
	Filtered	Chloramine	0.4
Spring	Raw	Chlorine	0.8
	Settled	Chlorine	0.3
	Filtered	Chlorine	0.3
	Raw	Chloramine	<MRL
	Settled	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	0.3
	Settled	Chlorine	0.8
	Filtered	Chlorine	0.6
	Raw	Chloramine	<MRL
	Settled	Chloramine	<MRL
	Filtered	Chloramine	<MRL

<MRL – below the minimum reporting limit

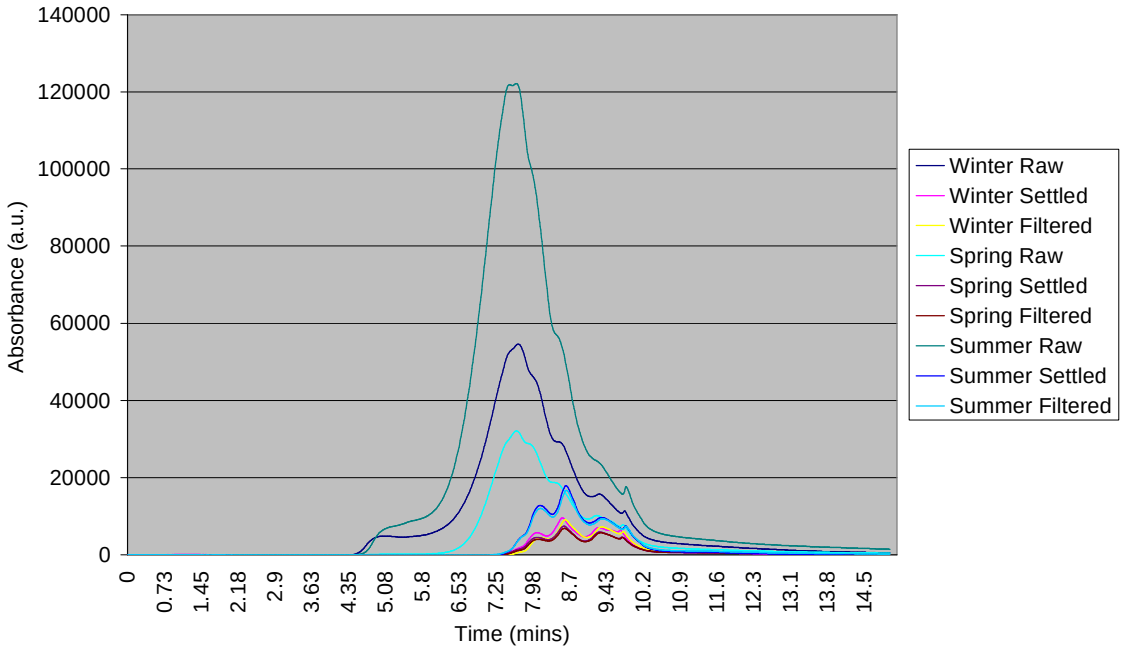

Figure B-3 HPSEC chromatogram of raw and treated waters

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Table B-4.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	22.4	12.1	13.2	1.9	49.6
	Dist 1	90.0	14.5	15.5	4.4	124.5
	Dist 2	369.7	19.6	21.8	7.8	418.9
Spring	Final	55.4	4.7	11.4	9.8	81.3
	Dist 1	59.4	4.5	9.6	7.5	80.9
	Dist 2	77.5	6.8	13.0	8.8	106.1
Summer	Final	55.1	9.2	11.2	4.5	80.0
	Dist 1	62.8	15.1	16.0	5.5	99.3
	Dist 2	33.4	24.5	24.8	7.4	90.2

Table B-4.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	<MRL	0.3	10.9	5.9	1.4	4.6	2.4	1.4	0.5	27.3
	Dist 1	<MRL	<MRL	10.6	6.9	2.0	5.8	2.8	1.8	1.1	32.2
	Dist 2	<MRL	<MRL	11.3	8.0	2.1	7.7	3.0	2.4	1.8	37.8
Spring	Final	<MRL	0.5	1.5	3.0	4.9	0.4	0.8	1.6	0.1	13.4
	Dist 1	<MRL	0.9	2.5	4.4	6.2	0.6	1.3	2.2	0.2	18.4
	Dist 2	<MRL	0.8	3.3	4.9	6.6	0.9	1.6	2.6	0.3	21.0
Summer	Final	<MRL	0.8	3.7	5.5	1.3	5.8	2.4	1.9	<MRL	21.3
	Dist 1	<MRL	1.0	5.4	6.7	2.4	5.9	3.5	2.1	<MRL	27.2
	Dist 2	<MRL	1.0	7.2	7.9	3.4	6.2	4.6	2.4	<MRL	32.8

<MRL – below the minimum reporting limit

Table B-4.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	0.2	1.5	1.2	2.9
	Dist 1	<MRL	0.2	1.9	1.6	3.6
	Dist 2	<MRL	0.1	2.0	2.0	4.1
Spring	Final	<MRL	0.1	1.4	0.2	1.7
	Dist 1	<MRL	0.2	1.5	0.3	2.0
	Dist 2	<MRL	<MRL	1.8	0.4	2.3
Summer	Final	<MRL	0.2	1.5	<MRL	1.8
	Dist 1	0.1	0.2	2.0	0.1	2.3
	Dist 2	0.1	0.3	2.1	0.1	2.6

<MRL – below the minimum reporting limit

Table B-4.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	0.1
	Dist 1	0.1
	Dist 2	0.1
Spring	Final	<MRL
	Dist 1	<MRL
	Dist 2	<MRL
Summer	Final	<MRL
	Dist 1	0.1
	Dist 2	0.1

<MRL – below the minimum reporting limit

Table B-4.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm
Spring	Final	0.4	<MRL	0.5
	Dist 1	0.5	<MRL	0.5
	Dist 2	0.6	<MRL	0.8
Summer	Final	3.7	<MRL	3.7
	Dist 1	3.1	<MRL	3.2
	Dist 2	0.7	<MRL	0.7

Nm – not measured
<MRL – below the minimum reporting limit

Table B-4.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm	Nm	Nm	Nm
Spring	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

<MRL – below the minimum reporting limit

Table B-4.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	12.5	40.2	3.2	224.4	6.8	230
	Filtered	3.3	4.4	1.4	192.3	2.5	323
Spring	Raw	4.2	12.0	2.8	222.0	8.1	281
	Filtered	1.5	1.9	1.2	207.0	4.2	345
Summer	Raw	7.8	32.3	4.1	165.0	12.1	270
	Filtered	2.2	4.1	1.9	152.0	6.7	380

Table B-4.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	142.3	66.9	14.6	1.1	224.9
	Filtered	Chlorine	28.6	26.6	9.9	1.0	66.0
	Raw	Chloramine	26.6	1.1	0.2	<MRL	28.0
	Filtered	Chloramine	4.9	0.4	0.3	<MRL	5.6
Spring	Raw	Chlorine	117.3	56.1	13.4	0.7	187.5
	Filtered	Chlorine	18.8	28.9	19.0	4.3	71.0
	Raw	Chloramine	25.2	<MRL	<MRL	<MRL	25.3
	Filtered	Chloramine	11.2	<MRL	<MRL	<MRL	11.3
Summer	Raw	Chlorine	210.1	37.5	3.4	<MRL	251.1
	Filtered	Chlorine	55.3	24.3	11.5	<MRL	91.3
	Raw	Chloramine	48.5	<MRL	<MRL	<MRL	48.5
	Filtered	Chloramine	36.1	<MRL	<MRL	<MRL	36.2

<MRL – below the minimum reporting limit

Table B-4.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	4.4	<MRL	49.2	3.2	84.8	0.1	2.8	<MRL	<MRL	144.7
	Filtered	Chlorine	<MRL	<MRL	5.3	1.9	4.7	0.4	3.3	0.9	<MRL	17.6
	Raw	Chloramine	<MRL	<MRL	17.4	1.2	1.1	<MRL	<MRL	<MRL	<MRL	21.8
	Filtered	Chloramine	<MRL	<MRL	<MRL	0.4	0.1	0.1	<MRL	<MRL	<MRL	1.5
Spring	Raw	Chlorine	<MRL	0.5	22.5	7.7	37.6	1.3	13.7	1.9	0.2	85.4
	Filtered	Chlorine	<MRL	0.7	4.9	4.1	2.4	2.3	3.1	2.5	0.2	20.3
	Raw	Chloramine	<MRL	<MRL	3.2	<MRL	0.1	<MRL	<MRL	<MRL	1.8	5.2
	Filtered	Chloramine	<MRL	<MRL	<MRL	0.2	0.1	0.1	<MRL	<MRL	1.4	2.9
Summer	Raw	Chlorine	<MRL	<MRL	13.1	1.8	31.0	0.1	4.1	<MRL	<MRL	51.3
	Filtered	Chlorine	<MRL	<MRL	2.2	1.3	1.7	0.4	1.6	0.6	<MRL	8.0
	Raw	Chloramine	<MRL	0.3	2.1	<MRL	0.1	<MRL	<MRL	<MRL	<MRL	4.0
	Filtered	Chloramine	<MRL	0.3	1.7	0.3	0.3	0.1	<MRL	<MRL	<MRL	4.7

<MRL – below the minimum reporting limit

Table B-4.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	0.9	2.5	1.4	2.2	7.0
	Filtered	Chlorine	<MRL	0.5	1.1	4.8	6.5
	Raw	Chloramine	<MRL	8.4	6.0	2.1	16.5
	Filtered	Chloramine	<MRL	0.8	0.6	0.5	1.9
Spring	Raw	Chlorine	<MRL	0.6	2.7	0.4	3.7
	Filtered	Chlorine	<MRL	0.3	1.2	0.2	1.7
	Raw	Chloramine	<MRL	0.2	<MRL	<MRL	0.2
	Filtered	Chloramine	<MRL	0.1	<MRL	<MRL	0.1
Summer	Raw	Chlorine	0.1	2.0	1.5	<MRL	3.6
	Filtered	Chlorine	<MRL	0.4	0.9	<MRL	1.3
	Raw	Chloramine	<MRL	0.3	<MRL	<MRL	0.3
	Filtered	Chloramine	<MRL	0.2	<MRL	<MRL	0.3

<MRL – below the minimum reporting limit

Table B-4.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	5.5
	Filtered	Chlorine	0.5
	Raw	Chloramine	6.0
	Filtered	Chloramine	0.6
Spring	Raw	Chlorine	0.8
	Filtered	Chlorine	0.1
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	1.2
	Filtered	Chlorine	0.2
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL

<MRL – below the minimum reporting limit

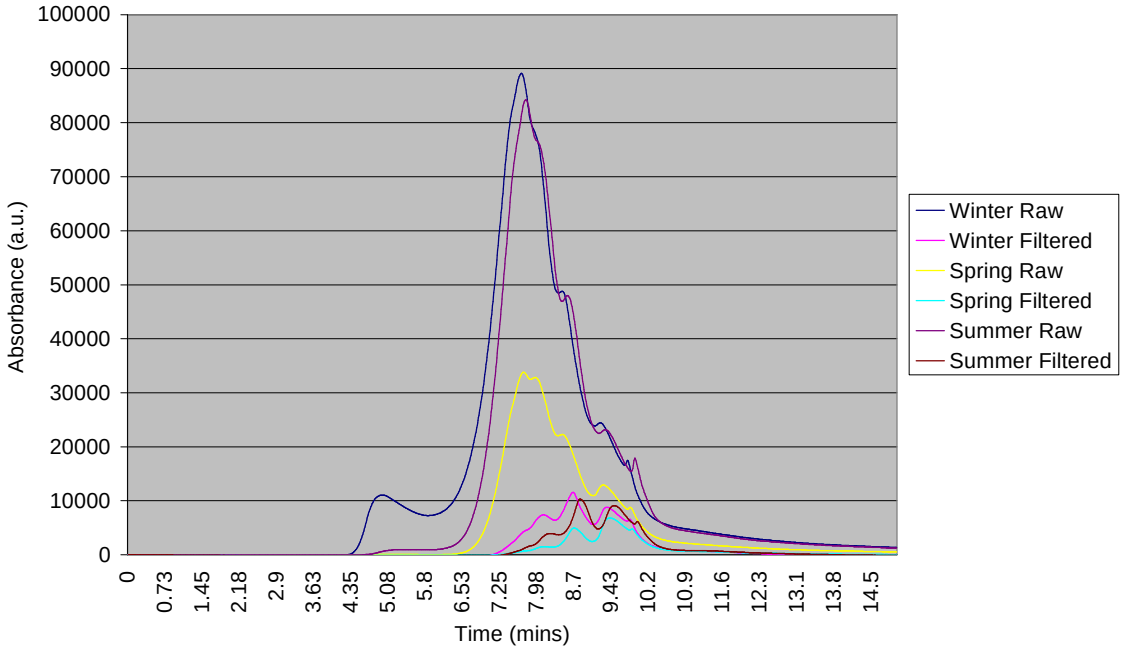

Figure B-4 HPSEC chromatogram of raw and treated waters

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Table B-5.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	191.1	2.0	0.6	<MRL	193.7
	Dist 1	147.6	3.3	0.7	<MRL	151.6
	Dist 2	156.6	2.9	0.6	<MRL	160.1
Spring	Final	78.2	2.0	0.3	<MRL	80.5
	Dist 1	50.7	2.9	0.6	<MRL	54.2
	Dist 2	89.3	1.9	0.3	0.1	91.5
Summer	Final	18.6	2.8	0.3	<MRL	21.7
	Dist 1	29.5	3.9	0.3	<MRL	33.7
	Dist 2	41.1	3.8	0.3	<MRL	45.2

<MRL – below the minimum reporting limit

Table B-5.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	<MRL	<MRL	10.7	1.5	1.8	0.2	1.0	<MRL	0.1	17.0
	Dist 1	2.7	<MRL	12.9	1.6	2.6	0.3	1.0	<MRL	0.2	21.7
	Dist 2	2.8	<MRL	27.4	2.3	17.5	0.2	1.8	<MRL	0.2	52.5
Spring	Final	2.6	<MRL	6.8	0.3	1.5	2.6	0.8	0.5	<MRL	15.3
	Dist 1	2.9	<MRL	7.6	0.3	1.6	2.9	0.8	0.3	<MRL	16.5
	Dist 2	<MRL	<MRL	8.9	0.3	1.3	2.8	0.5	<MRL	<MRL	16.3
Summer	Final	<MRL	<MRL	6.3	0.3	3.9	<MRL	0.6	<MRL	<MRL	12.1
	Dist 1	<MRL	<MRL	23.5	0.1	9.8	0.3	0.6	<MRL	<MRL	36.9
	Dist 2	2.8	<MRL	17.6	1.3	8.3	0.1	0.6	<MRL	<MRL	31.1

<MRL – below the minimum reporting limit

Table B-5.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	0.3	0.2	<MRL	0.5
	Dist 1	<MRL	0.9	0.1	<MRL	1.0
	Dist 2	<MRL	0.9	0.1	<MRL	1.1
Spring	Final	<MRL	0.3	0.2	0.6	1.1
	Dist 1	<MRL	0.5	0.1	<MRL	0.7
	Dist 2	<MRL	0.6	0.2	<MRL	0.8
Summer	Final	0.1	0.5	0.1	0.1	0.7
	Dist 1	<MRL	1.0	<MRL	<MRL	1.1
	Dist 2	<MRL	1.3	0.1	<MRL	1.4

<MRL – below the minimum reporting limit

Table B-5.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	0.1
	Dist 1	0.1
	Dist 2	0.3
Spring	Final	0.1
	Dist 1	<MRL
	Dist 2	0.1
Summer	Final	0.1
	Dist 1	0.1
	Dist 2	0.1

<MRL – below the minimum reporting limit

Table B-5.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm
Spring	Final	1.2	<MRL	1.2
	Dist 1	<MRL	0.5	0.6
	Dist 2	0.3	0.4	0.7
Summer	Final	1.4	<MRL	1.4
	Dist 1	<MRL	<MRL	<MRL
	Dist 2	1.8	<MRL	1.8

Nm – not measured
<MRL – below the minimum reporting limit

Table B-5.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm	Nm	Nm	Nm
Spring	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

<MRL – below the minimum reporting limit

Table B-5.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	5.2	21.2	4.1	71.3	1.8	88.1
	Filtered	2.3	3.1	1.4	73.6	0.3	130.7
Spring	Raw	3.0	8.6	2.9	43.8	1.9	80.8
	Filtered	1.5	2.3	1.6	41.3	2.2	109.7
Summer	Raw	6.2	4.2	0.7	32.8	6.1	68.4
	Filtered	3.3	3.8	1.2	17.0	4.4	110.3

Table B-5.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	222.9	13.1	0.3	<MRL	236.3
	Filtered	Chlorine	29.9	7.9	0.9	<MRL	38.7
	Raw	Chloramine	24.3	1.8	<MRL	<MRL	26.1
	Filtered	Chloramine	6.6	<MRL	<MRL	<MRL	6.7
Spring	Raw	Chlorine	183.6	15.1	0.5	<MRL	199.2
	Filtered	Chlorine	51.0	9.6	1.1	<MRL	61.8
	Raw	Chloramine	9.0	<MRL	<MRL	<MRL	9.1
	Filtered	Chloramine	11.0	0.3	<MRL	<MRL	11.3
Summer	Raw	Chlorine	405.1	10.4	0.2	0.5	416.2
	Filtered	Chlorine	75.2	4.0	0.2	<MRL	79.6
	Raw	Chloramine	50.5	<MRL	<MRL	<MRL	50.6
	Filtered	Chloramine	44.2	<MRL	<MRL	<MRL	44.3

<MRL – below the minimum reporting limit

Table B-5.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	5.0	<MRL	31.8	1.0	69.4	<MRL	1.8	<MRL	0.2	109.2
	Filtered	Chlorine	<MRL	<MRL	4.4	0.5	5.5	<MRL	0.9	<MRL	<MRL	12.5
	Raw	Chloramine	<MRL	<MRL	14.9	0.5	0.9	<MRL	<MRL	<MRL	0.1	18.6
	Filtered	Chloramine	<MRL	<MRL	<MRL	<MRL	0.1	<MRL	<MRL	<MRL	<MRL	1.0
Spring	Raw	Chlorine	<MRL	<MRL	35.3	2.0	76.9	<MRL	4.1	<MRL	<MRL	120.4
	Filtered	Chlorine	<MRL	<MRL	10.7	1.5	13.3	0.1	2.2	0.2	<MRL	28.1
	Raw	Chloramine	<MRL	<MRL	2.7	0.2	0.1	<MRL	<MRL	<MRL	0.5	3.7
	Filtered	Chloramine	<MRL	<MRL	1.5	<MRL	0.6	<MRL	<MRL	<MRL	1.1	3.3
Summer	Raw	Chlorine	<MRL	<MRL	22.8	0.4	71.4	<MRL	0.9	<MRL	<MRL	96.8
	Filtered	Chlorine	<MRL	<MRL	3.5	0.2	4.4	<MRL	0.3	<MRL	<MRL	8.4
	Raw	Chloramine	<MRL	<MRL	2.5	<MRL	0.1	<MRL	<MRL	<MRL	<MRL	4.4
	Filtered	Chloramine	<MRL	0.3	1.6	<MRL	0.2	<MRL	<MRL	<MRL	<MRL	3.6

<MRL – below the minimum reporting limit

Table B-5.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	0.1	1.2	0.6	7.5	9.5
	Filtered	Chlorine	<MRL	0.5	0.3	0.5	1.4
	Raw	Chloramine	<MRL	9.8	3.9	1.4	15.2
	Filtered	Chloramine	<MRL	0.9	0.8	0.1	1.8
Spring	Raw	Chlorine	<MRL	0.5	0.3	0.6	1.4
	Filtered	Chlorine	<MRL	0.3	0.2	0.3	0.9
	Raw	Chloramine	<MRL	0.3	<MRL	<MRL	0.3
	Filtered	Chloramine	<MRL	0.2	<MRL	<MRL	0.2
Summer	Raw	Chlorine	0.1	0.6	0.2	<MRL	0.8
	Filtered	Chlorine	<MRL	0.5	0.1	<MRL	0.7
	Raw	Chloramine	<MRL	0.4	<MRL	<MRL	0.4
	Filtered	Chloramine	<MRL	0.2	<MRL	<MRL	0.2

<MRL – below the minimum reporting limit

Table B-5.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	2.7
	Filtered	Chlorine	0.6
	Raw	Chloramine	3.9
	Filtered	Chloramine	0.8
Spring	Raw	Chlorine	0.6
	Filtered	Chlorine	1.3
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	1.0
	Filtered	Chlorine	0.6
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL

<MRL – below the minimum reporting limit

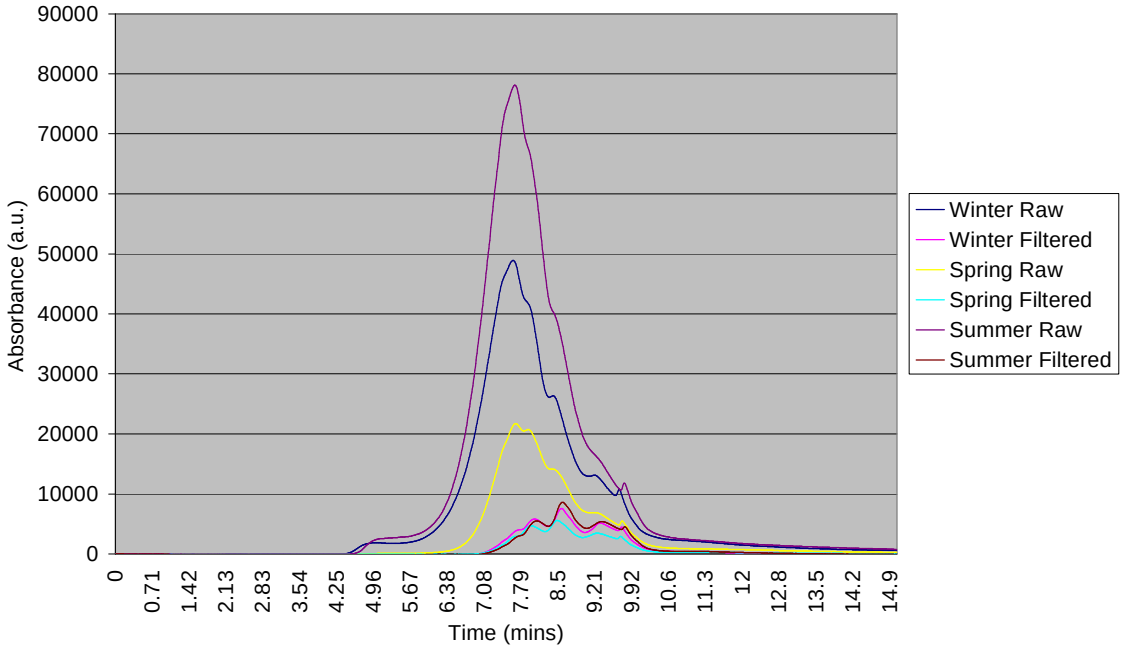

Figure B-5 HPSEC chromatogram of raw and treated waters

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Table B-6.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	115.4	0.7	0.1	<MRL	116.1
	Dist 1	111.6	0.6	0.1	<MRL	112.3
	Dist 2	197.9	0.6	0.1	<MRL	198.6
Spring	Final	41.9	0.7	0.1	0.1	42.8
	Dist 1	73.8	0.8	0.1	0.1	74.7
	Dist 2	82.8	0.8	0.1	<MRL	83.6
Summer	Final	38.2	1.4	0.1	0.1	39.8
	Dist 1	29.9	1.3	0.1	0.1	31.5
	Dist 2	20.6	1.4	0.1	0.1	22.2

<MRL – below the minimum reporting limit

Table B-6.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	3.4	<MRL	12.0	0.3	0.8	0.2	0.6	<MRL	0.2	17.6
	Dist 1	2.9	<MRL	10.7	0.4	0.4	0.1	0.5	<MRL	0.3	15.5
	Dist 2	3.3	<MRL	10.5	0.4	0.4	0.1	0.5	<MRL	0.3	15.7
Spring	Final	5.9	0.3	10.8	0.3	1.3	0.6	<MRL	<MRL	<MRL	19.4
	Dist 1	4.6	<MRL	8.7	0.2	0.6	0.6	<MRL	<MRL	<MRL	15.2
	Dist 2	7.0	0.4	11.5	0.4	1.5	0.7	0.1	<MRL	<MRL	21.7
Summer	Final	3.0	<MRL	12.8	1.1	1.6	0.2	0.2	<MRL	<MRL	19.2
	Dist 1	3.0	<MRL	12.0	0.9	1.5	0.2	0.2	<MRL	<MRL	17.9
	Dist 2	<MRL	<MRL	12.1	0.8	1.5	0.2	0.2	<MRL	<MRL	17.0

<MRL – below the minimum reporting limit

Table B-6.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	1.4	0.1	<MRL	1.5
	Dist 1	<MRL	1.0	<MRL	<MRL	1.0
	Dist 2	0.1	1.1	<MRL	<MRL	1.2
Spring	Final	<MRL	1.9	0.1	0.2	2.2
	Dist 1	<MRL	1.4	<MRL	0.1	1.5
	Dist 2	<MRL	1.6	<MRL	0.2	1.8
Summer	Final	0.1	2.1	0.2	<MRL	2.4
	Dist 1	<MRL	1.7	<MRL	<MRL	1.8
	Dist 2	<MRL	2.0	0.1	<MRL	2.2

