

eAppendix 1

Exposure assessment

Assessment of the chlorination by-products (CBP) concentration in tap water at the participant's residence: The strategy applied to assign CBP data (from sampling campaigns) to each participant's residence for each pregnancy trimester under study was based on spatial and temporal aspects. For each participant, this assignment was carried out as follows:

Spatial aspect: the participant's residence was positioned geographically in the appropriate system and sub-system using a geographical information system (MapBasic version 8.0 with Platinum Postal Suite™ 2008.3). Thereafter, the two closest sampling sites located in the same residence sub-system were selected. A spatial weighted factor was applied to these two sampling sites according to their distance from the participant's residence:

$$WF_{P_1} = 1 - \left(\frac{d_{P_1}}{d_{P_1} + d_{P_2}} \right) \quad (1)$$

$$WF_{P_2} = 1 - \left(\frac{d_{P_2}}{d_{P_1} + d_{P_2}} \right) \quad (2)$$

where WF represents the spatial weighted factor, P_1 and P_2 are the sampling sites selected to represent participant exposure to CBPs, and d denotes the distance between each sampling site and the participant's residence (without units: distances were standardized from coordinates).

In the case where a sub-system included a single sampling site, CBP data from the site were used directly to assess the CBP concentration in tap water at the participant's residence located in this sub-system.

Temporal aspect: for each selected sampling site (following the spatial aspect), the CBP concentration measured on each sampling date was considered as representative of the CBP concentration in tap water during a temporal window (denoted TW). The TW of each specific sampling date was calculated considering ± 15 days (for systems with a monthly sampling frequency) or ± 30 days (for systems with a bimonthly sampling frequency) from the date. CBP data from sampling dates for which the TW was included within each participant's pregnancy period were averaged according to the number of days of each TW included in the pregnancy trimester under study. For each selected sampling site, the CBP concentration in tap water during the pregnancy trimester under study was estimated as follows:

$$(C_P)_{it} = \left((Cm_{D1})_P * \left(\frac{n_{D1}}{n_{TOT}} \right) \right)_{it} + \dots + \left((Cm_{Dx})_P * \left(\frac{n_{Dx}}{n_{TOT}} \right) \right)_{it} \quad (3)$$

where C is the concentration ($\mu\text{g/L}$) of the CBP compound i estimated for each sampling site P (P1 or P2) selected to represent the exposure of the participant to CBPs during the pregnancy trimester t , Cm is the concentration ($\mu\text{g/L}$) of the CBP compound i measured at each sampling site P for each sampling date D selected (1 to x), n is the number of days of the TW of each sampling date D included in the pregnancy trimester t and n_{TOT} is the total number of days in the pregnancy trimester t .

Finally, the CBP concentration in tap water at the participant's residence during the pregnancy trimester under study was assessed by combining the two aspects (spatial and temporal) and was calculated as follows:

$$E_{it} = (C_{P1} * WF_{P1})_{it} + (C_{P2} * WF_{P2})_{it} \quad (4)$$

where E is the concentration ($\mu\text{g/L}$) of the CBP compound i estimated during the pregnancy trimester t at the tap of the participant's residence and C is the concentration ($\mu\text{g/L}$) of the CBP compound i estimated for each sampling site $P1$ and $P2$ selected to represent the exposure of the participant to CBPs during the pregnancy trimester t .

eAppendix 2

Corrective factors applied to concentrations of trihalomethanes (THM) to estimate their ingestion according to type of water handling or devices

Devices/Handling	Percentages of elimination				References
	Chloroform	DCBM	CDBM	Bromoform	
<u>Filtration at home</u>					
<u>Point of Entry</u>	86.8	86.8 ^a	86.8 ^a	86.8 ^a	Egorov et al. ¹
<u>Water Source</u>					
Bottled water	100 ^b	100 ^b	100 ^b	100 ^b	Savitz et al. ²

Hot tap water	-160 ^c	-70 ^{c d}	-70 ^{c d}	-70 ^{c d}	Dion-Fortier et al. ³
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Filtration at home

Point of Use

Not used – RO ¹	48.0 ^b	48.0 ^b	48.0 ^b	48.0 ^b	Weinberg et al. ^{4*}
Used – RO ¹	86.8	86.8 ^a	86.8 ^a	86.8 ^a	Egorov et al. ¹
Not used – AC ²	99 ^b	99 ^b	99 ^b	99 ^b	Weinberg et al. ^{4*}
Used – AC ²	86.8	86.8 ^a	86.8 ^a	86.8 ^a	Egorov et al. ¹

Additional

handling

Storage in fridge	13.0	9.6	12.7 ^e	12.7 ^e	Levesque et al. ⁵
Filtering pitcher	85.7	80.3	85.7 ^e	85.7 ^e	Levesque et al. ⁵
Boiling	81.6	84.9	81.8 ^e	81.8 ^e	Levesque et al. ⁵

^a Percentages were assumed to be the same as in the sole informed case of TCM.

