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RESPONSE TO SCIENTIFIC/TECHNICAL REQUEST

Trihalomethanes and Drinking Water

[redacted]

Key Messages

- In 2015, changes to Tottenham's drinking water system operations resulted in running annual average trihalomethanes (THMs) concentrations below the provincial drinking water standard and Health Canada's maximum acceptable concentration. Prior to 2015, elevated levels of THMs were detected in the Tottenham drinking water system.
- THMs are a group of chemicals including chloroform, bromoform, dibromochloromethane (DBCM), and bromodichloromethane (BDCM). The potential for THMs to cause cancer is assessed differently between Health Canada, the United States Environmental Protection Agency (US EPA) and the International Agency for Research on Cancer.
- A risk assessment was conducted based on drinking water THM concentrations before (2008 to 2015) and after (2016 to 2019) operational changes in Tottenham and US EPA toxicological reference values. Following exposure via ingestion and inhalation of average reported concentrations, the estimated risk was an additional 1-2 attributable cancers in a town the size of Tottenham (~5,000) over 70 years, assuming lifetime exposure. The current lifetime cancer risk for an individual is currently 1 in 2 for Canadians. Although estimates based on risk assessment are helpful for planning, the additional risk in this example would not be possible to detect in a community epidemiologic study or in an individual case of cancer.
- Using a recently updated US EPA approach where DBCM concentrations less than 60 µg/L are considered negligible, the estimated lifetime risk for cancer at the population level based on THM concentrations reported between 2008 and 2015 changes to 8.8 cancers per 100,000 people. In a population the size of Tottenham (approximately 5,000) this would be less than 1 cancer per lifetime.
- The risk assessment helps provide context for past community exposures. Regardless of these estimates, continued efforts are needed to reduce THM concentrations in drinking water to meet provincial standards and reduce community exposures.

Background

Elevated levels of trihalomethanes (THMs) have been detected in the Tottenham drinking water system. THMs are a group of chemicals formed as disinfection by-products and include chloroform, bromoform, dibromochloromethane (DBCM), and bromodichloromethane (BDCM). Following awareness of the elevated drinking water concentrations in 2007, the Simcoe-Muskoka Health Unit (SMDHU) has been engaged with local residents, the Town of New Tecumseth and the Ministry of the Environment, Conservation and Parks (MECP).

In 2015, changes in the operation of Tottenham's drinking water system lowered the running annual average of THMs below Health Canada's maximum acceptable concentration (MAC) of 100 µg/L. In the last few years, it has been noted that concentrations of THMs in Tottenham periodically exceed 100 µg/L; however, the running annual average of THMs continues to be below the MAC. The following response summarizes a risk assessment conducted to estimate and characterize potential drinking water exposures to THMs reported in Tottenham. The risk estimates are intended to support SMDHU's understanding of potential risks associated with drinking water concentrations reported in Tottenham.

Details of the risk calculation and supporting literature are provided as an appendix.

Methods

Risk assessment methods are used to set drinking water guidelines and standards. Risk assessments can also be used to estimate potential exposures to chemicals and predict incremental lifetime cancer risk. A risk assessment was conducted to characterize risk based on exposures to THM concentrations in drinking water reported in Tottenham between 2008 and 2019.

Routes of Exposure

The first step of a risk assessment is to determine if there is an exposure pathway of concern. The main routes of potential exposures to the four THMs (chloroform, bromoform, BDCM and DBCM) are via drinking water and inhalation of chlorinated water during swimming, showering, and bathing. Dermal absorption can also occur to a lesser extent.

The Ontario drinking water standard for total THMs is 100 µg/L. This drinking water standard is applied to a running annual average of (at least) quarterly samples. The drinking water standard was adopted from Health Canada's assessment and was derived based on chloroform toxicity.

For the risk assessment, total and individual THM water concentration data from various locations in the Tottenham drinking water system were calculated as yearly and total averages. The annual average concentrations of total THMs in Tottenham's drinking water ranged are summarized in Table 1.