<MRL – below the minimum reporting limit

Table B-6.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	<MRL
	Dist 1	<MRL
	Dist 2	<MRL
Spring	Final	<MRL
	Dist 1	<MRL
	Dist 2	<MRL
Summer	Final	0.2
	Dist 1	<MRL
	Dist 2	0.1

<MRL – below the minimum reporting limit

Table B-6.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm
Spring	Final	0.3	<MRL	0.5
	Dist 1	<MRL	<MRL	<MRL
	Dist 2	0.4	0.4	0.8
Summer	Final	0.3	<MRL	0.3
	Dist 1	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL

Nm – not measured
<MRL – below the minimum reporting limit

Table B-6.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm	Nm	Nm	Nm
Spring	Final	8.6	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	13.5	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	26.0	<MRL	<MRL	<MRL	<MRL	<MRL
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

Nm – not measured
<MRL – below the minimum reporting limit

Table B-6.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	4.3	15.1	3.5	54.2	2.9	37.9
	Ozonated	3.9	7.6	1.9	52.3	3.0	38.4
	Filtered	3.1	6.5	2.1	49.0	2.9	37.8
Spring	Raw	3.1	12.2	4.0	30.6	2.6	39.6
	Ozonated	2.9	5.6	1.9	30.9	3.0	38.9
	Filtered	2.7	5.3	2.0	31.6	3.3	42.9
Summer	Raw	3.7	15.8	4.2	21.5	6.1	37.2
	Ozonated	3.9	9.8	2.5	21.2	6.2	38.5
	Filtered	4.0	8.8	2.2	24.8	6.8	40.9

Table B-6.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	126.1	6.3	0.1	<MRL	132.5
	Ozonated	Chlorine	83.9	8.7	0.3	<MRL	93.0
	Filtered	Chlorine	71.0	7.2	0.3	<MRL	78.5
	Raw	Chloramine	15.2	0.1	<MRL	<MRL	15.2
	Ozonated	Chloramine	11.7	0.3	0.2	<MRL	12.2
	Filtered	Chloramine	6.1	0.1	<MRL	<MRL	6.1
Spring	Raw	Chlorine	158.4	8.1	0.2	<MRL	166.7
	Ozonated	Chlorine	131.7	11.1	0.5	<MRL	143.2
	Filtered	Chlorine	55.3	7.0	0.4	<MRL	62.7
	Raw	Chloramine	7.8	<MRL	<MRL	<MRL	7.8
	Ozonated	Chloramine	12.5	<MRL	<MRL	<MRL	12.5
	Filtered	Chloramine	9.7	<MRL	<MRL	<MRL	9.7
Summer	Raw	Chlorine	217.3	5.9	0.1	0.2	223.5
	Ozonated	Chlorine	154.1	5.9	0.2	<MRL	160.2
	Filtered	Chlorine	130.9	7.2	0.3	<MRL	138.6
	Raw	Chloramine	44.1	<MRL	<MRL	<MRL	44.2
	Ozonated	Chloramine	45.7	<MRL	<MRL	<MRL	45.7
	Filtered	Chloramine	30.6	<MRL	<MRL	<MRL	30.6

<MRL – below the minimum reporting limit

Table B-6.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	<MRL	<MRL	17.8	0.5	35.4	<MRL	0.7	<MRL	<MRL	56.6
	Ozonated	Chlorine	2.6	<MRL	12.3	0.5	22.7	<MRL	0.9	<MRL	<MRL	38.9
	Filtered	Chlorine	<MRL	<MRL	11.2	<MRL	21.6	<MRL	0.8	<MRL	<MRL	35.4
	Raw	Chloramine	<MRL	<MRL	7.9	0.2	0.3	<MRL	<MRL	<MRL	<MRL	9.4
	Ozonated	Chloramine	<MRL	<MRL	6.6	0.2	0.6	<MRL	<MRL	<MRL	<MRL	8.4
	Filtered	Chloramine	<MRL	<MRL	2.5	0.2	0.1	<MRL	<MRL	<MRL	<MRL	2.8
Spring	Raw	Chlorine	<MRL	<MRL	31.9	1.3	71.2	<MRL	2.1	<MRL	0.1	106.6
	Ozonated	Chlorine	<MRL	<MRL	27.2	1.4	57.7	0.1	3.0	<MRL	0.9	91.6
	Filtered	Chlorine	<MRL	<MRL	9.4	0.8	8.4	<MRL	0.6	<MRL	1.1	20.4
	Raw	Chloramine	<MRL	<MRL	1.7	<MRL	0.1	<MRL	<MRL	<MRL	3.0	4.9
	Ozonated	Chloramine	<MRL	<MRL	3.2	0.6	0.1	0.1	<MRL	<MRL	3.1	7.3
	Filtered	Chloramine	<MRL	<MRL	2.0	0.4	0.1	0.1	<MRL	<MRL	1.2	4.1
Summer	Raw	Chlorine	<MRL	<MRL	15.4	0.3	36.9	<MRL	0.6	<MRL	<MRL	54.3
	Ozonated	Chlorine	<MRL	<MRL	12.7	0.3	26.2	<MRL	0.6	<MRL	<MRL	40.8
	Filtered	Chlorine	<MRL	<MRL	8.2	0.3	18.5	<MRL	0.6	<MRL	<MRL	27.7
	Raw	Chloramine	2.6	0.3	3.4	<MRL	0.1	<MRL	<MRL	<MRL	<MRL	6.6
	Ozonated	Chloramine	<MRL	0.4	4.1	0.6	0.2	0.2	<MRL	<MRL	<MRL	7.8
	Filtered	Chloramine	2.5	0.3	2.5	0.4	0.1	0.2	<MRL	<MRL	<MRL	6.0

<MRL – below the minimum reporting limit

Table B-6.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	<MRL	0.4	0.2	0.3	0.9
	Ozonated	Chlorine	<MRL	1.1	<MRL	0.2	1.4
	Filtered	Chlorine	<MRL	0.6	<MRL	<MRL	0.8
	Raw	Chloramine	<MRL	4.7	1.6	0.7	7.1
	Ozonated	Chloramine	<MRL	4.9	2.6	0.5	8.0
	Filtered	Chloramine	<MRL	1.8	0.9	0.2	3.0
Spring	Raw	Chlorine	<MRL	0.7	0.2	0.3	1.2
	Ozonated	Chlorine	<MRL	0.5	0.2	0.6	1.3
	Filtered	Chlorine	<MRL	1.6	0.2	0.1	1.9
	Raw	Chloramine	<MRL	0.2	<MRL	<MRL	0.2
	Ozonated	Chloramine	<MRL	0.4	<MRL	<MRL	0.4
	Filtered	Chloramine	<MRL	0.3	<MRL	<MRL	0.3
Summer	Raw	Chlorine	<MRL	0.6	0.1	<MRL	0.8
	Ozonated	Chlorine	<MRL	0.9	<MRL	<MRL	1.0
	Filtered	Chlorine	<MRL	0.5	0.2	<MRL	0.7
	Raw	Chloramine	<MRL	0.4	<MRL	<MRL	0.4
	Ozonated	Chloramine	<MRL	0.5	<MRL	<MRL	0.6
	Filtered	Chloramine	<MRL	0.3	<MRL	<MRL	0.3

<MRL – below the minimum reporting limit

Table B-6.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	0.9
	Ozonated	Chlorine	2.1
	Filtered	Chlorine	1.0
	Raw	Chloramine	1.6
	Ozonated	Chloramine	2.6
	Filtered	Chloramine	0.9
Spring	Raw	Chlorine	0.9
	Ozonated	Chlorine	1.2
	Filtered	Chlorine	<MRL
	Raw	Chloramine	<MRL
	Ozonated	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	0.8
	Ozonated	Chlorine	1.0
	Filtered	Chlorine	1.0
	Raw	Chloramine	<MRL
	Ozonated	Chloramine	<MRL
	Filtered	Chloramine	<MRL

<MRL – below the minimum reporting limit

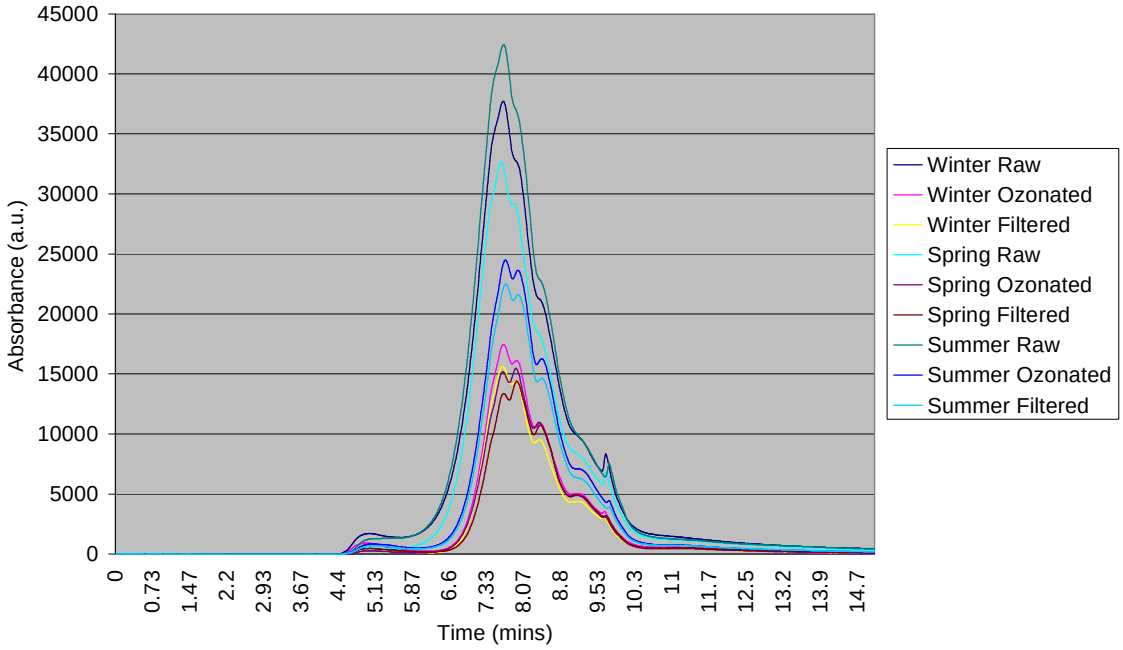

Figure B-6 HPSEC chromatogram of raw and treated waters

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Table B-7.1 Final and Distribution THMs (all data in μg/L)

Season	Sample	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Final	51.8	5.7	0.5	<MRL	58.0
	Dist 1	188.6	7.1	0.6	<MRL	196.3
	Dist 2	157.9	11.3	1.1	<MRL	170.3
Spring	Final	204.7	18.7	1.9	<MRL	225.2
	Dist 1	172.1	20.0	2.2	<MRL	194.2
	Dist 2	190.3	18.3	2.0	<MRL	210.6
Summer	Final	141.3	17.2	1.0	<MRL	159.4
	Dist 1	206.4	25.3	2.1	0.1	233.9
	Dist 2	153.1	18.2	1.0	0.1	172.4

<MRL – below the minimum reporting limit

Table B-7.2 Final and Distribution HAAs (all data in μg/L)

Season	Sample	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Final	2.8	<MRL	30.1	2.2	18.4	0.1	1.9	<MRL	0.3	56.0
	Dist 1	2.4	<MRL	17.0	<MRL	20.7	0.4	1.9	<MRL	0.1	43.4
	Dist 2	3.6	<MRL	48.0	2.7	32.5	0.1	2.7	<MRL	0.8	90.6
Spring	Final	5.1	<MRL	41.9	0.4	5.1	22.6	2.3	0.3	0.3	78.2
	Dist 1	3.0	<MRL	11.6	<MRL	1.3	24.8	2.3	0.3	0.4	44.0
	Dist 2	<MRL	<MRL	6.7	<MRL	0.5	23.6	1.8	0.2	0.3	35.1
Summer	Final	3.1	<MRL	52.9	3.9	40.3	0.2	2.2	<MRL	<MRL	102.7
	Dist 1	<MRL	<MRL	18.6	1.7	33.6	0.1	2.0	<MRL	<MRL	57.4
	Dist 2	4.9	<MRL	66.0	4.5	55.4	0.2	2.7	<MRL	<MRL	133.8

<MRL – below the minimum reporting limit

Table B-7.3 Final and Distribution HANs (all data in μg/L)

Season	Sample	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Final	<MRL	0.6	0.2	<MRL	0.8
	Dist 1	<MRL	0.4	0.2	<MRL	0.6
	Dist 2	0.1	0.5	0.2	<MRL	0.8
Spring	Final	<MRL	1.0	0.5	0.9	2.4
	Dist 1	<MRL	0.7	0.4	1.0	2.1
	Dist 2	<MRL	0.7	0.3	0.5	1.5
Summer	Final	0.1	1.0	0.5	0.2	1.8
	Dist 1	<MRL	0.6	0.4	0.3	1.4
	Dist 2	0.2	0.9	0.5	0.2	1.8

<MRL – below the minimum reporting limit

Table B-7.4 Final and Distribution HNM (all data in μg/L)

Season	Sample	CP
Winter	Final	0.2
	Dist 1	0.2
	Dist 2	0.1
Spring	Final	0.3
	Dist 1	0.2
	Dist 2	0.1
Summer	Final	0.3
	Dist 1	0.3
	Dist 2	0.4

Table B-7.5 Final and Distribution I THMs (all data in μg/L)

Season	Sample	DCIM	BCIM	I THM2
Winter	Final	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm
Spring	Final	1.6	<MRL	1.6
	Dist 1	1.9	<MRL	1.9
	Dist 2	1.1	<MRL	1.1
Summer	Final	1.8	<MRL	2.0
	Dist 1	0.9	<MRL	1.1
	Dist 2	1.4	<MRL	1.5

Nm – not measured
<MRL – below the minimum reporting limit

Table B-7.6 Final and Distribution Nitrosamines (all data in ng/L)

Season	Sample	NDMA	NMEA	NDPA	NPYR	NPIP	Nitro5
Winter	Final	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 1	Nm	Nm	Nm	Nm	Nm	Nm
	Dist 2	Nm	Nm	Nm	Nm	Nm	Nm
Spring	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
Summer	Final	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 1	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL
	Dist 2	<MRL	<MRL	<MRL	<MRL	<MRL	<MRL

<MRL – below the minimum reporting limit

Table B-7.7 In-Works Samples

Season	Sample	NPOC (mg/L)	UV (/m)	SUVA (L/m/mg)	Bromine (μg/L)	Iodine (μg/L)	Conductivity (μS)
Winter	Raw	17.7	52.6	3.0	69.7	3.9	63.5
	Filtered	3.1	4.8	1.5	54.0	0.0	114.9
Spring	Raw	11.2	41.8	3.7	64.8	4.2	85.5
	Filtered	3.6	5.3	1.5	54.2	1.3	127.9
Summer	Raw	26.2	47.1	1.8	56.1	9.0	63.1
	Filtered	4.3	8.2	1.9	24.0	2.4	136.9

Table B-7.8 Formation Potential Test THMs (all data in μg/L)

Season	Sample	Disinfectant	$CHCl_3$	$CHCl_2Br$	$CHClBr_2$	$CHBr_3$	THM4
Winter	Raw	Chlorine	990.4	14.6	0.1	<MRL	1005.1
	Filtered	Chlorine	60.0	6.3	0.3	<MRL	66.6
	Raw	Chloramine	33.5	0.1	<MRL	<MRL	33.6
	Filtered	Chloramine	6.6	0.1	<MRL	<MRL	6.7
Spring	Raw	Chlorine	303.6	9.9	0.1	<MRL	313.6
	Filtered	Chlorine	118.7	15.1	1.2	<MRL	135.0
	Raw	Chloramine	25.8	<MRL	<MRL	<MRL	25.8
	Filtered	Chloramine	11.3	0.1	<MRL	<MRL	11.4
Summer	Raw	Chlorine	439.4	7.7	0.6	<MRL	447.8
	Filtered	Chlorine	148.9	8.6	0.4	0.4	158.3
	Raw	Chloramine	39.5	<MRL	<MRL	<MRL	39.5
	Filtered	Chloramine	28.6	0.1	<MRL	<MRL	28.8

<MRL – below the minimum reporting limit

Table B-7.9 Formation Potential Test HAAs (all data in μg/L)

Season	Sample	Disinfectant	MC	MB	DC	BC	TC	DB	BDC	DBC	TB	HAA9
Winter	Raw	Chlorine	9.1	<MRL	143.1	1.3	379.3	<MRL	2.2	<MRL	0.3	535.2
	Filtered	Chlorine	<MRL	<MRL	8.5	0.4	13.1	<MRL	0.9	<MRL	<MRL	25.0
	Raw	Chloramine	3.0	<MRL	24.7	0.4	1.1	<MRL	<MRL	<MRL	<MRL	29.1
	Filtered	Chloramine	<MRL	<MRL	1.8	0.1	0.2	<MRL	<MRL	<MRL	<MRL	2.1
Spring	Raw	Chlorine	13.1	0.3	165.8	3.8	210.7	<MRL	3.8	<MRL	0.6	398.1
	Filtered	Chlorine	3.5	0.6	60.7	6.1	89.5	0.3	9.9	0.5	1.4	172.4
	Raw	Chloramine	<MRL	<MRL	4.0	<MRL	0.1	<MRL	<MRL	<MRL	0.9	5.1
	Filtered	Chloramine	<MRL	<MRL	2.8	<MRL	0.2	<MRL	<MRL	<MRL	1.3	4.4
Summer	Raw	Chlorine	4.4	<MRL	45.4	0.3	93.5	<MRL	0.5	<MRL	<MRL	144.2
	Filtered	Chlorine	<MRL	<MRL	8.7	0.4	13.9	<MRL	0.7	<MRL	<MRL	23.7
	Raw	Chloramine	<MRL	<MRL	<MRL	<MRL	0.2	<MRL	<MRL	<MRL	<MRL	2.2
	Filtered	Chloramine	<MRL	0.3	3.2	<MRL	0.2	<MRL	<MRL	<MRL	<MRL	6.2

<MRL – below the minimum reporting limit

Table B-7.10 Formation Potential Test HANs (all data in μg/L)

Season	Sample	Disinfectant	TCAN	DCAN	BCAN	DBAN	HAN4
Winter	Raw	Chlorine	0.1	1.8	0.2	4.7	6.8
	Filtered	Chlorine	<MRL	<MRL	<MRL	<MRL	0.1
	Raw	Chloramine	<MRL	14.0	4.3	1.7	20.1
	Filtered	Chloramine	<MRL	10.8	3.3	1.3	15.4
Spring	Raw	Chlorine	<MRL	5.6	<MRL	1.0	6.7
	Filtered	Chlorine	<MRL	0.4	0.4	0.5	1.4
	Raw	Chloramine	<MRL	0.7	<MRL	<MRL	0.7
	Filtered	Chloramine	<MRL	0.5	<MRL	<MRL	0.5
Summer	Raw	Chlorine	0.3	12.0	0.1	<MRL	12.3
	Filtered	Chlorine	<MRL	0.8	0.3	<MRL	1.0
	Raw	Chloramine	<MRL	1.0	<MRL	<MRL	1.0
	Filtered	Chloramine	<MRL	0.5	<MRL	<MRL	0.5

<MRL – below the minimum reporting limit

Table B-7.11 Formation Potential Test HNMs (all data in μg/L)

Season	Sample	Disinfectant	CP
Winter	Raw	Chlorine	2.9
	Filtered	Chlorine	0.4
	Raw	Chloramine	4.3
	Filtered	Chloramine	3.3
Spring	Raw	Chlorine	0.4
	Filtered	Chlorine	0.3
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL
Summer	Raw	Chlorine	1.0
	Filtered	Chlorine	0.4
	Raw	Chloramine	<MRL
	Filtered	Chloramine	<MRL

<MRL – below the minimum reporting limit

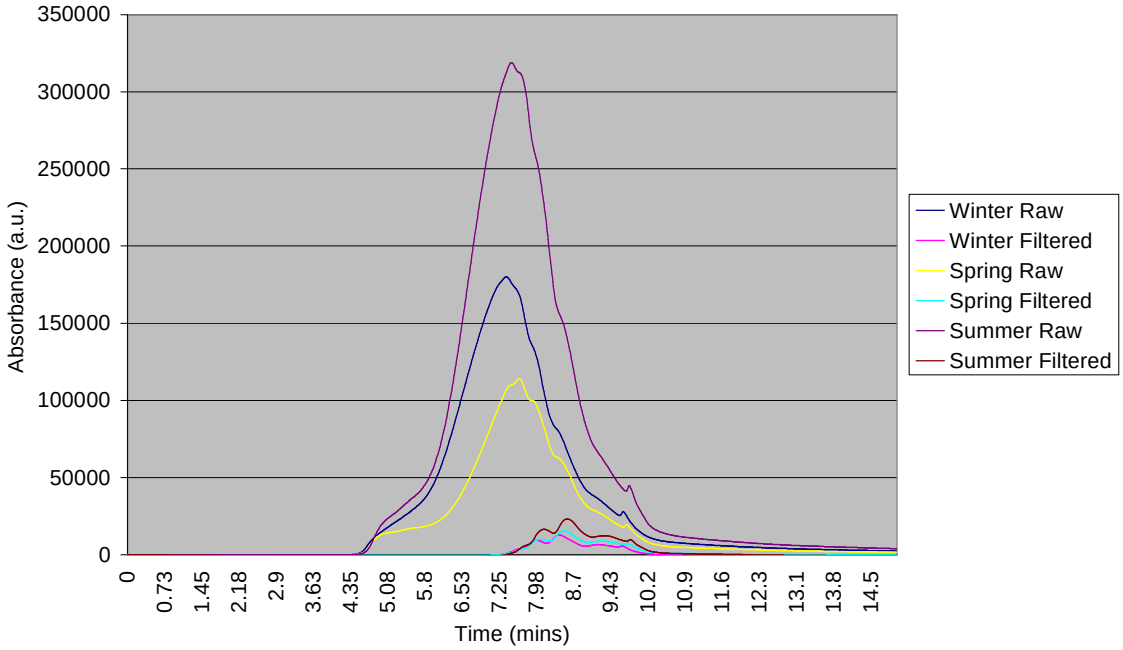

Figure B-7 HPSEC chromatogram of raw and treated waters

IEH Institute of Environment and Health

Cranfield UNIVERSITY

APPENDIX C TASK 3 REPORT

STUDY INTO THE FORMATION OF DISINFECTION BY-PRODUCTS OF CHLORAMINATION, POTENTIAL HEALTH IMPLICATIONS AND TECHNIQUES FOR MINIMISATION

Annex to Main Report — Report on Task 3: Review of toxicology data, assessment of risk and aesthetic data.

December 2008

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C1. Introduction

Since the late 1800's, the treatment of sewage and drinking water by filtration and, subsequently, chlorination has provided a major contribution to public health and well-being through its prevention of outbreaks of waterborne diseases – such as cholera. However, as discussed previously in this report, over 500 individual disinfection by-products (DBPs) may be formed as a result of chlorination (Parsons & Jefferson, 2006), and the presence of such compounds in drinking water may introduce potential health risks under certain circumstances (White, 1986). It is essential to consider that, although the potential health risks of DBPs are not fully elucidated and supporting data for certain compounds is incomplete, the well known benefits of disinfection must be weighed against the uncertain risks of adverse effects arising from disinfection processes (Craun *et al.*, 1994). The nature and extent of the by-products formed are dependent on multiple factors, including the disinfection method (e.g. chlorination or chloramination), the organic or humic content of the water and the distance of the sample point from the treatment plant. Thus, potentially a multitude of DBPs may be formed. The nature of the risks associated with the formation of DBPs has been the subject of some concern, and has been discussed in a number of published expert workshops and risk assessments. For example, a recent Gordon Research Conference (Massachusetts, USA, August 2006) entitled *Drinking Water Disinfection By-Products* brought together many of the world's experts to examine the most recent health findings with the purpose of integrating the knowledge on occurrence and formation of disinfection by-products, exposure, current toxicity, and epidemiology. The predominant DBPs that have been detected in treated drinking water in various countries can be separated into several chemical groups (Berry *et al.*, 1997) including: trihalomethanes (THMs; including the iodinated trihalomethanes, ITHMs); haloacetic acids (HAAs); haloacetonitriles (HANs); halonitromethane (HNMs); haloketones; cyanogen halides (CNX); haloaldehyde; nitrosoamines (NAs); haloacetamides; dimethylcyanamide; and the halogenated furanones.

In this phase of the study, IEH scientists considered the hazard profiles – including consideration of the basis for any acceptable daily intake (ADI), tolerable daily intake (TDI) or reference dose (RefD) established by any authoritative bodies – for each of the DBP categories or, where appropriate, individual compounds, using information obtained from a structured search of published and, where possible, 'grey' literature. Particular attention was given to the DBP's for which a difference in relative concentration was apparent between those Drinking Water Treatment Works (DWTWs) studied here that use chlorination and those that add ammonia after chlorination (chloramination) as a modified disinfection treatment (as informed by the sampling and analysis strategy undertaken during the course of the project).