- b Percentages were assumed to be the same as in the sole informed case of TTHMs.
- c Negative values indicate an increase rather than a decrease in contamination.
- d Percentages were assumed to be the same as in the informed case of brominated THMs.
- e Percentages assumed to be the same as the calculated average for TTHMs.
- 1 RO=Reverse osmosis.
- 2 AC=Activated carbon.
- * Only one datum was available for RO and three for AC.

eAppendix 3

Correction factors applied to estimate haloacetic acids (HAA) ingestion according to type of water handling or devices

Devices/Handling	Percentages of elimination						References
	MCAA	DCAA	TCAA	BCAA	HAA5	Other HAAs^a	Levesque et al.⁵
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<u>Water Source</u>							
Bottled water	100	100	100	100	100	100	
Hot tap water	0	0	0	0	0	0	
 <u>Filtration at home</u>							

Point of Use

RO and AC ¹	8	45	64	59	30	60
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Additional**handling**

Storage in fridge	0	0	0	0	0	0
Filtering pitcher	2	30	35	33	30	60
Boiling	0	0	0	0	0	0

^a Difference between HAA9 and HAA5¹ RO=Reverse osmosis, AC=Activated carbon.

Reference List

- 1 Egorov AI, Tereschenko AA, Altshul LM et al. Exposures to drinking water chlorination by-products in a Russian city. *Int J Hyg Environ Health*. 2003;206(6):539-551.
- 2 Savitz DA, Singer PC, Hartmann KE, Herring AH, Weinberg HS, Makarushka C, Hoffman C, Chan R, and Maclehose R. Drinking water disinfection by-products and pregnancy outcome. 212. 2005. AWWA Research Foundation.
Ref Type: Report
- 3 Dion-Fortier A, Rodriguez MJ, Serodes J, Proulx F. Impact of water stagnation in residential cold and hot water plumbing on concentrations of trihalomethanes and haloacetic acids. *Water Res*. 2009;43(12):3057-3066.
- 4 Weinberg HS, Pereira VR, Singer PC, Savitz DA. Considerations for improving the accuracy of exposure to disinfection by-products by ingestion in epidemiologic studies. *Sci Total Environ*. 2006;354(1):35-42.
- 5 Levesque S, Rodriguez MJ, Serodes J, Beaulieu C, Proulx F. Effects of indoor drinking water handling on trihalomethanes and haloacetic acids. *Water Res*. 2006;40(15):2921-2930.

eAppendix 4

Mean water consumption (l/day) among women during pregnancy by type of water

	Cases	Water	Controls	Water
	n (%)	consumption	n (%)	consumption
		(95%CI)		(95%CI)
Water consumption during				
last trimester				
Plain tap water	191 (34)	0.93 (0.83-1.03)	700 (37)	0.94 (0.89-0.99)
Filtered tap water	94 (16)	1.11 (0.94-1.27)	279 (15)	0.96 (0.87-1.05)
Water stand in the fridge	45 (8)	1.05 (0.77-1.32)	144 (8)	1.03 (0.85-1.20)
Bottled water	208 (37)	1.06 (0.95-1.16)	707 (37)	1.01 (0.95-1.07)
Boiled tap water	3 (1)	0.52 (0-1.69)	6 (0)	0.96 (0.09-1.83)
Other	13 (2)	1.25 (0.42-2.09)	55 (3)	0.93 (0.68-1.17)

eAppendix 5

Spearman Correlation between different concentrations of chlorination by-products species at the tap of participants' residence

	Bromodichloro- methane	Brominated Trihalomethanes	Total Trihalomethanes	Dichloro- Acetic acid	Trichloro Acetic acid	Total haloacetic acids (5 species)	Total haloacetic acids (9species)
Trihalomethanes							
Chloroform	-0.06	-0.22	0.99	0.84	0.91	0.89	0.87
Bromodichloromethane	-	0.96	0.04	-0.29	-0.20	-0.22	-0.21
Brominated trihalomethanes	-	-	-0.11	-0.43	-0.35	-0.36	-0.34
Total Trihalomethanes	-	-	-	0.91	0.88	0.86	0.85
Haloacetic acids							
Dichloro acetic acid	-	-	-	-	0.9	0.98	0.97
Trichloro acetic acid	-	-	-	-	-	0.98	0.97
Total Haloacetic acids (5 species)	-	-	-	-	-	-	0.99
Total Haloacetic acids (9 species)	-	-	-	-	-	-	-