Table 1: Average THM drinking water concentrations (µg/L)

Year	Bromoform	BDCM	DBCM	Chloroform	Total THMs
Average, 2008-2015	42.1	18.7	45	7.8	113.5
Average, 2016-2019	31.2	14.5	34.4	7.1	87.1
Average, all years	33.6	15.7	37.1	7.5	104.7

For the risk assessment, it was assumed that an adult consumes 2L of drinking water per day for a 70 year lifetime using 2008 to 2015 and 2016 to 2019 annual average concentrations.

Assessing Hazard

Health Canada, the United States Environmental Protection Agency (US EPA) and the International Agency for Cancer Research (IARC) reviewed toxicological and epidemiological literature to determine the health hazard of THMs. The conclusions of their reviews differ specifically in their designation of carcinogenicity with the US EPA ranking the evidence for some THMs as stronger than IARC or Health Canada and classifies all but DBCM as 'probably carcinogenic'. Overall, the differences between agencies were:

- In spite of referencing mostly the same studies, the EPA, Health Canada, and IARC disagreed on the potential for each THM to cause cancer. The US EPA were most conservative, then Health Canada followed by IARC.
- Importantly, the relative carcinogenicity was fairly consistent, meaning that the US EPA, Health Canada and IARC agreed that chloroform had the highest potential for cancer risk, and that DBCM had the least; bromoform and BDCM were in between.

A comparison of these classifications is provided in Table 2.

Note that the reported THM concentrations in Tottenham's drinking water reflect a predominantly "brominated" THM profile.

Table 2: THM carcinogenicity classification by organization

THMs	**EPA**	**IARC**	**Health Canada**
Chloroform	-Likely to be carcinogenic to humans at high exposures leading to cytotoxicity -Not likely to be carcinogenic to humans by any route of exposure under exposure conditions that do not lead to cytotoxicity	Possibly carcinogenic	Possibly carcinogenic
Bromoform	Probably carcinogenic	Unclassifiable as to carcinogenicity	Possibly carcinogenic
BDCM	Probably carcinogenic	Possibly carcinogenic	Probably carcinogenic
DBCM	Possibly carcinogenic	Unclassifiable as to carcinogenicity	Possibly carcinogenic

The US EPA drinking water and inhalation unit risks (where available) for individual THMs were used to estimate cancer risk. In the absence of inhalation unit risks, a drinking water unit risk was applied which

likely overestimates the risk via that exposure route. Therefore, the estimates of risk are best interpreted as an upper limit of what the risk might be and is likely substantially lower.

More recently, the US EPA updated their maximum contaminant level goal (MCLG) which is "the maximum level of a contaminant in drinking water at which no known or anticipated adverse effect on the health of persons would occur, allowing an adequate margin of safety". This assessment uses updated data to derive a MCLG for DBCM of 60 µg/L, a concentration above any of the annual averages for Tottenham.

Cancer Risk Estimates

Using the Tottenham THM concentrations for 2008-2015, the total population risk for cancer for all four THMs, is 29.8 attributable cancers per 100,000 individuals, and for 2016-2019, 22.9 attributable cancers per 100,000 individuals. For a water system serving approximately 5,000 people this would mean an additional 1-2 attributable cancers over 70 years assuming lifetime exposure. This increase in cancer risk would not appreciably change the lifetime cancer risk for an individual (which is currently 1 in 2 for Canadians), nor would it be large enough to be detectable in an epidemiologic study at the community level.

Using the updated US EPA approach, the associated risk per 100,000 due to the DBCM alone is negligible because all the measured DBCM concentrations in Tottenham were below the level where any additional risk of cancer would be expected (at 60µg/L). If we use these updated US EPA MCLG estimates, the lifetime risk for cancer at the population level using the higher 7 years of THM concentrations (2008-2015) is 8.8 cancers per 100,000 people. In a population the size of Tottenham (approximately 5,000) this would be less than 1 cancer in the town in a 70-year period, assuming residents were exposed for their lifetimes.

In Ontario, 1 in a million (1 in 1,000,000) is considered 'negligible' or 'acceptable'. This upper bound signifies an unlikely probability of a chemical exposure resulting in cancer in excess of background cancer risk. The risk assessment helps provide context for past community exposures. Regardless of these estimates, continued efforts are needed to reduce THM concentrations in drinking water to meet provincial standards and reduce community exposures.