Supported by the hazard profiles developed, appropriate ADIs, TDIs or RefDs were compared with the drinking water exposure information gathered during the course of the sampling campaign using standard defaults for intakes by particular population subgroups. Where no such reference value was available or where there was clear concern (because of more recent evidence on toxicity) as to the basis on which such values had been derived, a precautionary study-specific provisional acceptable daily intake (SPPADI) value was estimated using available information on the critical endpoint's no-adverse-effect or low-adverse-effect levels (NOAEL and LOAEL, respectively) based on toxicity studies. On this basis, the margin of safety for each

compound was calculated so as to inform on the extent and nature of any appreciable risk that might exist.

A further aspect considered was the potential that unexpected, difficult to predict, adverse effects might arise as a result of the complex chemical mixtures formed during the treatment processes, and the extent of any potential risk that might therefore be posed.

In this report, the methodology adopted is summarised in Section 2, and the hazard profiles for each group of chemicals in Section 3. Risk estimates are discussed in Section 4, while the possibility of mixture interactions influencing toxicity is addressed in Section 5.

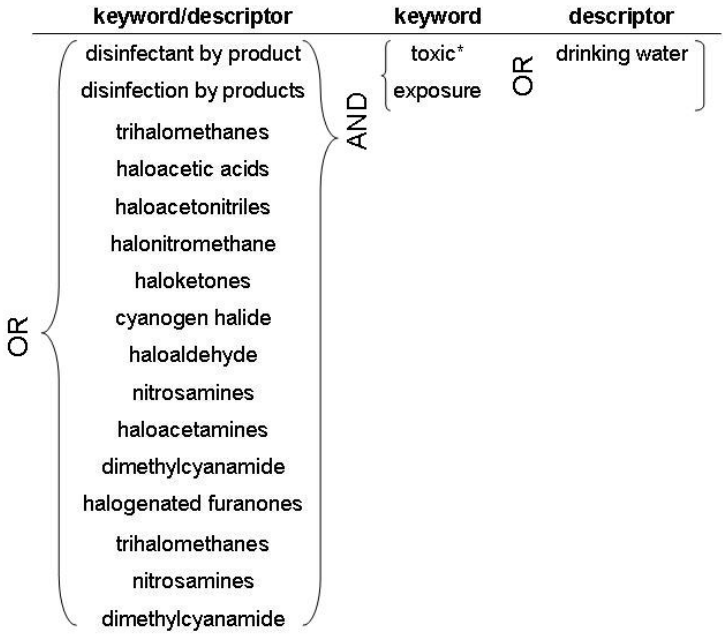
C2. Methods

C2.1 Literature search

On the basis of discussions between Institute scientists and the Institute's Information Scientist, a comprehensive search structure was applied to the published and 'grey' literature. Databases consulted included: BIOSIS Previews; EMBASE; MEDLINE; TOXLINE; Biological Sciences; Biology Digest; Conference Papers Index; Environmental Sciences and Pollution Management; Scopus; Science Direct; Web of Knowledge; PASCAL; SciSearch and ToxFile. The output of the search was reviewed by experienced scientists and selected material obtained for detailed consideration. In addition, the internet was searched to enable on-line access to authoritative reviews and assessments and databanks.

The search criteria used to identify the hazard information for selected DBPs are presented in Table 2.1. These criteria were linked by Boolean terms. Initially two searches considering the DBP keywords (all terms considered, first column) and the exposure keywords (last two columns) were performed and were then combined to obtain the initial output. This was considered in detail and further information requested for certain aspects where the Institute scientists deemed it appropriate. Whilst the initial focus of the literature review was on original papers, review papers were identified and used to ensure that the appropriate literature was captured.

Table C2.1 Search criteria used to identify hazard information for selected DBPs, terms linked by Boolean terms.



C2.2 Derivation of hazard profiles and acceptable exposures

The human and animal toxicity data were subject to critical review by experienced toxicologists and detailed hazard profiles developed for each group of chemicals. In particular, attention was given to determining the following key aspects of toxicity:

- Human evidence of adverse effects;
- Toxicokinetics;
- Acute toxicity;
- Repeat dose toxicity;
- Genetic toxicology and carcinogenicity;
- Reproductive and developmental toxicity;
- Mechanism(s) of action; and
- Authoritative or project specific provisional acceptable levels.

Efforts were made, wherever possible, to identify an established exposure standard or guideline value by an authoritative body for each of the chemicals and/or groups, and to document the basis on which this value had been established. Such standards may include, for example, ADIs, MRLs, TDIs or RefDs; preference was given to European standards and World Health Organisation (WHO) guideline values for Europe, as opposed to those of other regions (e.g. USA). Particular efforts were made to establish if the value was based upon the chemical's hazard potential (i.e. health-based) or if it represented a practical, technology-based, level of control or analytical determination.

For non health-based standards, the toxicological evidence was reviewed to confirm that the given value provided an adequate margin of safety, although it is noted that the standards may be established as a consequence of negotiation and are usually set below actual WHO health-based values. Wherever possible, the subsequent comparison with exposure (used for the risk assessment determinations, see below) was based on the use of standards or guidelines relating to drinking water (private communication with J Fawell). If unavailable, the possibility of using other standards (e.g. for food) relating to oral intake was investigated. Finally, if necessary, attempts were made to identify any health-related standard for other routes (e.g. inhalation) for which appropriate adjustment factors could be applied to derive a suitable oral standard using approaches in line with UK government guidance (Cantor *et al.*, 1989).

For some of the potential contaminants considered, no authoritative standard (ADI, MRL, TDI or RefD) exists. In these cases, the toxicological datasets were considered to identify the nature and dosimetry of any critical end points of effect. The toxicological profiles were based on a review of the most current review evaluations published by authoritative organisations and extensive literature searches. Where possible, an appropriate '*de novo'* specific project potential acceptable daily intake (SPPADI) was derived from the data available. In such instances, the relevant NOAEL was selected for the chemical, and an uncertainty factor applied that reflected the nature of the NOAEL and the degree of uncertainty regarding the dataset; the approach adopted followed that recommended by IGHRC (Cantor *et al.*, 1989). In the absence of any suitable NOAEL, then a LOAEL for the critical endpoint of concern was used, with appropriate adjustment of the uncertainty factors; this was only deemed necessary for DBPs, as discussed in Section 4.

For a number of chemicals, the toxicity dataset was grossly inadequate or absent. In such cases, read-across from other chemicals with similar properties was attempted to allow derivation of a putative SPPADI. However, despite these efforts in a few instances no suitable SPPADI could be identified and, for these, no hazard-based risk assessment is therefore possible.

C2.3 Risk assessment

The maximum measured concentration and the median measured concentration for each group of DBPs considered were used to calculate the total predicted daily (drinking water) intake values for an average consumer (adults and toddlers). These were then compared with the relevant authoritative standard or a derived SPPADI.

The potential exposure of the various sections of the human population considered were calculated by multiplying the maximum detected concentration of the compounds (from all chloraminated samples) present in drinking water supplies, with default assumptions regarding the average amounts of water consumed per day by adults and children. For this, daily water ingestion by an adult was assumed to be 2L; an 'oral correction factor' of 0.39 was applied to this value to derive an estimated value for a toddler (child aged 1–2 years, in this instance; (DEFRA/EA, 2002)).

Calculations of intakes per person on a bodyweight basis (µg/kg bw/day) were based on typical bodyweights of 60 kg for an adult and 11 kg for a child aged 1–2 years (DEFRA/EA, 2002). Where such data were available, the intake of each individual substance from drinking water was expressed as a proportion of the acceptable intake

derived from the authoritative standard or the SSPADI, for adults and toddlers separately.

In the initial assessments, a highly precautionary approach was adopted in which it was assumed that all of the drinking water consumed would contain residues at the estimated levels, on a long-term basis. Where the total predicted daily intake amounted to less than 5% of the authoritative standard or the SSPADI, there was considered not to be any appreciable risk associated with these sources. Where a potential for exceeding 10% of the selected authoritative standard or the SSPADI was estimated for either adults or toddlers, a more detailed assessment of the extent and character of the risk was undertaken.

C3. Hazard assessment for DBPs

C3.1 Epidemiological evidence of possible health effects in humans

While it is not the intention of this study to undertake a comprehensive critical assessment of the epidemiological evidence in relation to the presence of DBPs in drinking water supplies, it is noted that a number of epidemiology studies have reported associations between use of DBP and a range of toxicological effects in various communities (e.g. Villanueva *et al.*, 2007; Hwang *et al.*, 2008). Epidemiological studies in general have a number of limitations which confound assessment of the effects of DBPs including: indirect measurement of exposure (route or concentration and dose at target organ); validity of disease status assessment; individual exposure variables; variation in source of contaminant; other possible exposure routes to a contaminant (e.g. through smoking); duration of exposure; and historical water treatment data (separate to population data; Cantor *et al.*, 1989, Calderon, 2000). Of further concern is that any slight increases in relative risk will be difficult to detect in a population (diminishing the interpretability of such studies) and that any effect observed may be attributable to the actions of single or multiple substances within the complex mixture of chemicals to which individuals may be exposed. An acknowledged bias in epidemiological studies is that they are likely to underestimate the risk and distort the exposure-response relationship between DBP exposure and toxic end points (Bove *et al.*, 2002). Whilst epidemiological studies are of importance in establishing the potential human effects of DBPs. However, it is not possible to establish casual links solely on the basis of epidemiological studies of the type and nature currently available on this subject; this is, in part, a reflection of the number of potential confounding factors that may impact on study interpretation.

An affect of DBP exposure on foetal development has been suggested by some epidemiological studies. An analysis of full term pregnancies in Italian towns (Aggazzotti *et al.*, 2003, Aggazzotti *et al.*, 2004) reported a weak association between small at gestational age (SGA) and high exposure to THMs (30 μg/L) and chlorite (200 μg/L; 1194 births studied, with 239 SGAs identified). However, the mechanism of action and the specific chemical species responsible could not be identified, and this association can not be conclusively linked to DBP exposure. Separately, a study of Taiwanese births from 2001 to 2003 showed a correlation between a high concentration of total trihalomethanes in drinking water and increased incidences of ventricular septal defects, cleft palates, and anencephalus; this was corroborated by a meta-analysis of

three separate studies (Hwang *et al.*, 2008). However, together the four studies could not identify a causal agent and were unable to give an accurate indication of the DBP concentration within the water supply or other potential exposures to chlorinated compounds. Also, the relationship between total THMs and bladder cancer has been investigated in Taiwan (65 municipalities, cause of death taken from official records dating from 1996 to 2005) with comparisons addressing gender, age and age at death matched controls. This study showed a significant positive correlation between concentration of THM in drinking water (data obtained from government agencies) and risk of death from bladder cancer (Chang *et al.*, 2007). This possible association is further supported by a case-control study of 281 cases of bladder cancer and 272 controls in French hospitals where 70 % of residential exposure to DBPs was determined over a 30 year period; this showed that the risk of bladder cancer was increased with the duration of exposure to chlorinated surface water and with estimated THM content of the water (Chevrier *et al.*, 2004). A meta-analysis of 14 epidemiological studies has suggested that there is evidence to link exposure to THMs with adverse birth outcomes (Bove *et al.*, 2002), particularly at total THM levels greater than 100 ppb where reductions were noted in birth weight of full term births by 70.4 g (80938 births and 594 still births studied between 1985 to 1988 with exposure estimated from tap water sample data (Bove *et al.*, 1995). A study considering thte total THM concentration and the risk of stillbirth or low birth weight within three water regions within England between 1992 and 1998 (estimated water concentration determined by models and catagorised as low [less than 30 μg/K], medium [30 to 59 μg/L] and high [60μg/L or greater]) suggested that the maternal exposure to high concentrations of THMs was significantly associated with the incidence of still births (Toledano *et al.*, 2005). Separately, a study of the number of birth defects in Western Australia (official records compared to THM concentration data recorded during routine monitoring) showed a relationship in the likelihood of birth defects occurring in areas where the drinking water has high THM concentrations (>100 μg/L; Chisholm *et al.*, 2004). However, a UK-based project comparing congenital anomaly data from the National Congenital Anomalies System and the National Terminations Registry against the THM concentrations obtained from water companies suggested that there was little evidence for a relationship between THM concentrations in drinking water and risk of congenital anomalies. In the study, 2,605,226 live births, in which there were 22,828 cases of congential anomalies, showed no statistically significant trends across exposure catagories (total THM exposure defined as less than 30 μg/L, 30 to 60 μg/L or 60 μg/L; total brominated exposure of less than 10 μg/L, 10 to 20 μg/L or 20 μg/L; and bromoform exposure (less than 2 μg/L, 2 to 4 μg/L, or 4 μg/L modelled at the place of residence for the first trimester of pregnancy) for either broadly defined anomaly groups (including cleft palate/lip, abdominal wall, major cardiac, neural tube, urinary and respiratory defects) or a more restricted group of anaomalises (including isolated and multiple anomalies, data adjusted for sex, maternal age and socioeconomic status; Nieuwenhuijsen *et al.*, 2008).

Increased HAA levels have also been linked to reproductive effects. Total HAA levels associated with abruption placentae cases ending in stillbirths, an association not seen with total THM or BDCM concentrations in drinking water in the same population (695857 women; DBP exposure estimated from monthly DBP concentrations at treatment facilities; (Broers *et al.*, 2001). A study of cardiac defects in 58669 women and chlorination disinfection showed that the increased risk of congential defects (753 cases within population) associated with the use of chlorination processes and with increase of THM concentration, although the risk was considered small (Cedergren *et al.*, 2002). Male reproductive effects have also been noted with THMs; high total THM levels (>160μg/L in drinking water determined by water utility measurements) have

been linked to a decrease in percent normal morphology and increase in the percentage of head defects when compared to low total THM levels (≤ 40 μg/L), in a study of 157 healthy men (Fenster *et al.*, 2003).

DBPs have also been linked to cancer occurrence in populations with increased TBM levels associating with an increase in the odds ratio for rectal cancer in disease-free white males (35 to 90 years old, 128 cases and 253 controls); a weak association between dibromochloromethane or bromodichloromethane and increased risk of rectal cancer was also noted, although the total THM concentration did not show this association (Bove *et al.*, 2007). Other studies have shown a correlation between high THM concentrations (greater than 40 μg/L) and decreased foetal growth in genetically-susceptible newborns (those without the CYP2E1 gene; 458 cases) when compared to controls with CYP2E1 gene (426 cases; (Infante-Rivard *et al.*, 2002).

An association was also reported between brain cancer and exposure to chlorinated water in men with exposures either of 20 - 39 years, or greater than 40 years, to chlorinated water source, and in women exposed for 20 – 39 years (291 patients and 1983 controls with exposure estimated from water utilities records), where water quality information was available for over 70% of life span. However specific DBPs were not identified (Cantor *et al.*, 1999). A similar study comparing 2800 cancer patients (with a variety of cancers) against the incidence of chlorinated water supply indicated that the increased duration of exposure to chlorinated drinking water associated with increased bladder cancer incidence (data obtained from the National Bladder Cancer Survey; USA), although there was also an association between smoking and bladder cancer incidence that may have biased this finding (Cantor *et al.*, 1989).

There are also some reports of associations of DBP with gastrointestinal and urinary tract cancer (Koivusalo *et al.*, 1997, Koivusalo & Vartiainen, 1997), as well as a link between THM-containing drinking water and the increased risk of leukaemia in females (data from leukaemia incidence in locations with sampling data indicating volatile organic chemical exposure (Fagliano *et al.*, 1990)), whilst others have reported an increased risk of chronic myeloid leukaemia and chronic exposure to high concentrations of THMs (Kasim 2006). Another study has, however, reported no association between risk of leukaemia (childhood acute lymphoblastic leukaemia) and THM intake (Koivusalo *et al.*, 1997), and drew attention to the limitations of studies of this type.

Problems with drawing conclusions on causality based on the available types of epidemiological study have been noted to include a lack of information on the composition and extent of DBPs within the source water, lack of information on how DBPs interact, and a lack of data on the personal activity of subjects (including bathing habits and diet) and their water consumption patterns (Arbuckle *et al.*, 2002). Some indication of the extent of an individual's exposure to DBPs can be obtained from measurement of blood trichloroacetic acid concentration, which has shown to be suitable as a biomarker of exposure to DBPs (Froese *et al.*, 2002).

In estimating risk the route of exposure is an important variable (Gordon, 2006). Thus, for example, the highest blood concentrations of volunteers after exposure to drinking water have been found to occur in individuals who took 10 minute showers (n = 11) while the lowest levels were found in individuals who drank 1L of drinking water (n = 10; Backer *et al.*, 2000). In normal environments individuals may encounter volatisation of THMs which may lead to the increased importance of inhalation exposures to THMs, the extent of which may vary over time in ways difficult to predict. For example, THM

concentrations in the air of a swimming pool have been shown to vary between 6 $\mu g/m^3$ and 16.32 $\mu g/m^3$ over a two month period (Czajka *et al.*, 2003). Such variation may not be true for other DBPs however as, for example, home water filters have been shown to be effective at removing THM, HAA and MX from water samples (Egorov *et al.*, 2003).

In summary, some epidemiological studies have reported associations between THM exposure and adverse birth outcomes, low birth weight, rectal cancer and brain cancer, while HAA exposure has been associated with increases in numbers of stillbirths. However, these studies have significant limitations, such as not considering exposure to all DBPs and reliance on various measures estimating THM concentration. It is recognised that, in order to elucidate the mechanism of human toxicity from DBPs, further detailed toxicological assessments of commonly occurring DBPs in mixtures should occur (Nieuwenhuijsen *et al.*, 2000).

While it is acknowledged that inhalation and dermal exposure to DBPs may constitute an important proportion of the total DBP exposure of some individuals, it is not possible within the constraints of the current study design to estimate the extent of such exposures in the populations considered here. Therefore, the current assessment of risk posed by the various DBPs is restricted solely to consideration of oral exposure through consumption of drinking water.

C3.2 Influence of DBPs on aesthetic properties of drinking water.

Whilst the levels of DBPs in drinking water are generally unknown by the general public, consumers judge the quality of their drinking water on aesthetic properties including taste, odour and colour (Koivusalo *et al.*, 1997). There have been suggestions that the presence of 'off-flavours' in a water supply might indicate that levels of – for example – DBPs had exceeded regulatory thresholds and could therefore potentially be of possible concern (Koivusalo *et al.*, 1997). However, it must be appreciated that there are a number of other possible sources of odour/colouration in water supplies, and the importance and contribution to these aspects of water quality made by DBPs is as yet unclear. It is, however, apparent that there is little publically information available on odour threshold limits (OTLs) or odour threshold concentrations (OTCs) for the majority of DBPs.

The majority of chemical species for which OTLs in drinking waters are available are pesticides or phenolic compounds (Young *et al.*, 1996), although DBPs have been suggested, at high levels, to raise issues of odour and taste in drinking water (Koivusalo *et al.*, 1997). Currently, the only group of DBP's with an established OTC is the iodinated-THMs (Cancho *et al.*, 2001) and so these would be the main contaminants of concern with regard to this aspect in the current study. The OTC's of the iodinated-THMs (dichloroiodomethane, bromochloroiodomethane, chlorodiiodomethane, bromodiiodomethane and iodoform) were determined using flavour profile analysis (FPA) involving a panel of six assessors who – based on sniffing – then described and rated samples containing different concentrations of the listed iodinated-THMs. The experimental OTC was defined as the lowest concentration at which a smell was noticed by at least one panellist; values were in the low $\mu g/L$ range (diochloroiodomethane (5.8 $\mu g/L$); bromochloroiodomethane (5.1 $\mu g/L$); dibromoiodomethane (2.9 $\mu g/L$); chlorodiiodomethane (0.2 $\mu g/L$); bromodiiodomethane (0.1 $\mu g/L$); and iodoform (0.03 $\mu g/L$)).

It has, however, been noted that there have been few complaints from the public served by the water treatment plants considered in the current study and, therefore, the issues of odour and taste was not considered further in the study.

C3.3 Hazard profiles for each of the groups of DBPs considered

C3.3.1 Trihalomethanes

The trihalomethane (THM) group comprises the following principal compounds:

trichloromethane (chloroform; TCM; CAS number 67-66-3);

bromodichloromethane (BDCM; CAS number 75-27-4);

dibromochloromethane (DBCM; CAS number 124-48-1); and

tribromomethane (TBM; bromoform; CAS number 75-25-2).

In addition, a number of iodinated forms of THM (ITHMs) have been detected in drinking water and, as their properties differ slightly from those of the other THMs, particularly with regard to their influence on odour and taste, they are considered separately (Subsection 3.3.1.1).

The principal source of human exposure is thought to be from the consumption of chlorinated drinking water (Lin & Hoang, 1999) though other water uses, such as bathing, may contribute significantly to total exposures as a result of inhalation of THMs vaporized into the air or via dermal contact under certain scenarios (Lin & Hoang, 1999). Indeed, more generally the environmental release of THMs is largely to air during the chlorination of drinking water, with only small amounts retained in the water (Backer *et al.*, 2000) It has been reported that while less than 20% of THMs are volatilised after storage, pouring and serving of tap water at temperatures below 30°C, volatilisation increased to 75% if the water was boiled (even for a brief time) and up to 90% volatilised when boiled water was poured and served (Batterman *et al.*, 2000, Levesque *et al.*, 2006).

Toxicodynamics

THMs may be absorbed into the body through various routes, including ingestion, inhalation, and through the skin. However there is little information available on the percentage or rates of absorption from each route. Pharmacologically-based toxicokinetic models that considered the possible routes of THM exposure in various multimedia indoor exposure scenarios (including ingestion, inhalation and skin absorption) for humans, suggest that ingestion accounts for only 50 % of the total absorbed or metabolised dose of THMs (Haddad *et al.*, 2006).

Experimentally, oral administration of BDCM to male F344 rats (oral gavage, 200 mg/kg bw or 400 mg/kg bw with induction of CYP1A2 by dioxin for 24 hours) showed BDCM was metabolised primarily by CYP2E1 (Lilly *et al.*, 1997), with CYP1A2 playing a secondary role. Metabolic simulations suggested that BDCM would be completely metabolised after 5 hours at 200 mg/kg bw and approximately 7 hours at 400 mg/kg bw CYP2E1 (Lilly *et al.*, 1997).

Acute toxicity

TCM was used historically on humans for its acute effect as an inhalation anaesthetic. In addition to central nervous system (CNS) effects, TCM administration at high concentrations is also known to cause cardiac arrhythmia and liver and kidney toxicity in humans (IPCS, 1994).

Oral administration of 2000 mg/kg bw TBM (by gavage in corn oil) to male and female F344 rats and $B6C3F_1$ mice caused death, with the majority (3 out of 5 mice or rats) dying after administration of 1000 mg/kg bw TBM. Shallow breathing was noted in mice and rats treated with 2000 or 1000 mg/kg bw (NTP, 1989). The administration of TCM and DBCM to F344 rats (single gavage dose in an aqueous carrier 0.125 to 1.5 mmol/kg bw) resulted in dose-dependent hepatotoxicity (shown by increases in serum proteins, compared with control levels), and suggested that they were equipotent hepatotoxicants (Keegan *et al.*, 1998). In this study, the acute oral NOAELs were determined as 0.25 mmol/kg bw and LOAEL as 0.5 mmol/kg bw for both TCM and DBCM.

Inhalation exposure of male F344 rats to BDCM (4 hours at 100 to 3200 ppm) has been reported to result in dose-related increases in hepatic microsomal methoxyresorufin demethylase (MROD), ethoxyresorufin de-ethylease (EROD) and pentoxyresorufin dealkylase (PROD) activities, as well as in cytochrome P450 isoenzymes CYP1A2 and CYP2B1 (which showed an elevated response at the higher dose; (Allis *et al.*, 2001). When these results were compared with a repeat dose gavage study on BDCM in female F344 rats, findings were similar and the authors concluded that the liver response was similar in either sex (Allis *et al.*, 2001). BDCM hepatotoxicity was also noted to be increased in male F344 rats after induction of CYP1A2 using 2,3,7,8-tetrachlordibenzo-*p*-dioxin (TCDD; 1 μg/kg bw by gavage) when rats were dosed with BDCM (gavage, aqueous carrier at 0, 200 or 400 mg/kg bw) three days after induction (a significant increase in 400 mg/kg group and a trend in 200 mg/kg group), although no induction of CYP2E1 and CYP2B1/2 occurred, whilst inhibition of CYP1A2 reduced the metabolism and toxicity of BDCM (Allis *et al.*, 2002).

Repeat dose toxicity

Administration of TCM, BDCM, DCBM and TBM to female B6C3F1 for 11 days either by gavage (two dose levels: TCM at 130 or 260 mg/kg bw; BDCM at 150 or 300 mg/kg bw; DBCM at 100 or 300 mg/kg bw; and TBM at 200 or 500 mg/kg bw) or in the drinking water (75% saturation) caused an increase in liver:body weight ratio when administered by gavage; drinking water administration produced effects similar to those in the low dose gavage group. Proliferating cell nuclear antigen-labelling index (PCNA-LI) showed a similar pattern of response. TCM and BDCM exhibited the greatest hepatic effects whilst TBM and TCM provoked a greater PCNA-LI (Coffin *et al.*, 2000).