LIMITATIONS AND UNCERTAINTY

When conducting a risk assessment, a number of assumptions are made and require acknowledgment. The cancer risk estimates should be interpreted with caution as several assumptions overestimate exposures and risk.

- Applying US EPA unit risks for individual THMs to the Tottenham data (2008-2019) for the four individual THMs differs from Health Canada's approach.

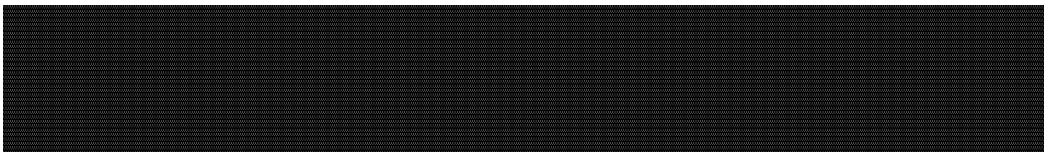
- The reported THM concentrations in Tottenham's drinking water reflect a predominantly "brominated" THM profile. All three agencies cited above generally deem the brominated THMs (particularly DBCM) less carcinogenic than chlorinated THMs. The main contributor to the overall estimate is from DBCM concentrations, the THM for which there is weakest evidence of carcinogenicity.

- The US EPA's drinking water unit risk adopted in this assessment is almost 30 years old. The EPA assessment associates a 40 µg/L concentration of DBCM with a 1 in 10,000 cancer risk over a 70 year lifetime (as we include inhalational exposure in our scenario our estimate exceeds the EPA estimate). The latest US EPA MCLG for the DBCM risk calculation assumes that there is no increased risk for cancer at DBCM concentrations below 60µg/L. The contribution of DBCM to the risk estimate in this approach would be zero. Note that DBCM was the highest contributor to the risk estimate, making up approximately 72% of the total risk estimate.

- Where the US EPA did not provide an inhalation unit risk for THMs (which was the case for BDCM), the risk from water consumption was doubled to account for potential exposures during showering, bathing, swimming, etc. This is likely an overestimate of risk as typically, a cancer risk would often not be calculated in the absence of sufficient toxicological and epidemiological data. Note that this would also apply to BDCM, the next highest contributor to the overall risk estimate, again emphasizing that the final estimates are calculated based on assumptions that tend to overestimate risk.

Disclaimer

Appendix: Cancer Risk Estimates for THM Exposures Using Tottenham Water Data (2008-2019)



Purpose:

To provide a scoping review of the recent scientific literature assessing the cancer risk associated with exposure to THMs, particularly brominated THMs. With this context, a cancer risk assessment, applying US EPA cancer unit risks for individual THMs to the Tottenham data (2008-2019) for the four individual THMs is provided to assist the local public health unit in communication with the public.

Methods:

A scoping review of the literature was performed. Using MEDLINE (entire duration of the database), the terms THM or trihalomethanes or "water disinfection by products" and Cancer, yielded 81 results, limited to meta-analysis or "review" or "systematic review," which yielded 9 articles, of which 4 were directly relevant. A Google Scholar search (using search terms “THMs,” “trihalomethanes,” “bromodichloromethane,” “BDCM,” and “cancer”) was also performed and relevant articles from the first 3 pages, as well as relevant citations found therein, were evaluated. Standard toxicologic databases (Health Canada, IRIS, EPA, ATSDR, and IARC) were also consulted.

Background/Summary of Relevant Literature:

Of the four trihalomethanes (THMs) found as disinfection by-products from chlorination of drinking water, chloroform is usually predominant.[1] Bromoform is usually found in lowest concentrations, with bromodichloromethane (BDCM) and dibromochloromethane (DBCM) somewhat higher.[1] Given that all 4 THMs are volatile at room temperature, the main routes of exposure are via ingestion and inhalation of chlorinated water during swimming, showering, and bathing.[2] Dermal absorption can also occur to a lesser extent.[2]

A number of relevant recent studies were identified to address the potential for carcinogenicity of THMs, with a few specifically looking at brominated THMs.

A cancer risk assessment comparing THM species in drinking water was performed in 2007, using data on THM levels in Taiwanese drinking water and US EPA information on toxicity and cancer risk.[3] Using the results of the US EPA cancer risk assessment available at that time, the authors found that chloroform was the predominant species implicated in increased cancer risk, with the brominated THMs (including BDCM) contributing less to the overall cancer risk; they suggest that in cases where brominated THMs are the dominant species, cancer risk may be lower than presumed.[3]

Recent epidemiological studies on THMs and cancer risk have produced mixed results:

- A 2018 case-control study in Spain looking at breast cancer risk and THM exposure did not find an association between elevated brominated (0.3-126µg/L, median 9.7µg/L) or total THMs (0.8-145.7µg/L, median 30.8µg/L) levels and breast cancer risk.[4] In the highest quartile of exposure to chloroform (>24 µg/L) was there an increase in associated risk (OR = 1.47, 95%CI =1.05, 2.06).[4]
- An ecological study looking at overall trends in bladder cancer diagnosis and THM levels in 8 countries over >45 years did not find evidence to support an association.[5]
- A pooled meta-analysis of European case-control studies looking at water disinfection by-products (including BDCM) found an increased risk in men only (OR 1.47) at total THM levels of >50µg/L after 30 years of exposure.[6]
- A case-control study in the US looking at bladder cancer in 1,213 cases compared to 1,418 controls used interviews to estimate exposure to THMs (including brominated species specifically), combined with data on THM water concentrations, to estimate exposure.[7] A modest increase was seen in the highest group of reported water intake only (OR = 1.98 for brominated and 1.78 for chlorinated THMs), but such an association was not seen in highest exposure concentrations (>34 µg/L), or in swimmers.[7]
- An attributable burden of bladder cancer study involving 28 European countries collected data on THM levels (median 10µg/L, range 0.01-771µg/L), and combined this with the exposure-response function used in the earlier cited European study[6] to estimate the THM-attributable fraction of bladder cancer of 4.9%, with Spain accounting for the largest estimated number (22%).[8]
- A systematic review of THMs and potential for carcinogenicity evaluated bench-level experiments (predominantly *in vivo* and *in vitro* studies) and found wide heterogeneity in the experiments (both exposures and outcomes) demonstrating cytotoxic, mutagenic and genotoxic effects, and calls for more research to reduce uncertainty regarding the carcinogenic mechanisms of THMs.[9] Given the heterogeneity seen and the nature of bench-level studies, no conclusions regarding health risk to humans can be drawn on the basis of these findings.

The inconsistencies seen in the literature cited above are reflected in the disagreement between agencies internationally. For example, BDCM has been classified by Health Canada as "probably carcinogenic" based on animal studies.[2] The International Agency for Research on Cancer (IARC) classified BDCM as "possibly carcinogenic", with inadequate evidence for cancer in humans but sufficient evidence in animal studies.[10] This is based on studies on rats and mice that found an increased incidence of tumors in the liver and kidneys.[10] The same designation has been given to chloroform.[11] The other two (DBCM and bromoform) have been classified by IARC as Group 3 ("not classifiable") based on inadequate evidence in human studies and limited evidence in animal studies.[12] The Unites States Environmental Protection Agency (EPA) classify all but DBCM as 'probably carcinogenic'.[13-16] A comparison of these cancer classifications is given in Table 1:

Table 3: THM carcinogenicity classification by organization

	EPA[13-16]	IARC[12]	Health Canada[2]

Chloroform	-Likely to be carcinogenic to humans at high exposures leading to cytotoxicity[14] -Not likely to be carcinogenic to humans by any route of exposure under exposure conditions that do not lead to cytotoxicity[14]	Possibly carcinogenic	Possibly carcinogenic
Bromoform	Probably carcinogenic[13]	Unclassifiable as to carcinogenicity	Possibly carcinogenic
BDCM	Probably carcinogenic[15]	Possibly carcinogenic	Probably carcinogenic
DBCM	Possibly carcinogenic[16]	Unclassifiable as to carcinogenicity	Possibly carcinogenic