BDCM (0.7 g/L) and TCM (1.8 g/L in drinking water; 17 weeks exposure) has been shown to alter the expression of caecal enzymes in male Long Evans rats; the activities of dechlorinase and beta-galactosidase were reduced and nitroreductase and azoreductase increased after BDCM treatment whilst TCM reduced the activity of dichloroinase (George *et al.*, 2004). Such alterations in the caecal enzymatic profile could lead to a change in the metabolism of other xenobiotics.

The lifetime exposure of male B6C3F1 mice to BDCM (8.1, 27.2, 43.4 mg/kg bw/day time weighted consumption in drinking water) did not result in any changes in food consumption, survival rate or overall bodyweight change. There were also no increases

in the incidence of neoplasia in the liver, kidney, spleen, testis, bladder, alimentary tract, excised lesions or other organs at any dose level but there was a significant decrease in kidney weights at 27.2 and 43.4 mg/kg bw/day dose levels. However, in the same study, when BDCM was administered in drinking water to male F344/N rats (time weighted consumption of 3.9, 20.6, and 36.3 mg/kg bw/day), there was an increase in the prevalence and multiplicity of hepatocellular adenomas at the lowest dose level and an increase in hepatocellular carcinomas in the medium dose level, when compared to controls. The combined incidence of neoplasms was increased at 3.9 and 20.6 mg/kg bw/day. However, at the highest dose level the incidence of liver neoplasia was lower than control levels. BDCM did not increase the incidence of cancer in the large bowel, renal tubes or other tissues. There were no changes in food consumption, survival rate or final body weight change, but there was significant decrease in kidney weight at the highest dose level (George *et al.*, 2000, George *et al.*, 2002). These results identify a species-specific response and suggest that, following repeated exposure, the liver is the principal target organ for BDCM toxicity and carcinogenicity in the rat.

Administration of TBM in corn oil by gavage to male and female F344 rats (400, 600 and 800 mg/kg bw/day) caused death in the mid and high dose groups, but only one death at 400 mg/kg/day. However, male rats given 400 mg TBM/kg bw/day showed reduced mean body weight at the end of the study period. The administration of TBM to $B6C3F_1$ mice resulted in only one death in each of the 600 mg/kg bw/day and 800 mg/kg bw/day groups but no other effects were apparent (NTP, 1989).

A repeat dose study on BDCM in the drinking water, in C57BL/6J mice (50, 125, 250 mg/kg bw for 16 days) and F344 rats (75, 150, 300 mg/kg bw for 5 days) found no effects in mice but deaths in rats (2 out of 6) at 300 mg/kg bw and significant decreases in body, spleen and thymus weights (French *et al.*, 1999). There was no evidence in either treated rats or mice to suggested suppressed humoral immunity (immunity mediated by secreted antibodies), and the authors suggest that the immune system is not a target for THM toxicity.

Administration of TBM in corn oil by oral gavage to male and female F344 rats (12 to 200 mg/kg bw/day for 13 weeks) caused lethargy in males (100 and 200 mg/kg/day) and in females (200 mg/kg/day), as well as an increased incidence of cytoplasmic vacuolisation of hepatocytes in males, where severity was increased at the highest dose. Similarly, administration to $B6C3F_1$ mice (at up to 400 mg/kg bw/day) caused a decrease in body weight of male mice (400 mg/kg/day) and cytoplasmic vacuolisation of hepatocytes was again observed in males (200 and 400 mg/kd/day; (NTP, 1989)). An extension of this study with dosing on 5 days/week for 2 years at concentrations of 100 and 200 mg TBM/kg bw/day resulted in a decreased mean body weight in rats but lower survival in male rats of the highest dose level. In treated female mice only a decrease in body weight was noted. A reduced survival rate was also noted in females but was attributed by the authors to an utero-ovarian infection (NTP, 1989).

The administration of BDCM (gavage in corn oil) to male and female F344 rats (300 mg/kg bw/day) and male and female $B6C3F_1$ mice (100 mg/kg bw/day) for 90 days, resulted in kidney damage and liver centrilobular degeneration in rats and kidney damage in mice (French *et al.*, 1999).

Oral gavage administration of DBCM to male and female F344/N rats (250 mg/kg bw/day, for 90 days) resulted in liver centrilobular necrosis and renal proximal tubular cell degeneration (NTP, 1985). In a longer term study on male and female F344/N rats (40 or 80 mg/kg bw on 5 days/week, for 104 weeks), liver toxicity (fatty metamorphosis

and ground-glass cytoplasmic changes) was noted. Similarly administration to B6C3F1 mice (50 or 100 mg/kg bw, 5 days/week, for 104 weeks) resulted in similar liver effects with hepatocytomegaly, necrosis and fatty metamorphosis. Both males and females had some evidence of nephrosis (NTP, 1985).

Genetic toxicology and carcinogenicity

TBM has been shown to have equivocal mutagenicity in *S. typhimurium* strain TA100 in the absence of exogenous metabolic activation and, with activation, in TA97 and TA98 but was negative in strains TA1535 or TA1357, with or without activation (NTP, 1989). TBM also increased sister chromatid exchange (SCE) and chromosome aberrations in Chinese hamster ovary (CHO) cells in the absence of metabolic activation at levels associated with cytotoxicity. An *in vivo* cytogenicity test in bone marrow cells of $B6C3F_1$ mice (intrapertioneal injection of 800 mg TBM /kg bw) showed an increase in the incidence of SCEs and micronucleated polychromatic erythrocytes but not of chromosomal aberrations (NTP, 1989). Following *in vitro* exposure of a human lymphoblastic leukaemia cell line (CCRF-CEM) to TCM, BDCM, DBCN or TBM (at 5 mM or 10 mM for 2 hours, with or without a 22 hour recovery period), there was an increase in DNA strand breaks when cells were exposed to brominated THMs at both dose levels when compared to control cells, but TCM had no effect. Furthermore, the DNA repair capacity (after 22 hour recovery) was compromised following TBM and BDCM exposure (Geter *et al.*, 2004b), suggesting that brominated THMs may be more genotoxic than the non-brominated forms.

In a study, TCM, BDCM, DCBM or TBM were administered to female B6C3F1 for 11 days either by gavage (at 130 or 260 mg/kg bw/day; 150 or 300 mg/kg bw/day; 100 or 300 mg/kg bw/day and 200 or 500 mg/kg bw/day; respectively) or in the drinking water (75% saturated solution). Hepatotoxicity was noted following gavage dosing (as discussed earlier) and levels of 5-methylcytosine in hepatic DNA were decreased after TCM and BDCM exposure. The hepatotoxic effects of TCM were increased when administered by gavage compared to drinking water (Coffin *et al.*, 2000). In general, THMs when administered by gavage enhanced cell proliferation and decreased the methylation of the *c-myc* gene, consistent with their carcinogenic potential but effects were less marked when administered via drinking water suggesting the rate of intake is important for toxicological outcome (Coffin *et al.*, 2000).

DBCM showed no mutagenic activity in *S. typhimurium* strains (TA98, TA100, TA1353 or TA1357), with or without metabolic activation (NTP, 1985). In contrast, BDCM was mutagenic in some *S. typhimurium* strains (TA98 and TA100) in the presence of metabolic activation and resulted, *in vitro,* in gene mutation in mouse lymphoma cells, chromosomal aberrations in CHO cells, and increased SCEs in human lymphocytes (Wilbourn, 1995).

Administration of TBM in corn oil by gavage to male and female F344 rats (100 or 200 mg/kg bw/day) resulted in tumours of the large intestine in high dose animals (NTP, 1989). However, an IARC Working Group concluded that TBM could not be classified as to its carcinogenicity, due to the limited nature of the evidence in experimental animals (Classified Group 3; (IARC, 1991)).

Gavage administration of DBCM to F344/N rats (40 or 80 mg/kg bw, 5 days/week, for 104 weeks) showed no evidence of carcinogenicity, while a similarly constituted study in $B6C3F_1$ mice gave equivocal evidence of carcinogenicity in male $B6C3F_1$ mice (increased incidence of hepatocellular carcinomas, but no increase in the combined

incidence of hepatocellular adenomas or carcinomas) while both tumour types were increased in female B6C3F1 mice (NTP, 1985).

The administration of BDCM in corn oil by oral gavage to male and female F344 rats (50 or 100 mg/kg bw/day) and male and female $B6C3F_1$ mice (25 or 50 mg/kg bw/day) for 2 years resulted in increased adenocarcinoma of the large intestine, renal tubular cell adenoma and carcinoma of male and female F344 rats. Renal tubular cell adenomas and adenocarcinomas were also observed in the kidneys of male mice (at both doses), and hepatocellular adenomas and carcinomas in female mice (at both doses; (NTP, 1987). Administration of BDCM in drinking water to male F344 rats over their lifetime (at 3.9, 20.6 and 36.3 mg/kg bw/day) also resulted in an increased incidence of hepatocelluar neoplasia; B6C3F1 mice were not thus affected (George *et al.*, 2002). On the basis of the then available evidence, an IARC Working Group (1992) concluded that BDCM was *possibly carcinogenic to humans* (Group 2B; (Wilbourn, 1995). However, it is noted that, in a more recently reported 2 year drinking water study with male F344/N rats (50 per group, average daily dose levels of 0, 6, 12, 25 mg/kg bw/day), no statistically signficiant differences in survival rates, mean body weights, or incidence of neoplasms were reported. Water intake of exposed rats was less than that of the controls, which was attributed to unpalatability of the treated water, but the presence of chronic liver inflammation in the two highest groups could not be explained (NTP, 2006). In a similarly designed experiment using female $B6C3F_1$ mice (50 per group) exposed to average daily doses of 0, 9, 18, or 36 mg/kg bw/day, no statistical difference in surviaval rate was noted. However, mean body weight and water consumption were reduced in treatment compared with control groups. When tumour incidences were considered, the incidence of hepatocellular adenoma or carcinoma were signficiantly decreased at 36 mg/kg bw/day compared with control incidence (NTP, 2006). These negative findings in two robust studies conducted on two rodent species, raises questions with regard to the robustness of the conclusions reached earlier by IARC. However, a definitive conclusion as to the carcinogenicity of BDCM is not possible until the current knowledge base has been reavaulated by a competent authority.

It has been established that brominated THMs require glutathione S-transferease theta1-1 (GSTT1-1) mediated metabolism to form mutagenic intermediates (Ross & Pegram, 2004). The genotoxicity of THMs in human whole blood cultures (*in vitro* exposure and analysis by Comet assay) was not affected by the presence or absence of GSTT1-1 and the genotoxic potency of TBM was calculated as 1.20 μm/mM. However, exposure of S. RSJ100 cells (expressing GSTT1-1 expression) to DBCM in the presence of red blood cells (which contain GSTT1-1) prevented the activation of DBCM to a mutagen (Landi *et al.*, 1999).

It has been suggested that dietary intake (including nutrients and fats) has a protective affect on the incidence of cancer precursors. In a study, 500 mg/L TBM was administered in drinking water to male F344/N rats fed on diets with either normal levels of, or without, folic acid for 26 weeks. An increase in serum folate concentration and serum homocysteine concentration was noted in the treated groups fed on diet without folic acid and an increase in aberrant crypt foci (ACF; precursors of colon cancer) was also noted when compared to animals receiving a diet normal in folic acid (Geter *et al.*, 2005). A similar effect was noted when TCM, BDCM, DBCM or TBM were given to male F344 rats in their drinking water for 26 weeks at dose of 0.5, 0.7, 0.9, 1.1 g/L which were fed either normal or high fat diets. With TBM only, an increase in ACF incidence was noted in those given the high fat intake, compared to those receiving a normal dietary

intake (Geter *et al.*, 2004a). These findings suggest that some dietary constituents may act protectively against oral TBM exposure, although the mechanism is unknown.

IARC has reviewed the carcinogenic potential of chlorinated and brominated trihalomethanes (IARC, 1991, IARC, 1987) and has evaluated TCM and BDCM as *possibly carcinogenic to humans* (Group 2B)). However, recent robust studies (NTP 2006) have failed to detect a carcinogenic potential in the case of BDCM. IARC also considered that DBCM and TBM are *not classifiable as to their carcinogenicity in humans* (Group 3).

Reproductive and developmental toxicity

There are a number of epidemiological studies suggesting an apparent association between THM exposure and adverse reproductive outcomes in humans (as discussed in Section 3.1 of this Annex).

Administration of BDCM (at 0, 50, 150, 450 or 1350 ppm) to Sprague-Dawley rats in drinking water for 63 to 70 days, with exposure starting 14 days prior to mating and continuing until lactation, caused a reduced water consumption at the two highest doses. However, DBCM was not detected in the plasma, placenta, amniotic fluid and milk of treated rats (samples taken on days 1 and 14 of initial dosing for male and female rats, gestation day 20 and lactation day 15 for female rats only, measured by gas chromatography), suggesting that it is rapidly metabolised (Christian *et al.*, 2001a). A number of effects attributed to the decreased water intake were seen in the parental generation including dehydration (assessment method not stated), reduced food intake and reduced weight gain (attributed by the authors). Reduced offspring birth weight was also noted but attributed by the authors to the differences in water intake. There were, however, no adverse effects on embryo-foetal viability and no gross signs of foetal toxicity. Delays in development were attributed to the reduced maternal weight gain. The authors suggest a material NOAEL for BDCM of 18.4 mg/kg bw/day and a developmental NOAEL of 45 mg/kg bw/day (Christian *et al.*, 2001a). Oral administration of BDCM at 0, 1.4, 13.4, 35.6 or 55.3 mg/kg bw/day (GD 6 to 29) to pregnant New Zealand White rabbits resulted in a significantly reduced absolute and relative (to body weight) water consumption, lower body weight gain and reduced food consumption at the two highest doses. There were no gross signs of foetal toxicity or reduction of foetal viability, and developmental delays were associated with the effect on maternal weight gain; the maternal NOAEL was 13.4 mg/kg bw/day and the developmental NOAEL was 55.3 mg/kg bw/day (Christian *et al.*, 2001a).

Marked strain differences have been noted between rats of the F344 and Sprague Dawley strains after oral gavage administration of BDCM at 75 mg/kd bw /day (GD 6 to 10). F344 rats showed a 62% incidence in full litter resorption (8 out of 13) compared to 0% (0 out of 14) in Sprague-Dawley rats (same treatment regime at either 75 or 100 mg/kg bw/day) (Bielmeier, Best & Narotsky, 2002). Differences in response depending on treatment days during gestation were also noted following oral administration of BCDM to F344 rats; treatment on GD 6 – 10 resulted in 75% full litter resorption, compared with 0% resorption when given either 75 or 100 mg/kg bw/day on GD 11 – 15 (Bielmeier, Best & Narotsky, 2001, Bielmeier *et al.*, 2001)}; it is noted that this period encompasses the LH-dependent period of pregnancy (GD 7 to 10) in this species.

Mechanism(s) of action

BDCM is metabolised primarily by CYP2E1 and CYP1A2 (Lilly *et al.*, 1997), and the main site of general toxicity for the majority of THMs is the liver. However, there is little

information on the underlying mechanism of action. It has been suggested that brominated THMs are mutagenically activated by GSTT1-1, but that this metabolic route is uncommon for chlorinated THMs (Pegram *et al.*, 1997).

Of the THMs considered, several (TCM, BDCM and DBCM) have been classified by the EPA as potential human non-genotoxic carcinogens. These compounds appear to operate through a mechanism not involving direct mutational effects on DNA but are believed to be mediated through induction of regenerative cell proliferation by a number of secondary mechanisms, including: release of nucleases; generation of reactive oxygen species; and DNA replication before adduct repair. Preferential growth of preneoplastic cells may then be caused by selective killing of normal cells or the expression of growth control genes (oncogenes; (WHO, 2005b).

With regard to the reproductive and developmental effects of THM, in a study on BCDM (75 mg/kg bw/day in 10% ethyoxylated caster oil) by oral gavage to female F344 rats daily (GD 6 to 9, with animals killed for study on GD 9) caused increased pregnancy loss (full-litter resorption) and decreased maternal serum progesterone and luteinising hormone (LH) levels (Bielmeier *et al.*, 2004, Bielmeier *et al.*, 2007). Collection of tail blood on 4 days from BCDM-treated F344 rats (at 75 mg/kg bw/day; oral gavage on GD 8 or 9; tail blood taken at regular intervals over test period), showed significantly reduced progesterone levels in rats with full litter resorption, 24 hours after dosing; no effect was noted for serum LH levels which actually increased on GD11, suggesting BCDM may disrupt luteal responsiveness to LH (Bielmeier *et al.*, 1999). Such changes have also been noted in other studies (including (Narotsky *et al.*, 2003, Narotsky *et al.*, 2006, Narotsky *et al.*, 2001, Narotsky *et al.*, 1993). Further studies provided evidence to suggest that BCDM at 100 mg/kg bw disrupts pregnancy by two mechanisms:

a) disruption of LH secretion, and

b) disruption of the copora lutea abilities' to respond to LH (Bielmeier *et al.*, 2007).

In an *in vitro* model of the human placenta using a primary culture of human trophoblast cells taken from the syncytium layer of the placenta (site of chorionic gonadotropin [CG] synthesis) allowed to differentiate into multinucleated syncytotrophoblast-like colonies, incubation for 24 hours with BDCM (at 20 nM to 2mM) followed by analysis of culture media for immunoreactive and bioactive CG, exposure to BDCM resulted in a dose-dependent decrease in secretion of immunoreactive and bioactive CG forms; the lowest effect concentration was 20 nM. However, there was no change in cell morphology or viability after BDCM exposure. This finding suggests that CG secretion by trophoblasts is decreased by BDCM exposure and might be a possible explanation for the effects noted *in vivo* (Chen *et al.*, 2003). BDCM was also shown to inhibit the differentiation of mononucleated cytotrophoblast cells (to form multinucleated syncytotrophoblast-like colonies) at 0.02 to 2 mM, as determined by immunocytochemical staining for desmosomes and nuclei (Chen *et al.*, 2004), again suggesting that the target organ for BDCM may be the placenta.

Authoritative or project specific provisional acceptable levels

The THMs possess a range of toxic properties and, in many instances, there is insufficient information on which to determine a definitive NOAEL. It is, however, noted that at the lowest doses studied in some experiments, the magnitude of effect was

small. A number of authoritative bodies have published health-based guideline values for these chemicals, which may be used as the basis for risk assessment, as follows:

- Trichloromethane (TCM)
  - 200 μg/L (WHO, 2005b)
  - 15 µg/kg bw - derived from the lower 95% confidence limit for 5% incidence of hepatic cysts, using pharmacologically-based pharmacokinetic (PBPK) modelling for beagle dogs given chloroform in toothpaste for 7.5 years; an uncertainty factor of 25 (10 for intraspecies differences in toxicokinetics and toxicodynamics, and 2.5 for interspecies differences in toxicodynamics) was applied; (WHO, 2005b)
- Bromodichloromethane (BDCM)
  - 60 μg/L (WHO, 2005b) - based on substance being considered carcinogenic; therefore represents concentration in drinking water associated with an upper-bound excess lifetime cancer risk of 10^{-5}
- Tribromomethane (TBM)
  - 100 μg/L (WHO, 2005b)
- Dibromochloromethane (DBCM)
  - 100 μg/L (WHO, 2005b)
- Bromoform
  - 17.9 µg/kg bw - based on absence of histopathological lesions in liver in 90-day study in rats; uses an uncertainty factor of 1000 (100 for intra- and interspecies variations. and 10 for possible carcinogenicity and short duration of exposure; (WHO, 2005b)
- DBCM
  - 21.4 µg/kg bw (WHO, 2005b) - based on absence of histopathological effects in liver in 90-day study in rats; uses uncertainty factor of 1000 (100 for intra- and interspecies variations, and 10 for short duration of the study); an additional uncertainty factor for potential carcinogenicity was not applied because of the questions regarding mouse liver tumours from corn oil vehicles and inconclusive evidence of genotoxicity

C3.3.1.1 Iodinated trihalomethanes

Iodinated trihalomethanes may be formed in the presence of iodine; these include:

dichloroiodomethane (DCIM)

chlorodiiodomethane (CDIM)

bromochloroiodomethane (BCIM)

bromodiiodomethane (BDIM) and

dibromoiodomethane (DBIM)

triiodomethane (or iodoform).

Of these, only two were specifically analysed for in this project; DCIM and BCIM. However, the total concentration of iodo-compounds was also measured.

In general there is little toxicological information available and they are not currently included in water quality regulations. However, existing odour and taste thresholds will effectively determine the tolerable concentrations of these compounds in drinking water as they are general described as possessing a medicinal, sweet or solvent odour (Cancho *et al.*, 2001).

Toxicodynamics

No toxicodynamic studies have been identified for this group of compounds.

Acute toxicity

No acute toxicity studies on these compounds have been identified. However, ITHMs were cytotoxic when CHO cells were exposed over a period of approximately three cell divisions (72 hours; tested for 10 exposure concentrations for each tested DBP); reduction cell density was noted, with the rank order for cytotoxicity being: iodoform > BDIM > DBIM > BCIM = CDIM > DCIM; ((Roldan-Arjona & Pueyo, 1993).

Repeat dose toxicity

No repeat dose studies have been identified.

Genetic toxicology and carcinogenicity

Quantitative structure-activity relationships (QSAR) computer modelling based on mechanistic data predicted that ITHMs are carcinogenic (Berry *et al.*, 1997) but there are currently no experimental data to substantiate this conclusion.

Iodoform was mutagenic in the absence of mammalian metabolic activation (S9), but showed decreased mutagenic potential in the presence of metabolic activation using the L-arbinose test of *S. typhimurium* (strain BA13; (Roldan-Arjona & Pueyo, 1993). However, iodoform did not induce chromosome abberations in SHE cells after incubation at up to 100 μM, for 24 hours (Hikiba *et al.*, 2005). The majority of tested ITHMs (iodoform, DBIM, DCIM, BCIM, BDIM) were also not genotoxic in a single-cell gel electrophoresis (SCGE) assay in which CHO cells were exposed for 4 hours, although cytotoxic effects were seen. However, CDIM was genotoxic in this assay (Richardson *et al.*, 2008).

Reproductive and developmental toxicity

No reproductive or developmental studies have been identified

Mechanism(s) of action

No mechanistic studies have been identified for this class of compound.

Authoritative or project specific provisional acceptable levels

No NOAELs, LOAELs or authoritative regulatory standards have been identified for this group of compounds. However, OTCs have been experimentally determined for DCIM (5.8 μg/L), BCIM (5.1 μg/L), DBIM (2.9 μg/L), CDIM (0.2 μg/L), BDIM (0.1 μg/L), and iodoform 0.03 μg/L, using a panel of human assessors (Cancho *et al.*, 2001). The validity of this assessment is supported by an OTC value of 0.02 μg/L previously established for iodoform (Bruchet *et al.*, 1989).

C3.3.2 Haloacetic Acids

The haloacetic acid (HAA) group comprises:

monochloroacetic acid (MCAA)

monobromoacetic acid (MBAA)

dichloroacetic acid (DCAA)

trichloroacetic acid (TCAA)

bromochloroacetic acid (BCAA)

dibromoacetic acid (DBAA)

bromodichloroacetic acid (BDCA)

dibromochloroacetic acid (DBCA)

tribromoacetic acid (TBAA)

iodoacetic acid

bromoiodoacetic acid

3-bromo-3-iodopropenoic acid

2-iodo-3-methylbutenedioic acid.

The most extensively studied are DCAA and TCAA, including data relating to their respective salts.

Toxicokinetics

The toxicokinetics of TCAA in humans has been determined by analysis of first morning urine samples following restricted drinking of public drinking water (containing TCAA) followed by two weeks of bottled water without TCAA. The elimination half-life was determined as 2.1 to 6.3 days and was modelled as a single-compartment exponential decay (Bader *et al.*, 2004).

The administration of radio-labelled sodium dichloroacetate (the sodium salt of DCAA, administered by gavage at 42.4 mg/kg bw) to rats showed the percentage of radio-label in tissues 24 hours after administration as: muscle (11.9%); liver (6.19%); gastrointestinal tract (3.74%); adipose tissue (3.87%); and kidney (0.53%) (James *et al.*, 1998). The average half life of sodium dichloroacetate (single i.v. dose) was determined in the plasma of rats, dogs, and humans as 2.97, 20.8, and 0.43 h, respectively, with metabolic transformation suggested as the rate-limiting step (Lukas *et al.*, 1980).

Toxicodynamics

Acute toxicity

When TCAA was instilled into the eye of rabbits (no other information available), severe irritation was observed characterized by severe and extensive loss of epithelium and endothelium, infiltration and haemorrhage about the limbal vessels, infiltration and hyperaemia of the iris, and damage to the anterior layers of the lens (ACGIH, 1991). TCAA has also been shown to be irritating and corrosive to the skin, eye, and mucous membranes in humans, but is not readily absorbed through the skin (ACGIH, 1991).