The EPA's assessment of BDCM was primarily based on an animal study which noted increased incidence of colon cancer in rats and kidney cancer in mice.[15] The lowest dose at which the earliest effect was observed (kidney cancer in male mice) was 50mg/kg/day of BDCM in corn oil for 5 days a week, for 102 weeks.[17] The authors note that this outcome should be interpreted with caution given that corn oil may increase the carcinogenicity of BDCM (as an inducer).[15] This study was the basis for the EPA's quantitative cancer risk assessment for oral exposure. Using their standard assumptions of daily exposure over a lifetime the specified lifetime risk levels of 1 in 10,000 to 1 in 1,000,000 individuals correspond to BDCM concentrations in water of 0.6 µg/L – 60µg/L.[15] For policy purposes, the EPA has used the 1 in 10,000 to 1 in 1,000,000 lifetime risk of cancer as a target risk range in their risk management decisions.

The Health Canada Drinking Water Guidelines describe BDCM as "probably carcinogenic to humans."[2] This was based on the same NTP rat study cited by the EPA; however, they focused on the outcome of colon cancer in rats (rather than kidney cancer in mice as the EPA did), with the rationale that some human epidemiological studies noted trends towards increased colon cancer risk and chlorinated drinking water use.[2] They too acknowledge that the corn oil may have affected the carcinogenic potential of the BDCM with potential for subsequent overestimation of risk.[2]

In the May 2006 assessment of THMs, Health Canada set a drinking water guideline of 16 µg/L for BDCM which in their assessment, assuming daily exposure over a lifetime, corresponded to a lifetime cancer risk between 3.3 in 1,000,000, to 1 in 100,000.[2] This is described by Health Canada as being within the range that is 'essentially negligible.'[18] Subsequent to that assessment, a study on cancer in rats exposed to BDCM by the US National Toxicology Program was published.[19] Water intake was noted to be lower in the exposed group compared to the control group, assumed due to decreased palatability of the increased dose of BDCM.[19] At all doses, including the highest of 700mg/L (equivalent to 36mg/kg/bw/day) for 2 years, no increase in cancer was seen.[19]

In 2009, after this study and other new scientific research on the health effects of THMs including BDCM, Health Canada rescinded the separate guideline for BDCM.[18] In the 2009 revision to the guideline, 100µg/L for total THMs is described as being protective of health effects from all THMs, including BDCM.[2]

Cancer Risk Assessment:

Under the approach currently used by Health Canada a running annual average of quarterly samples less than 100 µg/L is considered protective against adverse effects from THMs.[2] This is similar to the US EPA standard for drinking water which also for total THMs but specifies a limit of 80 µg/L.[20]

While the EPA only regulates total THMs in drinking water, their Integrated Risk Information System (IRIS) contains the results of the EPA's quantitative cancer risk assessment of the potency of the 4 THMs. We have used this framework along with the results of THM testing in the Tottenham water system to perform an assessment of the cancer risk from the 4 individual THMs using the EPA's cancer risk assessment which as we have outlined above differs from the assessment of IARC and Health Canada.

The results of this assessment should be interpreted with caution as it assumes all of the THMs are carcinogenic, which as outlined above is not supported by classifications in Table 1. In addition, the estimates assume daily exposure over a lifetime at the concentrations noted, which may over- or underestimate actual exposure.

For the purposes of this assessment, total and individual THM water concentration data from various locations in the Tottenham drinking water system, which were provided to PHO, were compiled into yearly and total averages, as can be seen in Table 2 below. The provided data was noted to demonstrate small discrepancies between "THM (total)" and the actual sum of the four THMs, with differences between -2 and 2 that could be accounted for from rounding of values; there were three exceptions (Oct. 14, 2014, Jan. 19, 2015, and Nov. 12, 2018) where the reported total THM was significantly greater than the actual sum of the four THMs measured. As such, for our calculations we used the raw data only of the four THMs to calculate averages for each on a yearly basis, and these were summed for yearly total THM averages (see Table 2).