Repeat dose toxicity

The administration of TCAA to female Sprague-Dawley albino rats (2000 ppm in drinking water given *ad libitum* for 50 days) resulted in a significant increase in serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine

phosphokinase (CPK) and acid phosphatase (ACP) activity. Malondialdehyde (MDA; a lipid peroxidation end product) was shown to be slightly increased in the erythrocytes, liver and kidney of the treated rats. Brain MDA was not altered but antioxidant enzyme activity (catalase and superoxide dismutase) was shown to be significantly increased in the brain, liver and kidney (Çelik, 2007). No clinical signs of toxicity were reported.

For male and female F344/N rats given DBA in drinking water for 2 weeks, 3 months or 2 years at 0, 125, 500, and 1000 mg/L, or given 2000 mg/L for 2 weeks or 3 months, significant increases were noted in hepatocellular cytoplasmic vacuolisation, delayed spermiation, and atypical residual bodies and atrophy of the germinal epithelium at 500, 1000 and 2000 mg/L after 3 months, when compared to control groups (Melnick *et al.*, 2007). In a similarly constituted study using B6C3F1 mice, significant increases in hepatocellular cytoplasmic vacuolisation, delayed spermiation and atypical residual bodies were noted, as well as neoplasms in liver (hepatocellular adenoma or carcinoma, at 50, 500 and 1000 mg/L for males and at 500 and 1000 mg/L for females and hepatoblastoma at 500 and 1000 mg/L in males only) and lung (alveolar adenoma or carcinoma at 1000 mg/L in females only; (Melnick *et al.*, 2007).

The administration of DBA to male and female F344 rats (in drinking water at average doses of 0, 20, 72, and 161 mg/kg bw/day) for 6 months resulted in depressed weight gain and activity, as well as early diarrhoea and hair loss at the high dose. Concentration-related neuromuscular toxicity (limb weakness and hypotonia) was also noted at mid and high doses, with symptoms present after one month of exposure. For neurobehavioural effects, the LOAEL was 20 mg/kg bw/day, while for neuropathological changes (spinal cord degenerating fibres and cellular vacuolation) this dose represented a NOAEL (Moser *et al.*, 2004).

Genetic toxicology and carcinogenicity

Iodoacetic acid exposure of CHO and *S. typhimuriam* (TA100) resulted in cytotoxic changes that were not reduced by co-exposure with the antioxidants catalase and butylated hydroxyamisole. However, the presence of antioxidants did reduce the mutagenic effect seen in *S. typhimurium* (catalase 33.5% and BHA 26.8% compared with no additional anitoxidant) or CHO cells (catalase 86.5% and BHA 42%), suggesting that the mechanism may involve oxidative stress (Cemeli *et al.*, 2006). Exposure of L5178Y/TK mouse lymphoma cells to DCAA or TCAA resulted in an increase in micronuclei and aberrations for TCAA with metabolic activation and DCAA without activation (0.5 to 3.5 g/L; (Harrington-Brock *et al.*, 1998). This suggests that both compounds are weakly mutagenic.

In vivo administration of TCAA at 500 mg/kg bw (daily administration for 5 days) by oral gavage to Swiss-Webster mice resulted in an increased incidence of abnormal chromosomes. In contrast, intraperitoneal injection at the same dose showed a lesser response (Bhunya & Behera, 1987). Oral gavage administration of TCAA to B6C3F1 mice at up to 10 mmol/kg, elicited no effect on DNA-strand breakage in hepatic cells (Chang *et al.*, 1992). In contrast, Nelson and colleagues (Nelson *et al.*, 2001) reported a significant increase in single strand breaks in hepatic cells when mice of the same strain were orally dosed at 0.006mmol/kg and in Sprague Dawley rats given 0.6 mmol/kg.

When male Fischer 344/N rats were given TCAA or MCAA in drinking water for 104 weeks (at 0.05, 0.5 and 2g MCAA/L or 0.05, 0.5, 5g TCAA/L), no effect was noted on neoplasia of the liver or other tissues at any doses. Rats given greater than 0.5 g

MCAA/L exhibited moderate to severe toxic symptoms (reduced water consumption and growth rate) which resulted in this dose group being replaced with one of 1.1 g/L (time weighted average). The authors were able to derive a NOAEL (for carcinogenicity) as 26.1 mg/kg bw/day for MCAA (based on the lack of induction of neoplasms) and NOAEL (for chronic toxicity) of 33 mg/kg bw/day for TCAA (based on decreased body weight in highest dose group) and a NOAEL (for carcinogenicity) of 364 mg/kg bw/day for TCAA (DeAngelo *et al.*, 1997). Administration of DCAA at 0.05, 0.5, 1.6 and 5g/L in drinking water for 100 weeks to male Fischer 344/N rats caused severe toxic effects in the high dose group; these comprised irreversible peripheral hind leg neuropathy requiring the group to be terminated early. Histopathologically, effects were noted in the nervous system, liver and myocardium and treatment-related neoplastic lesions were seen in the liver. Increased hepatocellular neoplasia (carcinoma and adenoma) was noted in groups given 1.6 g/L or 0.5 g/L, suggesting that DCAA is a hepatocarcinogen with a NOAEL of 3.6 mg/kg bw/day (DeAngelo *et al.*, 1996).

Reproductive and developmental toxicity

The exposure of CD-1 mouse embryos at GD 8 using a whole embryo culture, to a range of HAA (including MCAA, MBA, DCAA, DBA and TCAA) for 24 hour period, resulted in neural tube development effects ranging from prosencephalic hypoplasia to non-closure of defects throughout the cranial region (Hunter *et al.*, 1996). Incubation of GD 8 CD-1 mouse embryos with DCAA, DBA or BCA for 1, 3 6, or 26 hours, followed by 26 hours recovery, resulted an increase in dysmorphic embryos with DCAA at 6 to 26 hours at 104.5 pmol/μg protein or 2.5 pmol/μg protein, and 3 to 26 hours BCA at 2.6 pmol/μg protein (Hunter III *et al.*, 2006), suggesting that brominated HAAs may be more embryotoxic than the chlorinated forms of HAA (Hunter *et al.*, 2006).

In vitro incubation of rat embryonic neural crest (NC) cell explants and somatic tissue explants (taken GD 9.5 or 10.5, respectively) showed a concentration-dependant reduction in neural cell migration when exposed to 300 μM BCA (50% reduction), 342 μM DBA (15 % inhibition) but no inhibition with DCAA (up to 2500 μM). This suggests a selective sensitive of NC cells to BCA and DBA (Andrews *et al.*, 2000, Andrews *et al.*, 2001); no effects were observed in somatic cells.

Ex vivo exposure of GD 9.5 rat embryos to BCA, DBA and DCAA resulted in dysmorpology after 48 hours exposure, with rotation and heart defects and, less significantly, prosencephalic effects, visceral arch and eye defects. These showed a dose additivity correlation, and suggests that developmental toxicity was additive in whole embryo culture (Andrews *et al.*, 2004).

In vivo exposure of Long Evans female rats to DCAA via oral gavage at 0, 1990, 2400 or 3500 mg/kg on different GDs between day 6 and 15 (period of organogenesis) showed the greatest effect after exposure on GD 10 and 12, suggesting that DCAA may interfere with closure of the secondary and tertiary interventricular foramina (Epstein *et al.*, 1990).

DBA administered to female Sprague-Dawley rats (10/group) at 0, 1, 5 or 50 mg/kg bw on GD 17 to postnatal day (PND) 7 resulted in no effects on major organs, nor signs of maternal toxicity. No changes were seen in the follicular population in neonatal rats (Bodensteiner & Frederick, 2003).

Administration of DBA (at 0, 125, 250, 500 and 1000 ppm) to Sprague–Dawley rats in drinking water for 63 to 70 days (exposure began 14 days prior to mating and

continued until lactation) resulted in reduced water consumption at the two highest dose levels. DBA was detectable in the plasma, placenta, amniotic fluid and milk of treated rats (Christian *et al.*, 2001b). Secondary effects were seen in the parental generation attributed by the authors to the decreased water consumption; these included dehydration, reduced food intake and reduced weight gain. Similar effects were seen (reduced birth weight) in pups, thought to be related to reduced water and feed intake (Christian *et al.*, 2001b). The lack of direct toxic effects has also been reported in other studies (including (Narotsky *et al.*, 2001, Narotsky *et al.*, 1997, Narotsky *et al.*, 1996).

Male reproductive effects have been noted with HAA administration. Administration of DBA (at 0, 400, 600 and 800 ppm in drinking water) to rats from GD 15 through to PND 98 resulted in DBA being detected in the serum and milk of dams and in the serum of male offspring (at 0.24 μg/ml in the 800 ppm group). The weight of male offspring's epididymis was decreased at the two highest doses and the fertility of the proximal cauda sperm was decreased in treated offspring, along with SP22 levels, suggesting that DBA may disrupt spermatogenesis and fertility in the male rat (Klinefelter *et al.*, 2000). Possibly associated changes have been noted following such treatments for time of preputial separation and vagina opening in male and female rats, respectively (Klinefelter *et al.*, 2004). Spermatotoxic effects were noted after 14 days oral dosing of DBA (at greater than 10 mg/kg bw/day) to male rats; effects included reduced caput sperm count, mild effects on spermiation and, at 90 mg/kg bw/day, effects on spermiation, spermatid development, epidiymal sperm counts, sperm motility and morphology (Linder *et al.*, 1994). BCA has also been shown to affect development of meiotic spermaotcytes, spermatids and sperm (in the absence of systemic toxicity) in male C57BL/6 mice given BCA by oral gavage at 8, 24, 72 or 216 mg/kg bw/day for 14 days; a decrease in total number of foetuses and mean number of litters per male was noted (Luft *et al.*, 2000).

Mechanism(s) of action

Oral administration of DCAA to B6C3F1 mice (300 mg/kg bw, for 6 or 12 hours) resulted in an increase in liver and hepatic DNA single strand breaks that associated with an increase in lipid peroxidation at 6 hours after administration. By 12 hours after administration, an increase in DNA single strand breaks and lipid peroxidation were apparent but generation of superoxide anion was reduced. Administration of TCAA under the same conditions in this species/strain resulted in an increase in superoxide production in peritoneal lavage cells, as well as an increase in superoxide production, lipid peroxidation and DNA single strand breaks in hepatic cells by 12 hours after administration (Hassoun & Ray, 2003, Hassoun & Dey, 2008). These findings are further supported by an *in vitro* study in which exposure to DCAA or TCAA of a macrophage cell line (J774A-1) at 8 to 32 mM, for 24, 36 or 60 hours, resulted in a time- and concentration-dependent increase in cell death, lactate dehydrogenase release and superoxide production and altered superoxide dismutase activity (increased at low concentrations and shorter periods of exposure (Hassoun & Ray, 2003), indicating that DCAA and TCAA induce macrophage activity, and suggesting it is likely that oxidative stress plays a significant role in their toxicity.

Administration of DCAA, BCA and DBA in drinking water to male F344 rats (1 g/L for 5 weeks) resulted in changes in enzyme activation in the intestinal tract; effects included decrease in gamma linolenic acid (GLA) activity for all HAAs; reduction of glutamate racemase (GLR) activity with DCAA and DBA; and the increase in galactosidase (GAL) activity with BCA (George *et al.*, 2000). Other studies have also shown similar effects

with HAAs, except for BCA which was shown to be toxic to caecal microbiota (when incubated at 1 mg/ml to rat cecal homogenate for 15 hours). However, the mutagenicity of DBA, TBA and DCAA was not altered by the presence of intestinal flora (Nelson *et al.*, 2001), suggesting that BCA may have the potential to affect the biotransformation of other xenobiotic compounds.

There is some evidence for differences in susceptibility between the sexes. In ,male and female rats given oral gavage doses of DCAA or TCAA at 0.92 and 2.45 mmol/kg on three occasions over a 24 hour period, followed by an i.p. injection of TCM at 0.75mg/kg, resulted in no change after DCAA or TCAA in male rats only. In females, the increase in plasma alanine amino transferase (ALT) was elevated in those given DCAA and TCM, compared with untreated controls. In female rats, the extent of elevation of blood urea nitrogen (BUN) levels was also increased in the DCAA and TCAA treated groups (Davis, 1992).

Authoritative or project specific provisional acceptable levels

Currently, US regulations place a limit of 60 μg/L on the total concentration of five HAAs (MCAA, DCAA, TCAA, MBA and DBAA; (Koivusalo *et al.*, 1997). The WHO has issued TDIs for TCAA (32.5 μg/kg bw/day) based on chronic toxicological data, MCAA (3.5 μg/kg bw/day) based on chronic toxicological data), and a provisional guideline value for DCAA of 0.05 mg/L (based on tumour prevalence data). The current information base provided for brominated acetic acids was considered by the WHO as inadequate for the derivation of guideline values (WHO, 2004a).

Separately, IPCS has established a TDI for dibromoacetic acid (20 μg/kg bw/day; based on a male reproductive toxicity study). Identified NOAELs for bromochloroacetic acid were: systemic toxicity at 41 mg/kg bw/day; reproductive toxicity 50 mg/kg bw/day (WHO, 2004a) and therefore a SSPADI was calculated as 41 μg/kg bw/day using an safety factor of 1000 (based upon read across between species, and the high level of uncertainty with the identified values).

C3.3.3 Haloacetonitriles

Chemicals contained within the haloacetonitrile (HAN) group include:

trichloroacetonitrile (TCAN; CAS number 545-06-2)

bromochloroacetonitrile (BCAN; CAS number 83463-62-1), and

dichloroacetonitrile (DCAN; CAS number 3018-12-0)

dibromoacetonitrile (DBAN; CAS number 3252-43-5).

Toxicokinetics

HANs may be absorbed, metabolised and excreted relatively rapidly. In whole body radioactive studies on Sprague-Dawley rats following i.v. administration of CAN, the gastrointestinal (GI) tract, liver and kidneys showed increased radioactive signal by 5 minutes after administration. Furthermore, 65% of radioactively-labelled CAN was found to be excreted in the form of metabolites, within 12 hours (Ahmed *et al.*, 1991).

The administration of CAN to pregnant female CD-1 mice by oral gavage on GD 6 to 18 at 25 mg/kg bw/day, followed by pathological examination of foetal brains on GD 18, showed a significant increase in cortical neurodegeneration, with an increase in

apoptotic nuclei in the cortices and choroid plexuses, compared to controls. In treated animals, a three-fold decrease in glutathione level, concurrent with an increase in lipid peroxidation and DNA oxidation were noted in foetal brain tissue (Ahmed *et al.*, 2005). Foetal brain uptake of CAN was determined using a tracer dose of ^{14}C-CAN given by injection to CD-1 rats on GD 12, with sacrifice and analysis at either 1 or 24 hours after treatment. It was found that there was rapid transfer of ^{14}C-CAN across the placenta, and increased uptake in the foetal cortex and hippocampus (Ahmed *et al.*, 2005). These results suggest that HANs or their metabolites can cross the placenta and cause neurodegeneration involving oxidative stress.

HANs are also known to undergo *in vivo* metabolism by mixed function oxidase (MFO) to forms of cyanide (Daniel et al. 1986). In particular, they can be metabolised to thiocyanate which may be then removed in urine. TCAN is metabolised to phosgene and cyanoformyl chloride, while CAN forms formaldehyde and DHANs, resulting in subsequent generation of formyl cyanide or formyl halide (Pereira *et al.*, 1984).

There is some evidence of interspecies differences in metabolism. Thus, in a study using radioactively-labelled DCAN, the metabolism and excretion of carbons within DCAN differed in F344 rats and B6C3F$_1$ mice (Roby *et al.*, 1986).

Toxicodynamics

Acute toxicity

Male and female CD-1 mice and CD rats given single oral gavage doses of DBAN or DCAN in a corn oil vehicle resulted in ataxia, depressed respiration, depressed activity and coma prior to death; LD_{50} values were: DBAN - 245 mg/kg bw male rats, and 361 mg/kg bw female rats; DBAN 289 mg/kg bw male mice and 303 mg/kg bw female mice; DCAN 339 mg/kg bw male rats and 330 mg/kg bw female rats; and DCAN 270 mg/kg bw male mice and 279 mg/kg bw female mice (Hayes *et al.*, 1986). No consistent compound-related, gross pathological effects were noted at necropsy. Whilst lower oral LD_{50} concentrations have been reported for rats dosed with DBAN (98.9 mg/kg bw) and DCAN (202.4 mg/kg bw), further information was not obtained for this set of experiments (Ahmed & Hussein, 1987).

Repeat dose toxicity

In an oral gavage study, administration of male and female CD-1 rats with DCAN in corn oil, at 12, 23, 45 or 90 mg/kg/day, for 14 days caused a dose-dependant reduction in body weight gain. A further study in the same species using the same route on DCAN at 8, 33 or 65 mg/kg for 90 days found increased mortality at 33 mg/kg, together with reduced body weight gain and increased serum cholesterol and serum glutamic-pyruvic transaminase (GPT; otherwise known as alanine aminotransferase (ALT)). The latter findings are suggestive of liver involvement (Hayes *et al.*, 1986). In a similarly constituted study, CD-1 rats treated with DBAN at 23, 45, 90 or 180 mg/kg/day for 14 days showed 100% mortality at the highest dose and less than 50% mortality at 90 mg/kg bw/day. Although the highest dose had effects in the spleen and thymus of males and the liver, lungs and thymus in females, there was no reported cause of death and no other compound-related effects were reported. In a further study of the same design using 6, 23 or 45 mg/kg/day for 90 days, effects at 45 mg/kg, comprised increased mortality (no stated cause) and decreased body weight gain (Hayes *et al.*, 1986). NOAEL values for CD-1 rats for DCAN and DBAN were, for 90 day studies, 8mg/kg bw/day and 23 mg/kg bw/day respectively (Hayes *et al.*, 1986).

Administration of DBAN at 29 mg/kg bw/day for 6 months via drinking water to male and female F344 rats resulted in decreased water intake and body weight gain and, in males, a minimal decrease in body tone not considered by the authors to be suggestive of any significant neurotoxic potential (Moser *et al.*, 2007).

Genetic toxicology and carcinogenicity

DCAN and BCAN were mutagenic in *S. typhimurium* (strains TA98, TA1535 and TA100; the LC_{50} for these substances in this assay were: 12.4μmol DCAN/plate and 5.44 μmol BCAN/plate), in the presence or absence of metabolic activation. BCAN also showed mutagenic activity with TA100, which was not seen with DCAN. Other HANs tested (CAN, TCAN and DBAN) did not show any mutagenic activity (Bull *et al.*, 1985, Bull *et al.*, 1982).

The frequency of SCEs in a CHO cell line was affected by these compounds; the potency ranking was: DBAN > BCAN > DCAN = TCAN > CAN. However, none of the chemicals induced micronuclei in CD-1 mice when tested *in vivo* (oral gavage at 12.5, 25, and 50 mg/kg bw/day for 5 consecutive days; (Bull *et al.*, 1985).

The experimental evidence base on the carcinogenicity of BCAN, CAN, DBAN, DCAN and TCAN has been evaluated by IARC but the data were considered as inadequate. As a consequence, HANs were assigned to Group 3, not classifiable as to carcinogenicity to humans (Bull, 1982). Available evidence is limited to a small number of short duration studies of questionable reliability and robustness. In summary, in a study HANs (CAN, TCAN, DCAN, BCAN and DBAN) were applied to the skin of Sencar mice (occlusion status not specified) at 200, 400 or 800 mg/kg bw in 0.2 ml acetone on 6 occasions over a 2 week period (Bull *et al.*, 1985). A significant increase in cumulative papilloma count was seen with CAN and BCAN at 400 and 800 mg/kg. A significant increase in tumour incidence was also noted with DBAN at 400 mg/kg but tumour incidence was lower at 800 mg/kg. The authors suggest that the highest dose of DBAN might have caused cytotoxicity/cell death of initiated cells resulting in a resultant decrease in the extent of tumourogenic response. No statistically significant increase in tumours was noted for DCAN or TCAN. In another study, oral administration of CAN, TCAN and BCAN at 10 mg/kg/day, 3 times/week, for 8 weeks to female A/J mice resulted in a significant increased incidence of lung tumours; no such response was noted following treatment with either DBAN and DCAN (Bull *et al.*, 1985).

Reproductive and developmental toxicity

Oral administration of DCAN and TCAN at 0, 1, 7.5, 15, 35 and 55 mg/kg (in tricaprylin) to female Long Evans Hooded rats on GD 7 to 21, resulted in reduced maternal weight gain and significant reduction in the percentage of females delivering viable litters and increased resorption rates; reduced postnatal survival was also noted (at term), these effects were not present at other dose levels in dams. In contrast, administration of BCAN and DBAN at the same dose did not have any effect. All test substances reduced the mean birth weight of the pups and, for all treatments except DBAN, caused reduced offspring body weight at puberty (Smith *et al.*, 1987).

Oral administration of DCAN at 5, 15, 25 or 45 mg/kg/day (in tricaprylin) to female Long Evans Hooded rats on GD 6 to 18, resulted in a significant increase in embryo death and foetal resorption at 25 and 45 mg/kg/day. Evidence of maternal toxicity was, however, noted only at the highest dose. At the high dose, other effects included foetal soft tissue anomalies and a dose-dependant increase in skeletal abnormalities; the NOAEL for developmental toxicity was 15mg/kg bw/day (Smith *et al.*, 1989).

The oral administration of BCAN to Long-Evans rats on GD 6 to 18 at 5, 25, 45, or 65 mg/kg bw/day (in tricaprylin) resulted in reduced material weight gain and increased total litter loss at the two highest doses at GD 20. Signs of maternal toxicity (increased organ weights and death) were noted for the highest dose group. Reduced foetal crown-rump lengths and weight, and increased frequency of cardiovascular malformations, were noted for all treated groups (except for foetal weight at the lowest dose) (Christ *et al.*, 1995).

The oral gavage administration of TCAN (in tricaprylin) on GD 6 to 21 at 1, 7.5, 15, 35, or 55 mg/kg bw/day to Long Evans Hooded rats, resulted in embryodeaths in all treated groups; 100% resorption was noted at 7.5 mg/kg bw/day and above, while doses of 15 mg/kg bw/day or above associated with soft tissue abnormalities. The NOAEL was established (by statistical analysis) as 1 mg/kg bw/day (Smith *et al.*, 1988). However, in another study, oral gavage dosing with TCAN (in corn oil) to Long Evans Hooded rats on GD 7 to 21 produced cardiovascular defects at 55 mg/kg bw/day (Christ *et al.*, 1995), hence, effects were significantly less marked than in the study by Smith and colleagues (Smith *et al.*, 1989), which used tricaprylin as a vehicle. The authors suggest that this may reflect an interaction between the tricaprylin and TCAN, although these vehicles are not considered representative of actual human exposure via drinking water. Given these concerns, the available data on the developmental toxic potential of these chemicals should be treated with caution since, given the apparent potentiation of effects by the tricaprylin vehicle, they may represent a "worst case" scenario or provide a completely false result (i.e. raise concern where none is warranted).

Studies with CAN showed that, after daily oral gavage doses to pregnant mice (GD 6 to 18 at 25 mg/kg bw/day; results obtained at GD 18), CAN crosses the placenta and accumulates in foetal brain tissue causing oxidative stress and neuronal apoptosis (Ahmed *et al.*, 2005).

Mechanism(s) of action

As HANs are converted to forms of cyanide *in vivo* (Daniel *et al.*, 1986), some of the observed toxic effects may be attributable to the presence of these toxic metabolites.

DBAN exposure (0.6 to 4.4 μm) of cultured confluent monolayers of rat intestinal epithelial RIE cells for periods of 24, 48 and 72 hours resulted in increased glutathione disulphide activity at concentrations of 1 to 4.4 μM doses after 48 and 72 hours. Also noted was a decrease in reduced glutathione concentrations. An increase in malondialdehyde concentration (an indicator of oxidative stress) was apparent after 72 hours at all concentrations tested suggesting that there may be an increased oxidative stress with DBAN (Jacob *et al.*, 2006).

HANs can interfere with the metabolism of other chemicals. After oral administration of DBAN or TCAN to rats at 0.75 mmol/kg, the activity of hepatic dimethylnitrosamine demethylase (DMN-DM) was found to be inhibited after 3 and 10 hours by TCAN but not DBAN; this may be due to a difference in absorption or the nature of inhibition studied (Lin *et al.*, 1986). However, in a separate *in vitro* experiment using heptatic microsomes, DBAN, BCAN, DCAN and TCAN caused inhibition of high affinity DMN-DM activity through non-competitive or uncompetitive mechanisms. It was suggested that the mechanism for TCAN involved inhibition of a different form of the enzyme or operated via a different mechanism (Pereira *et al.*, 1984). Cytosolic GSTs have also been found to be inhibited by 50% by 2.49 mmol DCAN/L, 0.34 mmol TCAN/L, 0.82 mmol DBAN/L and >10 mmol CAN or BAN/L (Ahmed et al. 1989). Such changes in

metabolic capacity could potentially influence the metabolism and, hence the toxicity, of other compounds. This may be of particular concern with regard to some other DBPs (including HAAs) whose bioactivation and inactivation is known to be catalysed by isoforms of GST (Pegram *et al.*, 1997); (Tong *et al.*, 1998). As HANs are capable of inhibiting enzymes important in the metabolism of other xenobiotic chemicals, it may be conjectured that there is a potential for possible secondary detrimental effect under situations of multiple chemical exposure (Jacob *et al.*, 2006).

Authoritative or project specific provisional acceptable levels

DBAN has a WHO guideline value of 70 μg/L. DCAN has a provisional WHO guideline value of 20 μg/L, whilst TCAN has a calculated guideline value of 0.2 μg/kg bw/day derived from reproductive toxicity NOAEL (WHO, 2004c). No other authoritative values have been identified for any other HANs.

C3.3.4 Halonitromethanes

Chemicals considered in the halonitromethane (HNM) group include:

trichloronitromethane (also known as chloropicrin, CP; CAS number 76-06-2)

chloronitromethane

bromonitromethane

dichloronitromethane

bromochloronitromethane

dibromonitromethane

bromodichloronitromethane

dibromochloronitromethane

tribromonitromethane

Whilst HNMs are known to form as DBP, the incidence is low. Chloropicrin (CP), the most common HNM, is the only one formed in any significant amounts and the toxicological properties of this chemical has been investigated to a slightly greater extent than other HNMs.

Toxicokinetics

No information on toxicokinetics is available.

Toxicodynamic

Acute toxicity

A number of early studies of uncertain quality have reported on the acute toxicity of HNMs.

Inhaling chloropicrin has been reported to cause coughing, vomiting, methaemoglobinaemia and suffocation in humans, and death has been reported within one minute of a man exposed to 2.4 g/m^3 chloropicrin; acute pulmonary oedema was noted (Hanslian, 1921). Experimentally, when administered intravenously to rabbits, chloropicrin has been reported to have a minimal lethal dose of 10 mg/kg bw (in emulsion with lecithin; (Gildemeister & Heubner, 1921). Subcutaneous (SC) administration of chloropicrin to cats was also reported to cause death at 10 mg/kg bw (in an alcoholic solution; (Negherbon, 1959). A lethal concentration of 120 ppm was noted in dogs following inhalation exposure for 30 minutes (Negherbon, 1959).

Repeat dose toxicity

In subacute studies, dietary exposure at 1175 ppm to one cat and greater than 1.5 g one dog for two weeks elicited no toxic signs except decreased food consumption (Gildemeister & Heubner, 1921).

Inhalation studies with male Fisher 344 rats exposed to 0.1 ppm chloropicrin or above for 90 days resulted in upper respiratory tract toxicity; no further details were available (Yoshida *et al.*, 1987).

There was limited information available on these studies and no other studies were identified during the literature search.

Genetic toxicology and carcinogenicity

HMNs (chloropicrin, chloronitromethane, bromonitromethane, dichloronitromethane, bromochloronitromethane, dibromonitromethane, bromodichloronitromethane, dibromochloronitromethane, and tribromonitromethane) were tested for their mutagenic potential, in the presence and absence of metabolic activation. After incubation for 3 days with *S. typhurium* TA100 and with metabolic activation cytotoxic effects were noted for all HMNs (Kundu *et al.*, 2004).

No neoplastic response was produced by chloropicrin in Osborne-Mendel rats and B6C3F1 mice tested after administration of chloropicrin by oral gavage dosing (20 mg/kg bw/day and 25 mg/kg bw/day) with toxic effects noted as inflammatory and degenerative changes associated with chronic wound healing (WHO, 2005b, WHO, 2003).

Reproductive and developmental toxicity

No information is available.

Mechanism(s) of action

Chloropicrin has been shown to react with protein thiol groups on proteins, and are thus capable, for example, in causing changes in enzymic reactivity and function (e.g. for urease; (Fischer, 1944, Desreux *et al.*, 1946).

Authoritative or project specific provisional acceptable levels

The maximum tolerable concentration in air of chloropicrin has been set at 0.1 ppm (IPCS, 1965). There are no other identified authoritative levels for chloropicrin and no NOAEL or LOAEL values have been identified (WHO, 2003).

C3.3.5 Haloketones

Chemicals considered in the haloketone (HK) group include:

chloropropanone	1,1-dibromopropanone
1,1-dichloropropanone	1,1,1-trichloropropanone
1,3-dichloropropanone	1,1,3-trichloropropanone

1-bromo-1,1-dichloropropanone	1,1,3,3-tetrachloropropanone
1,1,1-tribromopropanone	1,1,1,3-tetrachloropropanone
1,1,3-tribromopropanone	1,1,3,3-tetrabromopropanone

There is little toxicological information available on any of these HKs.

Toxicokinetics

No toxicodynamic information was identified.

Toxicodynamics

No information is available on the acute, repeat dose and reproductive or developmental toxicity properties of HKs.

Genetic toxicology and carcinogenicity

No reliable information has been identified on the genetic toxicology and carcinogenicity of HKs.

Mechanism(s) of action

Administration of 1,3-dichloropropanone to suspensions of male rate hepatocytes (0.5 – 10 mM) resulted in a rapid decline in cellular GSH levels (Laurie *et al.*, 1986).

Authoritative or project specific provisional acceptable levels

No authoritative values have been identified for any chemical in the HK group. It was not possible to determine a NOAEL or LOAEL for any HKs, therefore it was not possible to calculate a SSPADI for this group of chemicals.

C3.3.6 Cyanogen halides

Cyanogen bromide (CNBr) is thought to be formed by the reaction of hypobromous acid with organic N-precursors present in, for example, lake water, and the concentration of CNBr has been shown to be stable in aqueous solution for 10 days (Heller-Grossman *et al.*, 1999). Cyanogen chlorine (CNCl) is also included within this group, which has been used as a war gas in the First World War (WHO, 2007b).

Toxicokinetics

No information was identified.

Toxicodynamics

There is little toxicological information available about the cyanogen halides, but cyanide (and hydrogen cyanide) is well characterised (Boening & Chew, 1999), and any toxic effects of the cyanogen halides are assumed to be due to the formation of cyanide after absorption of the cyanogen halides into the body. The cyanogen halides are thought to be metabolised to cyanide by either haemoglobin or glutathione (*in vitro* study with rat blood; (ALDRIDGE, 1951) or cyanide formed by the hydrolysis of cyanogen chloride (WHO, 2007b).

No information on the genetic toxicology, carcinogenicity, and reproductive or developmental toxicity of cyanogen halides have been identified.

Acute toxicity

Inhalation of CNCl causes irritation at low levels (2.5 mg/m^3) but is lethal at higher concentrations (120 mg/m^3). There was no other information identified during this project. However, the acute toxicity of cyanide (in the form of hydrogen cyanide) is well described (WHO, 2007b, WHO, 2007a). The LD_{50} of potassium cyanide in Sherman rats was determined to be 10 mg/kg bw for a single dose administered by gavage. However the route of administration has been shown to alter the lethality of cyanide as dietary intake of 250 mg/kg bw to rats for 90 days did not result in the death of the test species suggesting that the liver can metabolise cyanide before it reaches the circulation at low dose rates (WHO, 2007a).

Repeat dose toxicity

In an early study, dietary administration of hydrogen cyanide to male and female rats (10 per sex per group) at 0, 100 and 300 ppm diet (0, 73 and 183 mg/kg bw/day) for 2 years, was reported to have resulted in no treatment-related gross toxic signs, effects on growth rate, haematological parameters or on major organs (heart, lung, spleen, GI tract, kidneys, adrenals, thyroid, testes, uterus, ovaries, cerebrum and cerebellum). A NOAEL of 10.8 mg CN/kg bw was established (Howard & Hanzal, 1955). However, in another study, administration to male weanling rats of potassium cyanide via the diet at a dose equivalent to 30 mg CN/kg bw/day for 11.5 months resulted in decreased serum thyroxine level and weight gain. Vacuolisation and membrane degeneration were also reported in the spinal cord (Philbrick *et al.*, 1979).

Mechanism(s) of action

The toxic effects of cyanogen halides are thought to be due to the generation of cyanide after administration (as stated previously). Cyanide has an initial toxic effect of inhibiting cytochrome oxidase by binding the haem iron, which interrupts the mitochondrial electron transport chain resulting in impairment of oxidative metabolism. Cyanide will also inhibit other enzymes including catalase, periodiase, ascorbic acid oxidase and xanthine oxidase (Casarett *et al.*, 1996).

Authoritative or project specific provisional acceptable levels

No authoritative values have been identified for the CNX group.

The WHO has derived a TDI for cyanide in drinking water of 12 μg/kg bw/day based on a 6 month study in pigs (oral administration; 1.2 mg/kg bw/day) resulting in changes in behaviour and serum biochemistry (WHO, 2007a).

C3.2.7 Haloaldehyde

Chemicals considered in the haloaldehyde (HA) group include:

monochloroacetaldehyde	bromochloroacetaldehyde
dichloroacetaldehyde	tribromoacetaldehyde

trichloroacetaldehyde (also known as chloral hydrate; CAS number 302-17-0)

The toxicity of trichloroacetaldehyde is well characterised and reviewed thoroughly in WHO (2005). However there is little toxicological information available for other haloaldehydes.

Toxicokinetics

Trichloroacetaldehyde has been widely used as a sedative hypnotic drug in humans with a recommended dose in the adult of between 250 and 1000 mg (equivalent to 14 mg/kg; (Casarett *et al.*, 1996);(Gilman *et al.*, 1985). It is rapidly metabolised into trichloroethanol, TCA and DCA by the enzyme alcohol dehydrogenase mainly in the liver but also the kidney (Casarett *et al.*, 1996); (Gilman *et al.*, 1985). The half life of trichloroacetaldehyde in plasma for humans (therapeutic dose) was determined to be 4 to 5 minutes (Ellenhorn & Barceloux, 1988), suggesting that even at high doses trichloroacetaldehyde will not accumulate in the body.

Toxicodynamics

Acute toxicity

Instances of human overdoses of trichloroacetaldehyde have been reported, and it is known to be an addictive substance. Reported adverse reactions to trichloroacetaldehyde in humans include GI symptoms, depression of CNS, skin rash and bradycardia (Shapiro *et al.*, 1969); (Miller & Greenblatt, 1979).

One animal study was identified which gave the LD50 for trichloroacetaldehyde in mice of 1265 mg/kg bw (females) and 1442 mg/kg bw (males) and, in rats, of 285 mg/kg bw (newborn pups) and 479 mg/kg bw (adults;(Sanders *et al.*, 1982).

Repeat dose toxicity

In a study trichloroacetaldehyde was administered in drinking water to male and female Sprague Dawley rats at 0, 300, 600, 1200 or 2400 mg/L for 90 days. In the high dose (equivalent to 168 mg/kg/day), moderate signs of toxicity were noted including significant decreases in food and water consumption, and reduced weight gain. In a separate study, Sprague Dawley rats given 0.2, 2, 20 and 200 ppm in water for 90 days, showed no changes in food or water consumption or in weight gain. However, increased liver catalyse and aniline hydroxylase activity were noted together with significantly decreased liver aldehyde dehydrogenase activity. The NOAEL for this second study was calculated to be equivalent to 1.89 mg/kg bw/day in males and 2.53 mg/kg bw/day in females (Poon *et al.*, 2003).

The administration of trichloroacetaldehyde in drinking water to CD-1 mice (both sexes) at 0, 16 and 160 mg/kg bw/day (males) and 0, 18, 173 mg /kg bw/day (females) for 90 days resulted in a significant decrease in humoral immune function (determined by the number of splenic antibody-forming cells (AFC) in response to sheep erythrocytes) in

the low and high concentration groups in females, however no effects were observed in males. A NOAEL for humoral immunity as 16 mg/kg bw/day and a LOAEL of 160 mg/kg bw/day was determined for female CD-1 mice (Kauffmann *et al.*, 1982).

Genetic toxicology and carcinogenicity

Trichloroacetaldehyde was negative in most bacterial tests for point mutations, however positive results were seen in *S. typhimurium* point mutation assays using TA198 and TA100 strains with or without microsomal activation (WHO, 2005a). However, it has been shown that chloral hydrate may induce structural chromosomal aberrations *in vivo* after administration of doses between 125 and 500 mg/kg bw in a mouse bone marrow micronucleus test (NTP, 2002) and DNA strand breaks after *in vitro* administration of trichloroacetaldehyde to human lymphocytes (Gu *et al.*, 1981).

Trichloroacetaldehyde caused hepatic tumours in mice and was suggested to be linked with the incidence of prostate cancer (Haselkorn *et al.*, 2006). However it is unknown if the parent compound or its metabolites are the active form. Trichloroacetaldehyde also induces hepatic necrosis in rats at doses equal to or greater than 120 mg/kg bw/day (IARC, 2004).

In a study, trichloroacetaldehyde was given in drinking water to male C57BL × C3HF1 mice as a single dose of 5 mg/kg bw/day or 10 mg/kg bw/day for 92 weeks (animals sacrificed at intervals up to 92 weeks). In mice sacrificed at points after 48 weeks of treatment, the incidence of hepatic nodules (adenomas and trabecular carcinomas), the incidence of hepatic nodules, and the relative weight of the liver were increased for the high dose group compared with controls (Rijhsinghani *et al.*, 1986). The administration of trichloroacetaldehyde in drinking water to male B6C3F1 mice (166 mg/kg bw/day) for 104 weeks (with interim sacrifices at 30 and 60 weeks). After 60 weeks, hepatocellular carcinomas were found in treated mice but not in controls. At the end of the study period, there was a significant increase in the incidence of hepatocellular carcinomas and adenomas in treated animals compared with controls (Daniel *et al.*, 1992).

Reproductive and developmental toxicity

Trichloroacetaldehyde was given to male and female CD-1 mice at 14.4 and 144 mg/kg bw/day (calculated exposure for males and non-pregnant females) and 21.3 and 204.8 mg/kg bw/day to dams in drinking water with exposure for 3 weeks prior to breeding and females exposed during gestation until pups were weaned. In the high dose group, pups after weaning (23 days old) showed impaired retention of passive avoidance learning tests, and the authors determined a NOAEL for neurodevelopmental toxicity of 21.3 mg/kg bw/day with a reproductive and developmental effects NOAEL of 204.8 mg/kg bw/day (Kallman *et al.*, 1984).

The administration of trichloroacetaldehyde in drinking water to male F344 rats at 0, 55 and 188 mg/kg bw/day for 52 weeks resulted in a reduction in sperm motility in the high dose group compared with controls. The authors identified a NOAEL for effects on sperm motility of 55 mg/kg bw/day (Klinefelter *et al.*, 1995).

Mechanism(s) of action

It has been suggested that the subchronic toxicity of trichloroacetaldehyde is due to the presence of TCA, which has been shown to be a rodent peroxisome proliferator (Poon *et al.*, 2003).

Authoritative or project specific provisional acceptable levels

A provisional WHO guideline value for trichloroacetaldehyde has been determined as 4.5 μg/L based on a LOAEL for hepatic toxicity in mice with safety factors taking into consideration the interspecies variability, intraspecies variability, use of LOAEL and limited evidence of carcinogencitiy (WHO, 2005a).

C3.3.8 Nitrosamines

Chemicals in the nitrosamines (NA) group include:

N-nitrosodimethylamine (NDMA; CAS number 62-75-9)

N-nitrosomethylethylamine

N-nitrosodiethylamine

N-nitrosomorpholine

N-nitrosopyrrolidine

N-nitroosdipropylamine

N-nitrosopiperidine

N-nitrosodibutylamine.

The nitrosamines occur in large concentrations in processed food and cigarettes as well as other consumer products and have been extensively reviewed elsewhere (including (Abnet, 2007, Magee, 1971, Tricker & Preussmann, 1991).

NDMA is formed from the reaction between monochloramine and organic nitrogen containing compounds (e.g. dimethylamine), although the exact nature of the precusors is unclear (Walse & Mitch, 2008) NDMA has been detected in beer (8 μg/kg), bacon (17 μg/kg), cheese (5 μg/kg), cured meats (22 μg/kg), sausage (12 μg/kg), smoked pickled fish (32 μg/kg), and in broiled squid (300 μ/kg, Japan) and other nitrosamines have been detected in lower concentrations (e.g. N-nitrosodiethylamine at 20 μg/kg in cheese, N-nitrosopiperidine in spiced smoked meat at 9 μg/kg; (Lijinsky, 1999)). There are also other potential routes of exposure known — such as from chlorination of swimming pools and hot tubs where levels of NDMA up to 500-fold greater than those measured in drinking water have been reported (Walse & Mitch, 2008). NDMA has a reported $t_{1/2}$ in groundwater of 1008 – 8640 hours (Howard *et al.*, 2005). Studies in Alberta have shown NDMA concentrations up to 100ng/L and the occurrence of two other N-nitrosamines (N-nitrosopyrrolidine and N-nitrosomorpholine) in drinking water (Charrois *et al.*, 2007). However, it must be stressed that the proportion of daily oral intake arising from drinking water for NDMA has been estimated to be 0.02% of exogenous and endogenous sources combined or 2.7% when only exogenous sources are considered (Fristachi & Rice, 2007). Thus, exposure via drinking water is considered a relatively minor source of NDMA.

The occurrence, effects and toxicity of NDMA in drinking water has been thoroughly considered by the WHO when determing a guideline value (WHO, 2008).

Toxicokinetics

Oral administration of radio-labelled NDMA at 1, 5, 10, 50 or 100 μg/kg to female Sprague-Dawley rats demonstrated rapid absorption from the lower intestinal tract followed by a rapid metabolism (suggested as 5 mg/kg bw/hour). This occurred

predominately in the liver to an alkylating agent although small amounts are also similarly metabolised in the kidneys (Pegg & Perry, 1981).

The administration of ^{14}C-labelled NDMA (single i.v. dose, 4.2 μmol/kg) to male Syrian golden hamsters and the subsequent high performance liquid chromatography (HPLC) analysis of serial blood samples showed a biphasic first-order elimination with a terminal half-life of 8.7 ± 1.0 min (mean ± SE) for unchanged NDMA and 31.5 ± 5.5 min for total radioactivity. No unchanged NDMA was detected in the urine following an i.v. bolus dose of 15 μmol/kg ^{14}C-labelled NDMA, but 31% of the total radioactivity was eliminated by that route, suggesting that excretion of metabolites does occur to a degree in the urine of treated animals. The intrinsic hepatic clearance in the hamster was shown to be greater than that previously obtained for the rat suggesting that there are species differences in the potential end target organ (Streeter *et al.*, 1990).

NDMA is metabolised by either alpha-hydroxylation or denitrosation; both involve an intermediate radical species formed by the action of cytochrome P450 (CYP2E1)-dependent mixed function oxidase system ()(Haggerty & Holsapple, 1990). The metabolism occurs in both hepatic and extrahepatic compartments, and metabolites are excreted in the urine or exhaled as carbon dioxide.

Toxicodynamics

Acute toxicity

NDMA has an oral LD_{50} in rats of 23 – 40 mg/kg body weight (WHO, 2008). Acute hepatic effects noted after oral administration of NDMA include hepatocyte vacuolisation, portal venopathy (including portal obstruction and hypertension), and necrosis or haemorrhage of liver. Other reported effects include excessive blood or fluid in a number of organs, GI haemorrhage, and, in the kidney, glomerulus dilatation and thickening of the Bowman's capsule (WHO, 2008).

Repeat dose toxicity

In the study by Anderson (Anderson *et al.*, 1986), administration to Swiss mice of NDMA (1-4 weeks, dose levels of 0.5 - 5.0 ppm) resulted in hepatic centrilobular haemorrhage and necrosis at the highest dose. Co-administration of ethanol partially alleviated the hepatotoxic effect of NDMA, which (as noted below) is consistent with competitive inhibition.

No other studies on systemic effects of NDMA in repeat dose studies have been identified as the majority of studies concentrate on the carcinogenic effects of NDMA.

Genetic toxicology and carcinogenicity

NDMA has been classified by IARC as a "*probable human carcinogen (Group 2A*)" based upon sufficient evidence of a carcinogenic effect in experimental animal species and the demonstrated similarities in its metabolism by human and rodent tissues (IARC, 1987).

The genetic toxicity of NDMA in drinking water has been reviewed (WHO, 2008). An *in vivo* study in mice given 6 or 9 mg NDMA/kg bw by i.p. injection showed germ cell effects including micronucleated spermatids (Cliet *et al.*, 1993).

Exposure of both male and female Colworth rats to NDMA (natural lifetime exposure) resulted in hepatic toxicity with effects noted at 0.01 to 0.02 mg/kg bw/day (little information presented in paper) with the TO50 value of 0.12 mg/kg bw/day). Other tumours or effects were not stated (Peto *et al.*, 1991). These results have been used to calculate a TDI (as seen below).

Reproductive and developmental toxicity

Male rats given a single i.p. injection of NDMA (30 or 60 mg/kg bw) induced testicular damage evidenced as necrosis or degeneration of the seminiferous epithelium (Hard & Butler, 1970).

Female mice exposed to NDMA via drinking water (estimated intake of 0.02 mg/kg bw/day) for 75 days prior to mating and throughout pregnancy and lactation showed a significant increase in the proportion of deaths (total number of stillborn and neonatal deaths) when compared with controls. There was no effect upon maternal fluid consumption, litter size or average body weight of the weanlings, and no consistent gross or histopathological abnormalities were observed in the stillborn foetuses or dead neonates to account for the increased mortality (Anderson *et al.*, 1989).

Mechanism(s) of action

In the study by Anderson (Anderson *et al.*, 1986), co-administration of ethanol to Swiss mice given NDMA (1-4 weeks, dose levels of 0.5 - 50 ppm) partially alleviated the hepatotoxic effects of NDMA at 50 ppm which is consistent with competitive inhibition of metabolic activation of NDMA by ethanol.

Authoritative or project specific provisional acceptable levels

An Australian-modified Benchmark Dose Model (mBMD) has reported that the 5% risk dose for NDMA is in the range of 0.02 to 0.028 mg/kg bw/day based on a cancer dose response in rat liver tumour data and incidence data for hepatocellular carcinomas and haemoangiosarcomas. This would equate to a TDI of 4 to 9.3 ng/kg bw/day (Fitzgerald & Robinson, 2007).

WHO has published a TDI for NDMA in drinking water of 2.77 x 10^{-3} μg/kg bw/day (27.7 ng/kg bw/day), based on the unit risk of cancer in humans.

C3.3.9 Haloacetamides

The haloacetamide group (HAMs) include:

chloroacetamide (CAM; CAS number 79-07-2)

bromoacetamide (BAM; CAS number 79-15-2)

dichloroacetamide (DCAM; CAS number 689-72-7)

dibromoacetamide (DBAM; CAS number 598-70-9) and

trichloroacetamide (TCAM; CAS number 594-65-0).

There is little toxicological information available for HAMs, although the chemically-related chloroacetamide (CAM) pesticides have been associated with cancers at various sites in rodents, including the nasal epithelium, thyroid, liver and stomach (Hodgson & Rose, 2005).

Toxicokinetics

There was no information identified on the toxicokinetics of HAMs or CAM.

Toxicodynamics

Acute toxicity

Oral gavage administration of CAM at 75 mg/kg bw to Sprague-Dawley rats resulted in liver lesions and an increase in lipid peroxidation products after 3 to 6 hours. Reversible changes, including hydropic degeneration, were noted after 24 and 48 hours (Anundi *et al.*, 1980). After 24 hours elevated lipid peroxidation products were still apparent, however these had returned to normal levels after 48 hours; this was reflected by changes in glutathione concentration over the same time period. No regenerative growth was observed 1 week after administration.

Repeat dose toxicity

There was no information identified on the repeat dose toxicity of HAMs.

Genetic toxicology and carcinogenicity

There was no information identified on the genotoxicity of HAMs.

Reproductive and developmental toxicity

There was no information identified on the reproductive or developmental toxicity of HAMs.

Mechanism(s) of action

There was no information identified on the mechanism of HAM action.

Authoritative or project specific provisional acceptable levels

There was no authoritative standard, nor NOAEL or LOAEL identified from which it would be possible to derive a SSPADI for any of the HAMs or CAM.

C3.3.10 Dimethyl cyanamide

Dimethyl cyanamide (DMC; CAS number 1467-79-4) is a clear liquid (Gigiena Truda i Professional'nye Zabolevaniya, 1975), which is volatile and flammable in liquid and vapour form (MSDS, Cole Palmer Ltd 2005). It decomposes to produce carbon monoxide, carbon dioxide, and nitrogen oxides.

There is little published data on the toxicity profile of dimethyl cyanamide (DMC), with the only information identified for this review being drawn from secondary sources (e.g. from MSDS listings).

Toxicokinetics

In rats given DMC followed by ethanol (oral administration, no indication of dose) there was a marked elevation in ethanol-derived blood acetaldehyde, depression of specific mitochondrial aldehyde dehydrogenase (ADH) activity and depletion of hepatic glutathione levels (Shirota *et al.*, 1982). *In vitro* exposure of intact rat liver mitochondria to DMC (dose not stated) did not result in inhibition of aldehyde dehydrogenase. This was interpreted as suggesting that DMC may undergo N-demethylated before conversion to an active metabolite capable of inhibiting a mitochondria ADH isozyme (Shirota *et al.*, 1982).