Table 4: Average THM drinking water concentrations, in µg/L

Year	Bromoform	BDCM	DBCM	Chloroform	Total THMs
2008	45.2	18.3	46.7	7.2	117.4
2009	44.7	19	50.6	7.7	122
2010	44.3	18.5	47	7.3	117.1
2011	35.6	18.9	44.6	8.3	107.4
2012	37.7	24.3	47.1	8.2	117.3
2013	44.8	17.4	44.1	7.7	114
2014	43.4	17.8	38.3	8.2	107.7
2015	41	15	41.3	7.5	104.8
Average, 2008-2015	**42.1**	**18.7**	**45**	**7.8**	**113.5**
2016	35.4	14.9	36.8	7.2	94.3
2017	32.2	15.3	36.8	7.7	92
2018	31.3	13.4	32.6	6	83.3
2019	25.7	14.2	31.5	7.4	78.8
Average, 2016-2019	**31.2**	**14.5**	**34.4**	**7.1**	**87.1**
Average, all years	**33.6**	**15.7**	**37.1**	**7.5**	**104.7**

A summary of the variables used is provided in Tables 3a and 3b below. The EPA drinking water unit risks, and where available inhalation unit risks, have been used which assume lifetime exposure. Where inhalation unit risks were not available, we doubled the drinking water unit risk to account for inhalation of the THM while showering or bathing. This approach is unconventional will result in an overestimate of risk. Our use of the EPA inhalation unit risk in this scenario is not in keeping with their current assessment of chloroform's carcinogenicity and will again serve to inflate the risk estimate.

Table 5a: Summary of variables and risk estimates for cancer assuming lifetime exposure at Tottenham water data concentrations from 2008-2015

THM	Avg Conc, µg/L	EPA Drinking Water Unit Risk per µg/L	EPA Inhalation Unit Risk per µg/m^3	Tottenham ingestion cancer risk, per 100,000	Tottenham inhalation cancer risk, per 100,000	**Tottenham overall risk estimate, per 100,000**
Bromoform	42.1	$2.3x10^{-7}$	$1.1x10^{-6}$	0.97	0.1	**1.1**
BDCM	18.7	1.8×10^{-6}	N/A – use the DWUR risk	3.4	3.4	**6.8**
DBCM	45	2.4×10^{-6}	N/A – use the DWUR risk	10.8	10.8	**21.6**
Chloroform	7.8	N/A (RfD used instead)	2.3×10^{-5}	0	0.3	**0.3**
TTHM	113.5	N/A	N/A	N/A	N/A	**29.8**

Table 6b: Summary of variables and risk estimates for cancer assuming lifetime exposure at Tottenham water data concentrations from 2016-2019

THM	Avg Conc, µg/L	EPA Drinking Water Unit Risk per µg/L	EPA Inhalation Unit Risk per µg/m^3	Tottenham ingestion cancer risk, per 100,000	Tottenham inhalation cancer risk, per 100,000	**Tottenham overall risk estimate, per 100,000**
Bromoform	31.2	$2.3x10^{-7}$	$1.1x10^{-6}$	0.72	0.08	**0.8**
BDCM	14.5	1.8×10^{-6}	N/A – use the DWUR risk	2.6	2.6	**5.2**
DBCM	34.4	2.4×10^{-6}	N/A – use the DWUR risk	8.3	8.3	**16.6**
Chloroform	7.1	N/A (RfD used instead)	2.3×10^{-5}	0	0.3	**0.3**
TTHM	87.1	N/A	N/A	N/A	N/A	**22.9**

a) Bromoform: For bromoform, the EPA drinking water unit risk (DWUR) is $2.3x10^{-7}$ per µg/L (assuming a 70 kg adult, consuming 2L of water daily for a lifetime).[13] The DWUR is interpreted that for each µg/L of bromoform in the drinking water, 2.3 cancers (of any kind, noting the basis is from intestinal neoplasms in female rats) are expected per 10 million individuals, if exposed at

these levels daily for a lifetime. With the Tottenham average bromoform concentration from 2008-2015 of 42.1µg/L, this confers a population level risk of $96.8x10^{-7}$, or 9.7 attributable cancers per 1,000,000 individuals over a lifetime of exposure. With the Tottenham average bromoform concentration from 2016-2019 of 31.2µg/L, this results in a population level risk of $71.8x10^{-7}$, or 7.2 attributable cancers per 1,000,000 individuals over a lifetime of such exposure.