Toxicodynamics

Acute toxicity

The oral LD_{50} of DMC is 73 mg/kg in mice and 146 mg/kg in rats; toxic effects include convulsion, effect on seizure threshold, muscle weakness and dyspnea (Gigiena Truda i Professional'nye Zabolevaniya, 1975). In guinea pigs, the oral LD_{50} is 146 mg/kg (Gigiena Truda i Professional'nye Zabolevaniya, 1975). Inhalation LC_{50} for DMC are 2800 mg/m^3 in mice and 2500 mg/m^3 in rats; toxic effects were similar to those reported following oral administration (Gigiena Truda i Professional'nye Zabolevaniya, 1975).

The LD_{50} following the IP or dermal administration of DMC to mice have been reported to be identical at 125 μg/kg (Gigiena Truda i Professional'nye Zabolevaniya, 1975), but to be much higher (5 mg/kg) in guinea pigs (Gigiena Truda i Professional'nye Zabolevaniya, 1975).

Repeat dose toxicity

There was no information identified on the repeat dose toxicity of DMC.

Genetic toxicology and carcinogenicity

In an Ames test, DMC has been reported to be negative, and it has been suggested not to be carcinogenic (Haworth *et al.*, 1983).

Reproductive and developmental toxicity

No human or experimental data on the reproductive or developmental toxicity of DMC is available (Haworth *et al.*, 1983).

Mechanism(s) of action

There was no information identified on the mechanism of DMC action.

Authoritative or project specific provisional acceptable levels

There was no information identified on the authoritative levels of DMC and, as no NOAEL or LOAEL was identified, no specific project provisional acceptable (SSPADI) can be calculated.

C3.2.11 Halogenated furanones

3-Chloro-4-(dichloromethyl)-5-hydroxy-2(5*H*)-furanone (MX, CAS number 77439-76-0) has been found at nanogram-per-litre levels in sample of drinking-water, and is thought

to arise as a result of disinfection processing using chlorination or chloramination techniques (Philbrick *et al.*, 1979). Other halogenated furanones are analogues of MX, and include E-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (E-MX), although these are less well studied.

Toxicokinetics

After the administration of a single oral dose of radioactively-labelled MX to Han:Wistar rats, 20 to 35% of the dose was absorbed, with distribution occurring to the circulation, GI tract lining, kidney, stomach, small intestine, and bladder. The mean elimination half-life was 3.8 hours, with excretion occurring mainly via the urine (77% in 12 hours, 90% in 24 hours; (Komulainen *et al.*, 1992).

After oral administration of MX to male CD-1 mice, a similar absorption pattern was observed, with peak blood concentrations being attained within 15 minutes of dosing. The pattern of elimination in the mouse differed however, with 57% of radioactivity being excreted in urine and 28% in faeces (Horth et al., 1991). When the i.v. route of administration was studied, the mean elimination half life was increased in Han:Wistar rats to 22.9 hours (Komulainen *et al.*, 1992).

MX is excreted rapidly in urine (Komulainen *et al.*, 1992) with less than 6% retained in F344 rats after 48 hours (Gigiena Truda i Professional'nye Zabolevaniya, 1975) and less than 1% retained in CD-1 mice 120 hours after administration (Meier *et al.*, 1996).

Overall, studies suggest that MX is readily absorbed from the GI tract and rapidly excreted in the urine although a small fraction of MX or its metabolites may be retained in blood for a longer period of time. However, there is little suggestion of any accumulation of MX within the body (Komulainen *et al.*, 1992).

Toxicodynamics

Acute toxicity

MX by oral gavage in distilled water to male Wistar rats was tolerated at up to 200 mg/kg body weight but did cause severe symptoms including dyspnoea, depressed motor activity, GI inflammation, and oedema in lungs and kidneys. The 48-hour LD_{50} was 230 mg/kg body weight (Komulainen *et al.*, 1994).

A single oral dose of 144 mg/kg bw to weanling CD-1 mice caused only limited deaths but resulted in focal epithelial hyperplasia of the stomach and vacuolation of the superficial villus epithelium in duodenum and jejunum, and increased numbers of mitotic figures in liver and cytotoxicity in the urinary bladder (Mullins & Proudlock, 1990).

Repeat dose toxicity

In a subacute study, administration of MX by gavage on 2 consecutive days at a dose of 128 mg/kg bw to mice (species not stated) resulted in enlarged stomachs and moderate haemorrhagic areas in forestomach. The majority of deaths occurred within 24 hours whilst doses of 70% LD_{50} or less ($<$ 90 mg/kg) had no significant effect on body weight or mortality rate (Meier *et al.*, 1987a).

MX has been shown to reduce hepatic levels of catalase, cytochrome P450 reductase, aminopyrine demethylase, and aromatic hydrocarbon hydroxylase in a sub-chronic study of 14 days duration in which F344 rats were dosed at 64 mg/kg bw/day by gavage (no effects noted at 0, 8, 16, 32 mg/kg bw/day). No effect was noted on fatty

acyl CoA oxidase, glutamylcysteine synthetase, GST or glutathione peroxidase (Meier *et al.*, 1996). MX has also been shown to cause a dose-related decrease in ethoxyresorufin-O-deethylase activity in the liver and kidney in Wistar rats (30 mg/kg bw/day, for 18 weeks, or 45, 60 or 75 mg/kg body weight/day, for 7, 2, and 5 weeks, respectively, by gavage). Increased uridine diphosphate glucuronosyl transferase and GST was also noted in the kidneys of the females suggesting that sex differences may exist (Heiskanen *et al.*, 1995). However, the high concentrations studied here are unlikely to be relevant to human exposure through drinking water.

In a chronic study of 14 to 18 weeks, MX was given by oral gavage to Wistar rats (15 per sex per group) on 5 days per week, at doses of 30 mg/kg of body weight (low dose; 18 weeks) or 45 to 75 mg/kg of body weight for 14 weeks. The high dose resulted in some deaths (two males and one female) and also caused hypersalivation, wheezing respiration, emaciation and tangled fur. High dose males had increased water consumption, decreased body weight and food consumption, elevated plasma cholesterol and triglycerides, and increased urine excretion associated with lower specific gravity. At the highest two doses the relative weights of liver and kidneys were increased compared with control values and duodenal hyperplasia was noted. Sex differences in response observed included: epithelial hyperplasia in forestomach (in males); and splenic atrophy and haemosiderosis (in high dose females). Epithelial cell atypia was seen in the urinary bladder of high dose males and females, while bone marrow polychromatic erythrocytes with micronuclei were slightly increased only in low dose males (Vaittinen *et al.*, 1995).

Genetic toxicology and carcinogenicity

MX and its analogues (including E-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (E-MX)) have been suggested as responsible for much of the mutagenic activity attributed to DBPs in drinking water (Meier *et al.*, 1987b).

MX has been classified by IARC (IARC, 2004) a*s possibly carcinogenic in humans on the basis of limited animal data (Group 2B)*, and the majority of research has concentrated on MX. It has also been shown that chlorinated-MX analogues and other E-MX, are genotoxic in mammalian cells *in vitro* (Komulainen, 2004), and that they may have an additive or synergistic genotoxic interaction in mammalian cells *in vitro* (Maki-Paakkanen *et al.*, 2004). This suggests that any exposure calculations should consider the amount of total halogenated furanones and safety factors should be adjusted appropriately.

There is no human toxicity data available for MX or its analogues.

Experimentally, exposure of primary hepatocytes from F344 rats or L5178Y mouse lymphoma cells to MX *in vitro* caused genotoxic effects (Le Curieux *et al.*, 1999). MX has also been shown to induce chromosomal aberrations in CHO cells (4 μg/ml; (Meier *et al.*, 1987a) as well as to induce DNA damage, in a concentration-dependent manner, in suspensions of rat hepatocytes and, an increased frequency of SCE at 2 to 5 μmol/L when incubated with V79 Chinese hamster cells for 2 hours and at 30 - 300 μmol/litre when incubated with isolated rat testicular cells for 1 hour (Brunborg *et al.*, 1991). *In vitro* incubation of rat and mouse hepatocytes with MX also showed a dose-dependent increase in unscheduled DNA synthesis (UDS) at subcytotoxic concentrations (1 - 10 μmol/L, 20 hour incubation; (Nunn *et al.*, 1997). Studies have also shown that, whilst MX has clastogenic effects (chromatid breaks and rearrangements, concentration 0.75 μg/ml; (Harrington-Brock *et al.*, 1995), it does not have a significant effect on

hypoxanthine-guanine phosphoribosyltransferease mutation induction when administered to V79 Chinese hamster cells at 30 to 300 μM for 1 hour (Brunborg *et al.*, 1991). MX has also been shown not to induce UDS in mouse hepatocytes *ex vivo* at 3 to 16 hours after oral administration of 100 mg MX/kg body weight (Nunn *et al.*, 1997) and it did not increase the frequency of micronuclei in the bone marrow of Swiss-Webster mice (at 70% of $LD_{50,}$ i.e. 90 mg/kg bw/day, for 2 days; (Meier *et al.*, 1987a).

Studies using repair-competent and repair-deficient *Escherichia coli* have shown that after intravenous administration of MX to mice at 200 mg/kg bw, there is reduced recovery in a repair-deficient strain in the stomach, lung, intestine, liver, kidney and spleen (Fekadu *et al.*, 1994), which has also been seen at dosages as low as 4.3 mg/kg bw.

After oral gavage administration of MX at 64 mg/kg bw/day to rats for 14 days only 0.3% of the dose was excreted in a genotoxically-active form in rat urine; no significant mutagenic activity was seen in hepatocytes from rats given 32 mg/kg bw/day, and there was no evidence of micronuclei induction detected in peripheral blood erythrocytes from the mice (Meier *et al.*, 1996). MX has also been shown not to induce DNA strand breaks after IP dosing at 18 mg/kg bw (Brunborg *et al.*, 1991) or following oral administration at 125 mg/kg bw (Brunborg *et al.*, 1991). However, dose-dependent increased SCE of peripheral lymphocytes was noted at both 30 or 45 – 75 mg/kg bw/day when given to male and female Han:Wistar rats via gavage for 14 to 18 weeks (Jansson *et al.*, 1993). Similarly, a dose-related increase in chromosomal damage (micronuclei formation) and increased SCE was noted in Han:Wistar rats given 25 - 150 mg/kg by oral gavage, on only 3 consecutive days (Maki-Paakkanen *et al.*, 2004, Jansson *et al.*, 1993).

Nuclear anomalies in duodenum epithelial cells were reported at doses above 0.37 mmol/kg bw but not at 0.28 mmol/kg bw after oral administration to B3C6F1 mice (Daniel *et al.*, 1991). Increases in the incidence of nuclear anomalies were also reported in non-glandular stomach, urinary bladder, jejunum and ileum of rats dosed with 144 mg/kg bw (Mullins & Proudlock, 1990), which also caused significant irritation, inflammation and evidence of apoptotic cells in the GI tract.

In Wistar rats given MX at up to 50 mg/l in drinking water for 5 weeks, a dose-dependent and statistically significant increase in cell proliferation and an increase in lipid peroxidation level was noted in gastric mucosa and urine (at up to 25 mg/L). Gastric erosion was also seen at >25 mg/L, suggesting that MX might potentially promote gastric tumours even at low, apparently non-toxic, doses (Nishikawa *et al.*, 1994). Oral administration of MX to Wistar rats (50/sex/group) in drinking water at 0.4, 1.3 and 5.0 mg/kg bw/day (males) and 0.6, 1.9 and 6.6 mg/kg bw/day females, for 104 weeks, resulted in no over general toxic changes but did show increased tumours of the lung, mammary gland, haematopoietic system, liver, pancreas, adrenal gland and thyroid (Komulainen, 1996). MX has also been shown to exert promotional effects on rat glandular stomach carcinogenesis after initiation (with N-methyl-N theta-nitro-N-nitrosoguanidine at 100 ppm in a 5% NaCl diet for 8 weeks) in male Wistar rats at 30 ppm for 57 weeks, but no effect on tumour profile was noted at 10 ppm (Nishikawa *et al.*, 1999).

Reproductive and developmental toxicity

No information identified.

Mechanism(s) of action

With regard to the mechanism of genotoxicity of MX, mutations arising from this compound have been noted to be similar to the bulky adduct forming carcinogens that block replication leading to base substitutions (Strauss, 1991). Mutagenetic activity of MX is thought to be reliant on the chlorine substitution on C_3 (Ishiguro *et al.*, 1988). MX has shown been shown to be a potent mutagen in the bacterial Ames-test without metabolic activation (*Salmonella typhimurium* TA100-strain, weaker responses in strains TA92, TA97, TA98, TA102, and TA1535) but the addition of the metabolic fraction decreased the mutagenic response (Meier *et al.*, 1987a).

The exposure of BALB 3T3 cells to MX *in vitro* at concentrations of 0.005, 0.05, 5 and 50 μM for 15 minutes, 30 minutes, 1 hour or 2 hours, resulted in an inhibition in the gap junctional intercellular communication (GJIC) at all doses and all time points; the most significant inhibition occurred after 30 minutes exposure although some recovery was noted after an prolonged exposure period of 6 hours (Hakulinen *et al.*, 2004). It was suggested that this is one mechanism by which MX may cause the production of malignant foci.

Authoritative or project specific provisional acceptable levels

No authoritative values have been identified for the halogenated furanone group and, as no NOAEL or LOAEL was identified, no specific project provisional acceptable (SSPADI) can be calculated.

C3.4 Overall assessment of hazard profiles and key determinants of toxicity for chemicals detected in experimental investigations

Whilst it is known that the number of chemicals generated as disinfection by-products is extensive (believed to be over 500 different chemical species; Parsons and Jefferson, 2006), current analytical methods are limited by the level of detection and therefore only selected DBPs are routinely measured. Within the experimental procedures outlined in Sections 3 and 4 of the main report, the detected DBPs were: trihalomethanes (TCM, BDCM, DBCM, TBM, DCIM and BCIM); haloacetic acids (MCAA, MBAA, DCAA, TCAA, BCAA, DBAA, BDCA, DBCA, and TBAA); haloacetonitriles (TCAN, DCAN, BCAN, and DBAN); halonitromethanes (chloropicrin); and nitrosoamines (NDMA). Although the potential for formation of cyanogen chloride was also determined, this is a qualitative measurement and cannot be used for risk assessment purposes therefore has been excluded from the consideration of the risk assessment in this report.

From the trihalomethane group, TCM is the most common form and is formed preferentially unless there is sufficient bromide concentration, at which point the brominated forms increase (WHO, 2005). The toxic end points for THMs are the liver and thyroid. The tolerable daily intake for the THMs was determined as 15 μg/kg bw/day for TCM; 21.4 μg/kg bw/day for DBCM; and 17.9 μg/kg bw/day for TBM, all of which result in the same toxic end point of liver toxicity evidenced by histopathological lesions in the liver or hepatic cysts. IARC has classified BDCM in Group 2B (possibly carcinogenic to humans) as it has given unpredictable results from in vitro and in vivo genotoxicity assays. The WHO guideline value for BDCM has been derived as 0.06

mg/L on the basis of scientific uncertainty (calculations based on same study) and practical limitations of reducing DBP whilst maintaining robust disinfection standards (WHO, 2005b, WHO, 2004e). It was not possible to identify a reference standard or to derive a SSPADI for DCIM or BCIM. It is noted that the identified guideline value for THM4 is not health-based. It has been suggested (WHO, 2006; J Fawell, private communication) that the sum of the observed concentrations of the identified THMs divided by the sum of guideline values ($THM4_{obv}$:$THM4_{guide}$) for those chemical species should be calculated and the result compared to 1. If the ratio of $THM4_{obv}$:$THM4_{guide}$ is greater than 1, then the observed concentrations are of concern and should be considered further.

Studies on the toxicity of haloacetic acids have mainly concentrated on TCAA, DCAA and MCAA compounds, with TDIs being derived for these as 32.5 μg/kg bw/day, 7.6 μg/kg bw/day, and 3.5 μg/kg bw/day, respectively (WHO guideline values). TDIs have also been derived for BCAA (41 μg/kg bw/day), DBAA (20 μg/kg bw/day) and HAA9s (SSPADI calculated from US guidance of total intake less than 60 μg/L). WHO derived a provisional guideline value for DCAA of 0.05 mg/L (based on tumour prevalence data). The current information base provided for brominated acetic acids was considered by the WHO as inadequate for the derivation of guideline values therefore other sources were considered. IPCS derived a TDI for dibromoacetic acid of 20 μg/kg bw/day (reproductive toxicity). A TDI for bromochloroacetic acid was not identified during this project but did identify relevant NOAELs for systemic toxicity (41 mg/kg bw/day) and reproductive toxicity (50 mg/kg bw/day). A SSPADI was calculated as 41 μg/kg bw/day, using the NOAEL for systemic toxicity and a safety factor of 1000 due to the high level of uncertainty and the potential toxic end points. The HAA9 SSPADI is not health-based and a similar approach as for THM4 has been suggested (J Fawell, private communication), i.e. that the sum of the observed concentrations of the identified HAAs divided by the sum of guideline values ($HAA9_{obv}$:$HAA9_{guide}$) and the result compared to 1.

The haloacetonitrile group has TDIs derived for reproductive toxicity in the case of TCAN (0.2 μg/kg bw/day), liver toxicity for DCAN (0.66 μg/kg bw/day) and the reduction of body weight in the case of DBAN (2.33 μg/kg bw/day). No TDI has been derived for BCAN and there were no identified appropriate NOAEL or LOAEL values obtained for this compound.

DBAN has a WHO guideline value of 70 μg/L. DCAN has a provisional WHO guideline value of 20 μg/L. No other authoritative values have been identified for any other HANs.

The halonitromethane group is represented by chloropicrin. The TDI of chloropicrin has been derived as 11.3 μg/kg bw/day for its systemic toxicity.

Nitrosoamines (NDMA) are known carcinogens. WHO has derived a TDI for NDMA in drinking water as 2.77×10^{-3} μg/kg bw/day, based on the unit risk of cancer in humans, which equates to 27.7 ng/kg bw/day.

A summary of the identified DBP, their associated toxic end points and the standard value to be used in the risk assessment is shown in Table 3.

Table C3. Summary of key toxic endpoints of concern and appropriate standard values for use in risk assessment of DBP

DBP	Toxic Endpoint	NOAEL or LOAEL mg/kg bw/day	Uncertainty Factor	Standard value to be used in risk assessment μg/kg bw/day
Trihalomethanes				
Trichloromethane	Liver toxicity	-		15 μg/kg bw/day[1]
Bromodichloromethane	Possible carcinogen (renal and intestinal)	-		2 μg/kg bw/day [Derived from guideline value 0.06 mg/L[1]]
Dibromochloromethane	Liver toxicity			21.4 μg/kg bw/day[1]
Tribromomethane	Liver toxicity			17.9 μ/kg bw/day[1]
Total Trihalomethanes (THM4)				3.33 μg/kg bw/day [Derived from UK limits of 100μg/L[1]]
THM4 (sum)				Sum of observed concentrations divided by sum of guideline values[2]
Haloacetonitriles (HAN)				
Trichloroacetonitrile (TCAN)	Reproductive/teratogenic toxicity			0.2 μg/kg bw/day[3]
Dichloroacetonitrile (DCAN)	Liver toxicity			0.66 μg/kg bw/day [Derived from WHO TDI of 20μg/L][2]
Bromochloroacetonitrile (BCAN)				
Dibromoacetonitrile (DBAN)	Reduced body weight			0.66 μg/kg bw/day [Derived from WHO TDI of 70 μg/L][2]
Haloacetic acids				
Monochloroacetic acid (MCA)	Spleen toxicity	-		3.5 μg/kg bw/day[3]
Monobromoacetic acid (MBA)		-		
Dichloroacetic acid (DCAA)	Possible carcinogen	-		7.6 μg/kg bw/day[4]
Trichloroacetic acid (TCAA)	Liver toxicity	-		32.5 μg/kg bw/day[5]
Bromochloroacetic acid (BCA)	Systemic toxicity	41 mg/kg bw/day	100	41 μg/kg bw/day
Dibromoacetic acid (DBA)	Reproductive toxicity	-		20 μg/kg bw/day
Bromodichloroacetic acid (BDCA)		-		
Dibromochloroacetic acid (DBCA)		-		
Tribromoacetic acid (TBA)		-		
Haloacetic acids				2 μg/kg bw/day

(HAA9)				[Derived from US limits of 60μg/L]
HAA9 (sum)				Sum of observed concentrations divided by sum of guideline values[2]
Halonitromethane				
Chloropicrin				
Nitrosoamines				
N-nitrosodimethylamine	Carcinogen			2.77 x 10^{-3} µg/kg bw/day[6]

[1](WHO, 2005b)
[2.] WHO2006
[3] (WHO, 2004c)
[4] (WHO, 2004d)
[5] (WHO, 2004b)
[6] (WHO, 2004f)
[7] (WHO, 2008)

C4 Risk assessment

C4.1 Patterns of contamination identified in water samples, and implications for risk assessment

In general the highest concentrations of the DBPs were found in samples from sewage treatment plants (STP) using chlorination techniques. However, three DBP (dichloroacetonitrile, monochloroacetic acid, and NDMA) occurred at higher levels in those STP's that utilise chloramination treatments. This difference is also apparent when data are expressed in terms of the relative average percentages for each chemical group and analysed using a one-tailed Student's T-test. The percentage of some chemicals, DCAN, NDMA, MCAA and DCAA, showed significant increases ($p>0.05$) in the chloraminated samples, compared with those for chlorination (see Figure 4.1). As NDMA was detected only in one sample from one chloraminated source, it was considered inappropriate to analyse this statistically.

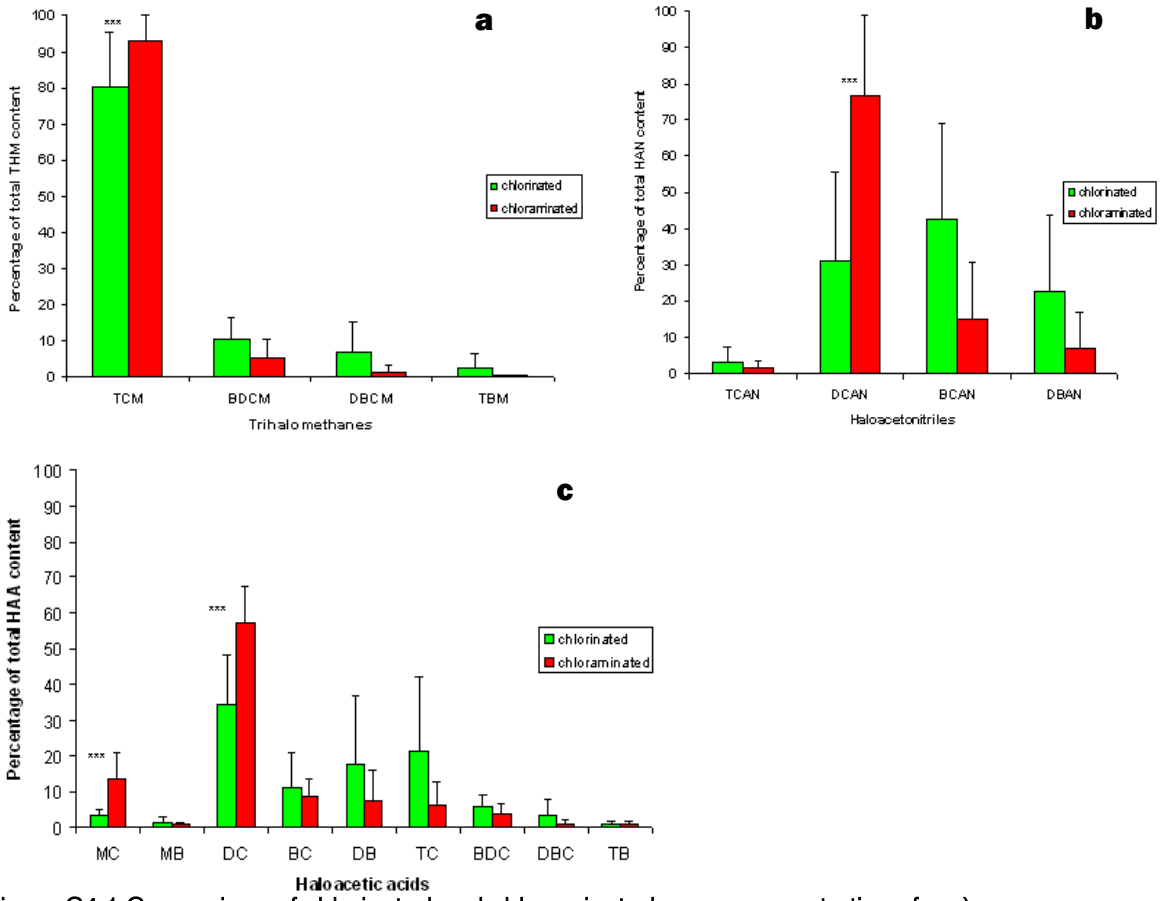


Figure C4.1 Comparison of chlorinated and chloraminated mean concentrations for a) trihalomethane group b) haloacetonitrile group and c) haloacetic acid group with individual chemical concentration considered as a percentage of the total group concentration.