The additional cancer risk for inhalational exposure is calculated using the EPAs inhalational unit risk (IUR) of $1.1x10^{-6}$ per µg/m^3.[13] One study measured average bromoform air concentrations during showering at 2.69µg/m^3 from tap water containing 1µg/L average concentrations, and these levels quickly declined post-shower.[21] Applying this ratio of 1 to 2.69 (water to air bromoform concentration) to the Tottenham 2008-2015 average concentration of 42.1µg/L would result in breathing zone air concentrations of approximately 113.3µg/m^3 bromoform during showering. Assuming a daily 10 minute shower, a 24-hour time-weighted average for inhalational exposure to bromoform from these concentrations would equal 0.94µg/m^3. Applying this to the EPA IUR this confers a population level risk of $1.04x10^{-6}$, or approximately 1 attributable cancer per 1,000,000 individuals. Applying this to the 2016-2019 concentration of 31.2µg/L would result in breathing zone air concentrations of approximately 83.9µg/m^3 bromoform during showering. Assuming a daily 10 minute shower, a 24-hour time-weighted average for inhalational exposure to bromoform from these concentrations would equal 0.7µg/m^3. Applying this to the EPA IUR this confers a population level risk of $0.77x10^{-6}$, or 0.8 attributable cancers per 1,000,000 individuals.

Summing the two risk estimates for bromoform exposures from 2008-2015 gives a value of 10.7 attributable cancers per 1,000,000 (1.1 per 100,000) exposed individuals over a lifetime of such exposure (see Table 3a). Summing the two risk estimates for bromoform exposures from 2016-2019 gives a value of 7.9 attributable cancers per 1,000,000 (0.8 per 100,000) exposed individuals over a lifetime of such exposure (see Table 3b).

b) For BDCM, the EPA drinking water unit risk is 1.8×10^{-6} per µg/L based on kidney cancer in male mice.[15] With the Tottenham average BDCM concentration from 2008-2015 of 18.7µg/L, this results in a population level risk of $33.7x10^{-6}$, or 3.4 cancers per 100,000 individuals. With the Tottenham average BDCM concentration from 2016-2019 of 14.5µg/L, this results in a population level risk of $26.1x10^{-6}$, or 2.6 cancers per 100,000 individuals.

   The EPA does not have an inhalational unit risk for BDCM, so for our purposes in order to account for inhalational exposure, we somewhat arbitrarily elected to assume the inhalation risk was the same as that estimated for ingestion. Comparison with the ratio of the ingestion risk to inhalation risk for bromoform shows that this procedure may result in a considerable overestimation of the risk. This results in a summary risk for BDCM from 2008-2015 of 6.8 cancers per 100,000 individuals over a lifetime of such exposure, and for 2016-2019, 5.2 cancers per 100,000 individuals over a lifetime of such exposure (see Tables 3a and 3b).

c) For DBCM, the EPA drinking water unit risk is 2.4×10^{-6} per µg/L, based on liver cancer in female mice.[16] With the Tottenham average DBCM concentration from 2008-2015 of 45µg/L, this results in a population level risk of 108×10^{-6}, or 10.8 cancers per 100,000 individuals. With the Tottenham average DBCM concentration from 2016-2019 of 34.4µg/L, this results in a

population level risk of 82.6 x 10^{-6}, or 8.3 cancers per 100,000 individuals. The EPA does not have an inhalational unit risk for DBCM so we made the same assumption as for BDCM above. The same caveat made above for BDCM regarding our use of this approach applies for DBCM as well. This results in an estimate for DBCM from 2008-2015 of 21.6 cancers per 100,000 individuals over a lifetime of such exposure, and from 2016-2019 of 16.6 cancers per 100,000 individuals over a lifetime of such exposure (see Tables 3a and 3b).

d) For chloroform, the EPA does not have a drinking water unit risk but uses a reference dose of 10µg/kg/day.[14] The RfD is the dose below which, with a lifetime of exposure, no adverse effect (including cancer) is expected. In a 70kg adult consuming 2L of water at the Tottenham average chloroform concentration from 2008-2015 of 7.8µg/L, 15.6ug total would be consumed per day, a dose of 0.22µg/kg/day, which is 45 times lower than the RfD, and according to the EPA, "can be considered protective against cancer risk."[14] Performing the same calculation to the average chloroform concentration from 2016-2019 of 7.1µg/L gives a dose of 0.2µg/kg/day, or 50 times lower than the RfD.