Where *** represents $p < 0.005$ (using a one-tailed Student's T-test) when a statistically significant in compound concentration is noted in chloraminated samples compared to chlorinated samples.

C4.2 Estimation of intake from drinking water by population subgroups

The exposure of human populations was modelled using the derived estimates of concentration of each compounds or group present in the sampled drinking water supplies (based on the sampling programme undertaken; see Section 4 of Main Report).

C4.2.1 Chemicals not detected in water samples

The following individual or groups of chemicals were not measured in the chloraminated or chlorinated water samples analysed and, therefore, no risk assessment can be performed in the absence of any evidence of exposure:

- Trihalomethanes: water samples were not analysed for the presence of dichloroiodomethane, bromochloroiodomethane, dibromoiodomethane, chloroiodomethane, bromodiiodomethane, or triiodomethane due to the analytical

methods used, other trihalomethanes were analysed for and detected in both chlorinated and chloraminated samples;

- Haloacetic acids: water samples were not analysed for the presence of iodoacetic acid, bromoiodoacetic acid, 3-bromo-3-iodopropenoic acid, or 2-iodo-3-methylbutenedioic acid due to the analytical methods used, other haloacetic acids were analysed for and detected in both chlorinated and chloraminated samples;

- Halonitromethanes: water samples were analysed for the presence of trichloronitromethane (also known as chloropicrin; detected in both chlorinated and chloraminated samples), no other halonitromethane was included in the analysis;

- Haloketones: samples were not analysed for haloketone concentrations;

- Haloaldehydes: samples were not analysed for haloaldehyde concentrations;

- Cyanogen halides: whilst analytical investigations identified that there was the theoretical potential for the formation of cyanogen halides, this only indicates the possibility of their generation. No evidence is available that this contaminant is actually present, and in the absence of any data on exposure occurring at a quantifiable level, quantitative risk assessment is not possible.

- Haloacetamides: samples were not analysed for haloacetamide concentrations;

- Dimethyl cyanamide: samples were not analysed for DMC concentration;

- Halogenated furanones: samples were not analysed for halogenated furanone concentrations.

C4.2.2 Chemicals detected in water samples

For the remaining chemicals included in the analysis suite, some evidence of exposure was found during the sampling programme and intake estimates were derived based on the highest detected obtained in the sampling programme from all three sample collection periods (Section 4 of Main Report). As described in detail in Section 2.3 of this Annex, the intakes were calculated in terms of units per kg bodyweight per day for adults and for children.

The intake value of each chemical and/or group, as appropriate, was then compared with the most appropriate reference standard (be it an established guideline or standard value) or with the SPPPADI, for adults and toddlers separately. This approach is considered highly precautionary since it assumes the worse-case scenario in which all drinking water consumed by relevant individuals would contain residues at the worst-case levels on a long-term basis and, in addition, makes no allowance for only partial absorption of a chemical into the gastrointestinal tract or for volatilisation of compounds from the water during processing prior to consumption (e.g. as would be the case for THMs when water is boiled prior to making a hot drink or preparation of infant milk formula). A different method was also used for THM4 and HAA9s, as described in Section 3.4, where the ratio of the sum of observed concentrations of THM4 against the sum of the guideline values was determined and compared to 1. The compound group were of concern if the ratio exceeded 1.

As a slightly more realistic, though still highly precautionary approach, intakes were also derived using the median detected values obtained in the sampling programme.

The values derived for both these scenarios are presented in Tables 4.1 to 4.4. Where the percentage of the derived intake value was greater than 5% of the appropriate reference standard, these are highlighted in the tables

Table C4.1 Percentage of Derived reference standards for highest concentrations (chloraminated data) for a) adults and b) toddlers

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	*6.60*	15	**44.0**
Bromodichloromethane	*0.29*	2	**14.7**
Dibromochloromethane	*0.09*	21.4	**0.4**
Tribromomethane	*0.02*	17.9	**0.1**
THM4obs:THM4guide	*6.99*	56.3	**0.1**
THM4	*6.62*	3.33	**198.9**
Trichloroacetonitrile	*0.00*	0.2	**2.2**
Dichloroacetonitrile	*0.07*	0.7	**10.6**
Dibromoacetonitrile	*0.02*	2.3	**0.8**
Monochloroacetic acid	*0.23*	3.5	**6.6**
Dichloroacetic acid	*0.91*	7.6	**12.0**
Bromochloroacetic acid	*0.09*	41	**0.2**
Dibromoacetic acid	*0.33*	20	**1.6**
Trichloroacetic acid	*0.58*	32.5	**1.8**
HAA9obs:HAA9guide	*2.15*	78.6	**0.0**
HAA9 (sum)	*1.75*	2	**87.4**
NDMA	**0.00**	**0.0277**	**3.1**

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	*14.03*	15	**93.5**
Bromodichloromethane	*0.63*	2	**31.3**
Dibromochloromethane	*0.19*	21.4	**0.9**
Tribromomethane	*0.03*	17.9	**0.2**
THM4obs:THM4guide	*14.88*	56.3	**0.3**
Sum (trihalomethanes)	*14.09*	7.09	**198.7**
Trichloroacetonitrile	*0.01*	0.2	**4.6**
Dichloroacetonitrile	*0.15*	1.4	**10.6**
Dibromoacetonitrile	*0.04*	5	**0.8**
Monochloroacetic acid	*0.49*	3.5	**14.1**
Dichloroacetic acid	*1.94*	7.6	**25.5**
Bromochloroacetic acid	*0.19*	41	**0.5**
Dibromoacetic acid	*0.70*	20	**3.5**
Trichloroacetic acid	*1.24*	32.5	**3.8**
HAA9obs:HAA9guide	*4.57*	104.6	**0.0**
Sum (haloacetic acids	*3.72*	4.25	**87.5**
NDMA	**0.00**	**0.0277**	**6.7**

Table C4.2 Percentage of Derived reference standards for median concentrations (chloraminated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	1.41	15	9.4
Bromodichloromethane	0.06	2	2.8
Dibromochloromethane	0.01	21.4	0.0
Tribromomethane	0.002	17.9	0.0
THM4obs:THM4guide	1.48	56.3	0.0
Sum (trihalomethanes)	**1.60**	**3.33**	**48.0**
Trichloroacetonitrile	0.00	0.2	0.2
Dichloroacetonitrile	0.03	0.7	4.9
Dibromoacetonitrile	0.00	2.3	0.0
Monochloroacetic acid	0.08	3.5	2.2
Dichloroacetic acid	0.35	7.6	4.7
Bromochloroacetic acid	0.05	15	0.3
Dibromoacetic acid	0.02	20	0.1
Trichloroacetic acid	0.02	32.5	0.1
HAA9obs:HAA9guide	0.52	78.6	0.0
Sum (haloacetic acids)	**0.55**	**2**	**27.6**
NDMA	**0.00**	**0.0277**	**1.6**

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	3.01	15	20.0
Bromodichloromethane	0.12	2	5.9
Dibromochloromethane	0.01	21.4	0.1
Tribromomethane	0.004	17.9	0.0
THM4obs:THM4guide	3.14	56.3	0.1
Sum (trihalomethanes)	**3.40**	**7.09**	**47.9**
Trichloroacetonitrile	0.00	0.2	0.4
Dichloroacetonitrile	0.07	1.4	4.9
Dibromoacetonitrile	0.00	5	0.0
Monochloroacetic acid	0.16	3.5	4.6
Dichloroacetic acid	0.75	7.6	9.9
Bromochloroacetic acid	0.10	41	0.2
Dibromoacetic acid	0.04	20	0.2
Trichloroacetic acid	0.05	32.5	0.2
HAA9obs:HAA9guide	1.11	104.6	0.0
Sum (haloacetic acids	**1.17**	**4.25**	**27.6**
NDMA	**0.00**	**0.0277**	**3.5**

Table C4.3 Percentage of Derived reference standards for highest concentrations (chlorinated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	12.32	15	82.2
Bromodichloromethane	0.84	2	42.1
Dibromochloromethane	0.83	21.4	3.9
Tribromomethane	0.33	17.9	1.8
THM4obs:THM4guide	14.32	56.3	0.3
Sum (trihalomethanes)	**13.96**	**3.33**	**419.3**
Trichloroacetonitrile	0.01	0.2	2.6
Dichloroacetonitrile	0.03	0.7	5.2
Dibromoacetonitrile	0.07	2.3	2.8
Monochloroacetic acid	0.17	3.5	4.9
Dichloroacetic acid	2.20	7.6	28.9
Bromochloroacetic acid	0.27	41	0.7
Dibromoacetic acid	1.85	20	9.2
Trichloroacetic acid	1.08	32.5	3.3
HAA9obs:HAA9guide	5.57	78.6	0.1
Sum (haloacetic acids)	**4.46**	**2**	**223.1**

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/ TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	26.21	15	174.8
Bromodichloromethane	1.79	2	89.6
Dibromochloromethane	1.76	21.4	8.2
Tribromomethane	0.69	17.9	3.9
THM4obs:THM4guide	30.46	56.3	0.5
Sum (trihalomethanes)	**29.70**	**7.03**	**422.5**
Trichloroacetonitrile	0.01	0.2	5.5
Dichloroacetonitrile	0.07	1.4	5.2
Dibromoacetonitrile	0.14	5	2.8
Monochloroacetic acid	0.36	3.5	10.4
Dichloroacetic acid	4.83	7.6	61.5
Bromochloroacetic acid	0.57	41	1.4
Dibromoacetic acid	3.93	20	19.6
Trichloroacetic acid	2.30	32.5	7.1
HAA9obs:HAA9guide	11.84	104.6	0.1
Sum (haloacetic acids	**9.49**	**4.25**	**223.4**

Table C4.4 Percentage of Derived reference standards for median concentrations (chlorinated data) for a) adults and b) toddlers.

a.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	2.58	15	17.2
Bromodichloromethane	0.40	2	19.9
Dibromochloromethane	0.07	21.4	0.3
Tribromomethane	0.00	17.9	0.0
THM4obs:THM4guide	3.05	56.3	0.0
Sum (trihalomethanes)	3.54	3.33	106.2
Trichloroacetonitrile	0.00	0.2	0.5
Dichloroacetonitrile	0.01	0.7	1.4
Dibromoacetonitrile	0.01	2.3	0.3
Monochloroacetic acid	0.05	3.5	1.5
Dichloroacetic acid	0.57	7.6	7.5
Bromochloroacetic acid	0.14	15	0.9
Dibromoacetic acid	0.11	20	0.6
Trichloroacetic acid	0.19	32.5	0.6
HAA9obs:HAA9guide	1.07	78.6	0.0
Sum (haloacetic acids)	2.11	2	105.6

b.

	Calculated intake /kg (µg/kg bw/day)	SSPADI/TDI (µg/kg bw/day)	% SSPADI/TDI
Trichloromethane	5.49	15	36.6
Bromodichloromethane	0.85	2	42.3
Dibromochloromethane	0.14	21.4	0.7
Tribromomethane	0.00	17.9	0.0
THM4obs:THM4guide	6.49	56.3	0.1
Sum (trihalomethanes)	7.52	7.03	107.0
Trichloroacetonitrile	0.00	0.2	1.1
Dichloroacetonitrile	0.02	1.4	1.4
Dibromoacetonitrile	0.01	5	0.3
Monochloroacetic acid	0.11	3.5	3.2
Dichloroacetic acid	1.21	7.6	15.9
Bromochloroacetic acid	0.30	41	0.7
Dibromoacetic acid	0.24	20	1.2
Trichloroacetic acid	0.41	32.5	1.3
HAA9obs:HAA9guide	2.27	104.6	0.0
Sum (haloacetic acids	4.49	4.25	105.7

C4.2.2.1 Consideration of risk for individual or groups of compounds for which predicted daily intake from drinking water amounted to less than 5% of the reference standard

The following individual or groups of compounds (in Table 4.5) were detected in water samples at amounts below 5% of the reference standard, even on the basis of a worst case scenario (toddler exposure) using the highest water concentration detected.

Table C4.5 Individual or groups of compounds that present in water samples at less than 5% of reference standard for worse case scenario (using the highest recorded concentration).

Chloraminated samples	Chlorinated samples
Dibromomethane	Tribromomethane
Tribromomethane	Dibromoacetonitrile
Triacetonitrile	Chloropicrin
Dibromoacetonitrile	Bromochloroacetic acid
Chloropicrin	Trichloroacetic acid
Bromochloroacetic acid	THM4 (sum)[1]
	HAA9 (sum)[1]
Dibromoacetic acid	
Trichloroacetic acid	
THM4 (sum)[1]	

HAA9 (sum)[1]	

[1]THM4 (sum) and HAA9 (sum) have been determined by taking the ratio of the sum of the observed concentrations against the sum of the guideline values.

The presence of these above contaminants at such low levels is not considered to represent a significant risk to human health and will not be considered further.

C4.2.2.2 Consideration of risk for individual or groups of compounds for which predicted daily intake from drinking water amounted to between 5 and 10% of the reference standard

The only compounds that were identified as having a predicted daily intake for adults of between 5 and 10% of the relevant reference standard or SSPADI (as shown in Tables 4.1 to 4.4) when the highest measured chloraminated sample concentrations were considered, was MCAA (6.6%). When the same criteria are applied to chlorinated water samples, only DBA (9.2%) and DCAN (5.2%) were identified. As can be seen, even continuous exposure of humans to these compound through drinking water at the highest concentrations detected in the sampling programme would represents only a small percentage of the health-based reference standards for these chemicals and is not considered to represent a significant issue with regard to human safety, Furthermore, when the more representative values based on median measured concentrations are used to calculate predicted daily intake, only TCM reached this nominal threshold intake for chloraminated samples whilst DCAA was the only DBP identified for the chlorinated water samples.

When intakes predicted for toddlers were considered, the highest predicted daily intake of NDMA (6.7%) marginally exceeded 5% of the SSPADI. NDMA was the only detected form of nitrosamine, and was only detected in samples at one location in one sampling period. The significance of this single occurrence within the context of a quantitative risk assessment is questionable. While, because of its toxicological properties, any exposure to NDMA is considered undesirable, the frequency of occurrence of this pollutant in the water supply is unclear on the basis of the current limited sampling programme. However, if viewed as an isolated occurrence then this finding is unlikely to represent any quantifiable risk to human health and should be viewed in the context of the established major routes of human exposure to nitrosamines which are known to be through use of tobacco products and through some food stuffs (such as cured meats, fish and cheese; (Lijinsky, 1999). Indeed, it has previously been estimated that consumption of drinking water accounts for considerably less than 1% of the total intake of nitrosamines (Fristachi & Rice, 2007).

Comparisons based on the median measured concentrations (excluding NDMA, for which no medium value was appropriate) resulted in the predicted daily intake of BDCM (5.9%) and DCAA (9.9%) slightly exceeding 5% of the SSPADI, but these were again considered to represent only marginal diminutions of the margin of safety implicit for exposures lower than the reference standard. When the same criteria are applied to chlorinated water samples, the highest measured sample concentration resulted in a predicted daily intake of DBCM (8.2%) exceeding 5% of SSPADI, but when the median concentration levels were used there were no DBP that could be included in this data set.

C4.2.2.2 Consideration of extent of risk for compounds or groups for which predicted daily intake from drinking water amounted to 10% or greater of the reference standard

A number of compounds were found to have predicted daily intakes in excess of 10% of the relevant standard. For adults, exceedence of 10% of TDI or SSPADI was noted for TCM (44.0%), BDCM (14.7%), THM4 (198.9%), DCAN (10.6%) DCAA (12.0%) and HAA9 (87.4%) when the highest measured value of chloraminated samples was used in the calculation. Of these, only the predicted daily intake THM concentration exceeded the reference value and thus represents a slight erosion of the safety margin. However, when the more representative median measured concentration was used to calculate the predicted daily intake for adults, the percentage was significantly less for each compound or compound group (THM4 and HAA9 at 48.0% and 27.6 % of SSPADI, respectively). When chlorinated water samples were considered for adults, exceedence of 10% of SSPADI (or TDI) was noted for TCM (82.2%), BDCM (42.1%), THM4 (419.3%), DCAA (28.9), DBAA (9.2%), and HAA9 (223.1%). When the median measured concentration was used, the compounds exceeding 10% of TDI or SSPADI were: TCM (17.2%), BDCM (19.9%), THM4 (106.2%), DCAA (7.5%) and HAA9 (105.6%).

In the case of toddlers, seven compounds or groups were found to exceed the 10% of standard value when the highest measured values of chloraminated samples were considered, as follows: TCM (93.5%), BDCM (31.3%), DCAN (10.6%), THM4 (198.7%), MCAA (14.1%), DCA (25.5%), and HAA9 (87.5%). However, when median measured concentrations were considered, only the predicted daily intake for TCM (20.0%), THM4 (47.9%), and HAA9 (27.6%) exceeded 10% of SSPADI. When chlorinated water samples were measured, seven compounds or groups were found to exceed the 10% of SSPADI: TCM (174.8%), BDCM (89.6%), THM4 (422.5%), MCAA (10.4%), DCA (61.5%), DBA(19.6%), and HAA9 (223.4%). When median measured concentrations were considered, only the predicted daily intake for TCM (at 36.6%), BDCM (42.3%) THM4 (107.0%), DCAA (15.9%), and HAA9 (105.7%) exceeded 10% of the SSPADI.

Thus, the two groups of compounds that exceeded 10% of the SSPADI were trihalomethanes and haloacetic acids. For both groups, the chlorinated and brominated compounds have been shown to have different potencies with regards to mutagenicity. In these cases it may not be appropriate to consider the total concentration of the compound group for use as the risk assessment but instead to consider the individual compounds separately.

If individual compounds are considered for chloraminated water samples, the relevance of the predicted highest intakes of TCM, BDCM, and DCAA to human health are considered questionable and of limited concern given that there is still a significant margin between these calculated intakes and the reference standard which is itself highly precautionary and designed to ensure the safety of the general population. If THM4 and HAA9 are considered, this safety margin is somewhat eroded. However, when median concentrations are used, no compound or compound group exceeds the reference standard. When chlorinated water samples are considered using the same criteria, the relevance of the predicted highest intakes of TCM, BDCM, DCAA, and MCAA to human health are considered questionable and of limited concern given that there is still a margin between these calculated intakes and the reference standard. When the predicted intake is calculated using the median measured concentration, the reference standard is exceeded only by THM4 and HAA9; this represents a slight

erosion of the margin of safety. It should be noted, however, that when a modified approach is used to comparing $THM4_{obs}$:$THM4_{guide}$ and $HAA9_{obs}$:$HAA9_{guide}$ (see Section 3.4), neither ratio exceeded 1 suggesting that, in practice, there is little cause for concern across the whole population considered. However, it is noted that the ratio method takes into account the health-based guideline values for the individual chemical species but may not take into account chemical mixtures.

C5. Consideration of potential for mixture interactions influencing overall toxic outcome

Current good practise in chemical risk assessment requires that the potential for interactions of chemical substances in the same matrix, to which humans might be exposed, should be considered. The presence of over 500 individual chemicals caused by the disinfection of drinking water, either by chlorination or chloramination, presents an excellent, but challenging, example of this principle. Recently, the UK Interdepartmental Group on Health Risks from Chemicals (IGHRC) has produced guidelines to encourage best practice in this area. The guidelines (Chemical mixtures: a framework for assessing risks to human health, GHRC, 2008) provide a comprehensive framework for undertaking risk assessments of mixtures in a structured fashion using the best available methodology.

One of the principles in the framework states,
"A key factor in risk assessments for chemical mixtures is the availability, or absence, of reliable data for the whole mixture or components. Where mixture risk assessments follow component-based approaches it is particularly important to have reliable data on the identity, toxicokinetics, metabolic pathways, mechanisms of action and levels of exposure for the key components in order to make science-based judgements about the potential for interactions between components to affect the overall toxicity. Where this information is lacking regulators may need to make precautionary default assumptions. Where there is no clear information on the potential for interactions to occur, there is no scientific basis from which to consider interactions in either a quantitative or a qualitative sense".
This presents a great challenge to undertaking risk assessments for the DBPs due to both their large number and, the paucity of data on which to make informed assessments. As has been shown in the above sections, there is a lack of toxicological data for many of the identified DBPs and thus expert-judgement is either used to "read-across" conclusions based on information from similar compounds or, make a judgement that nothing can be done. The framework notes the particular situation for undertaking risk assessment for drinking water and states:

"Drinking water, both tap and bottled, also contains a diverse range of residues. Any water-soluble chemical present in the environment and not completely removed by the treatment process may potentially be present in the water supply. In addition, the treatment process itself can introduce residues and by-products into the supply. Which contaminants are present in the supply will depend on whether the water is obtained from a groundwater or surface water source and factors such as the local geology and

land-use. Potential contaminants include naturally occurring metal salts, products used in agriculture, substances discharged from industrial processes and other environmental contaminants as well as drinking water treatment chemicals and disinfection byproducts. Regular and frequent analyses are performed to ensure that levels of regulated contaminants do not exceed permitted levels. In the case of both food and drinking water although the identity and quantity of the natural constituents, residues and contaminants present is likely to be highly variable, in general, these substances will be present at very low concentrations. In the case of pesticide and veterinary medicine residues, specific residues are likely to be associated with particular foods but there may be variations in the levels of these residues depending on the season and geographic region from which the food was obtained. [Current] understanding of the hazardous properties of residues and contaminants in food and drinking water is based on information for individual substances. It will not be possible to obtain meaningful whole mixture data because of the variable nature of these mixtures. However, data may be available for certain commonly occurring groups of components."

In risk assessment of mixtures in specific situations, the risk assessor is expected to consider where chemicals in a mixture may influence the effects of each other. This should be done in a systematic fashion and is best undertaken via a series of steps. Fundamentally, an assessment should be made as to whether or not being simultaneously exposed to two or more chemicals can make the toxic/harmful effect greater than the effect of the individual substances. Such interactions may lead to potentiation or synergism and should consider are: 1) chemical-chemical interactions; 2) Toxicokinetic interactions (interactions affecting absorption, interactions affecting distribution, interactions affecting metabolism and interactions affecting elimination); 3) Toxicodynamic interactions (effects with and without thresholds). A few years ago, the UK Committee of Toxicology (COT, 2002) considered these issues in relation to the many chemical contaminants, primarily pesticides that occur in food at very low levels, a situation that has certain similarities to DBPs in drinking water. Their key conclusions regarding the risk assessment of mixtures were:

- Direct chemical reactions can occur between components of a mixture, though relatively few studies have been conducted to investigate such reactions.

- Mixtures of chemicals that affect the same target organ and have the same mode of action will show additivity (dose addition), which results from simple similar action, over the whole dose range.

- Where components of a mixture have different modes of action and exposures to each component are below any threshold of effect, no additivity and no potentiating interactions are generally found, suggesting that adverse reactions to the mixture at this level of exposure would be unlikely.

- A few studies have found evidence for potentiation when exposure to the mixture exceeded the threshold of effect for some or all of the components. However, it is not scientifically valid to extrapolate these findings to much lower dose levels.

- The probability of any health hazard due to additivity or potentiating interactions of mixtures at (low) non-toxic doses of the individual chemicals is likely to be

small, since the dose of pesticides in food to which humans are exposed is generally much lower than the NOAEL, at least through food.

In this current study, best practice indicates that compounds should be grouped together where the available evidence would suggest that they have a similar mode of action (THM and HAA). However, it should be noted that the measured amounts of DBPs are in general extremely low and the estimated human uptake likewise low in relation to any potential toxic endpoints. Helpfully, the IGHRC 2008 document states that: “In the case of toxicodynamic interactions, the document notes that these will only occur where exposures are above thresholds of effect. Providing the exposure level for each component is below its threshold of effect there should be no toxicodynamic interactions.” This, taking into account the low levels of exposure estimated in this study should provide a good measure of reassurance that any estimation of toxic effect will be no greater that that reported in previous sections.

Risk assessment of DBP is a rapidly evolving research area and as individual chemicals are identified and toxicity data becomes available, various component-based and whole-mixture techniques are being developed which may allow risk assessments to be further refined (Simmons *et al.*, 2004). In addition, other models will allow cumulative risk assessment models for DBPs to take account of toxicokinetics and dose addition integrated over time (Teuschler *et al.*, 2004).

C6. Conclusions and Recommendations

Most DBPs are present at levels markedly below the level of concern in the water samples tested.

In general, the concentrations of DBPs in chloraminated samples were at lower levels than chlorinated samples. Therefore, this suggests that chloramination of water samples generally reduces exposure when compared to chlorination of water samples.

Certain DBPs were present in samples at levels which exceeded 10% of the reference standard, namely THM4 and HAA9 in chloraminated samples and TCM, BDCM, THM4, DCAA, and HAA9 in chlorinated samples. However when a modified approach was used to calculate THM4 (sum) and HAA9 (sum), there appeared to be little concern. Given that this adopts a health-based guideline value approach, that has been suggested by the WHO, it seems appropriate to adopt this for the current risk assessment.

Risk assessment of DBPs is a rapidly evolving research area and as individual chemicals are identified and toxicity data becomes available, various component-based and whole-mixture techniques are being developed which will allow risk assessments to be further refined and cumulative risk assessment models to be developed.

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