   The cancer risk for inhalational exposure for chloroform is calculated using the EPA's inhalational unit risk of 2.3 x 10^{-5} per µg/m^3 based on liver cancer in female mice.[14] In one study measuring normalized air shower concentrations, chloroform concentrations in the air were measured at 1.91 µg/m^3 per µg/L in the tap water.[22] Applying this to the 2008-2015 Tottenham data, in a scenario of a daily 10-minute unventilated shower with baseline tap chloroform concentrations averaging 7.8µg/L, corresponding air concentrations during the shower would be expected to be approximately 14.9µg/m^3. As a 24 hour average this is 0.12µg/m^3. Applying the EPA inhalational unit risk, this confers a population level risk of 0.3 x 10^{-5}, or 0.3 cancers per 100,000 individuals. Applying this to the 2016-2019 data, baseline tap chloroform concentrations of 7.1µg/L would result in shower air concentrations of 13.6 µg/m^3, which would average 0.11µg/m^3 over 24 hours, conferring a risk of 0.26x10^{-5} or 0.3 cancers per 100,000 individuals. Strictly speaking our use of the inhalational unit risk to estimate a cancer risk in this scenario is contrary to EPA guidance as chloroform is not likely to be carcinogenic via any route of exposure at low doses. If one adds the inhalational exposure to the exposure via ingestion one would still be well below the RfD. However, consistent with our other assumptions we erred on the side of overestimating the risk.

Summary/Conclusion:

A review of the current and past literature demonstrates conflicting assessments between various organizations regarding the carcinogenicity of THMs. In the case of the US EPA, their initial assessment of chloroform as 'probably carcinogenic' changed when additional scientific information became available. Their current assessment of chloroform as likely to be carcinogenic under exposure conditions leading to cytotoxicity and not likely to be carcinogenic in the absence of cytotoxic effects takes account of the variety of mechanisms by which cancer can occur and that in some cases there is a threshold for these effects.

The US EPA has rated the evidence of carcinogenicity for some THMs as stronger than have IARC or Health Canada. We applied the EPA unit risks for individual THMs to the THM results for Tottenham water. We made assumptions about exposure that result in higher estimates of risk than conventional risk assessments that consider only consumption of the water for drinking and cooking. Therefore our

estimates of risk are best interpreted as an upper limit of what the risk might be and that it is likely substantially lower.

Using the Tottenham THM concentrations for 2008-2015, the total population risk for cancer for all four THMs, is 29.8 attributable cancers per 100,000 individuals, and for 2016-2019, 22.9 attributable cancers per 100,000 individuals. For a water system serving approximately 5,000 people[23] this would mean 1.5 attributable cancers over 70 years assuming lifetime exposure. This increase in cancer risk would not appreciably change the lifetime cancer risk for an individual which is currently 1 in 2 for Canadians, [24] nor would it be large enough to be detectable in an epidemiologic study at the community level.

Our estimates should be interpreted with caution as we made several assumptions that will inflate the estimated risks. The main contributor to the overall estimate is from DBCM concentrations, the THM for which there is weakest evidence of carcinogenicity. The DWUR we retrieved from the IRIS database is almost 30 years old. The EPA assessment associates a 40 µg/L concentration of DBCM with a 1 in 10,000 cancer risk over a 70 year lifetime (as we include inhalational exposure in our scenario our estimate exceeds the EPA estimate). It is not likely this represents the EPA's current view. A review of the US EPA maximum contaminant level goals (MCLG) which were set more recently than the unit risk provides a further indication that our assessment of the DBCM risk is unrealistically high. Although the MCLGs are not legally enforceable, according to the EPA, they represent *the maximum level of a contaminant in drinking water at which no known or anticipated adverse effect on the health of persons would occur, allowing an adequate margin of safety*. For DBCM, the EPA MCLG is 60 µg/L, a concentration above any of the annual averages for Tottenham.[20] In contrast, the EPA MCLGs for bromoform and BDCM are 0 which is standard practice for non-threshold carcinogens.[20]

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