N-Nitrosamines and Halogenated Disinfection Byproducts in U.S. Full Advanced Treatment Trains for Potable Reuse

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Abstract

Water utilities are increasingly considering indirect and direct potable reuse of municipal wastewater effluents. Disinfection byproducts (DBPs), particularly *N*-nitrosamines, are key contaminants of potential health concern for potable reuse. This study quantified the concentrations of *N*-nitrosamines and a suite of regulated and unregulated halogenated DBPs across five U.S. potable reuse Full Advanced Treatment trains incorporating microfiltration, reverse osmosis, and UV-based advanced oxidation. Low $\mu\text{g/L}$ concentrations of trihalomethanes, haloacetic acids, dichloroacetonitrile, and dichloroacetamide were detected in the secondary or tertiary wastewater effluents serving as influents to potable reuse treatment trains, while the concentrations of *N*-nitrosamines were more variable (e.g., <2-324 ng/L for *N*-nitrosodimethylamine). Ozonation promoted the formation of *N*-nitrosamines, haloacetaldehydes, and haloacetamides, but biological activated carbon effectively reduced concentrations of these DBPs. Application of chloramines upstream of microfiltration for biofouling control increased DBP concentrations to their highest levels observed along the treatment trains. Reverse osmosis rejected DBPs to varying degrees, ranging from low for some (e.g., *N*-nitrosamines, trihalomethanes, and haloacetonitriles) to high for other DBPs. UV-based advanced oxidation eliminated *N*-nitrosamines, but only partially removed halogenated DBPs. Chloramination of the treatment train product waters under simulated distribution system conditions formed additional DBPs, with concentrations often equaling or exceeding those in the treatment train influents. Overall, the concentrations of DBPs were fairly consistent within

individual treatment trains for sampling campaigns separated by months and across different treatment trains for the same sampling time window. Weighting DBP concentrations by their toxic potencies highlighted the potential significance of haloacetonitriles, which were not effectively removed by reverse osmosis and advanced oxidation, to the DBP-associated toxicity in potable reuse waters.

Key Words

Potable reuse, *N*-Nitrosamines, Halogenated disinfection byproducts, Advanced treatment trains

1. Introduction

Expanding water supplies beyond traditional sources will likely become a necessity in many water-stressed regions worldwide (Jiménez and Asano, 2008; Fatta-Kassinos et al., 2016). In the wake of recent droughts in the United States, water utilities are increasingly considering highly-treated municipal wastewater effluents as a local, reliable supply of potable water (National Research Council, 2012; Gerrity et al., 2013). To ensure adequate removal of chemical and microbiological contaminants, conventional wastewater effluents (e.g., secondary effluents) are further purified by multi-barrier advanced treatment trains. Existing potable reuse Full Advanced Treatment (FAT) trains typically consist of microfiltration (MF) and reverse osmosis (RO) as broad-screen physical removal processes, followed by a UV/hydrogen peroxide (H₂O₂) advanced oxidation process (AOP), a broad-screen chemical oxidation process that produces hydroxyl radicals to destroy poorly-rejected contaminants. The product water generally is routed either to reservoirs, aquifers, or other environmental buffers (i.e., indirect potable reuse), but there is increasing interest in blending directly into drinking water treatment plant influents or distribution systems (i.e., direct potable reuse) (Gerrity et al., 2013).

The National Research Council has indicated that *N*-nitrosamines, particularly *N*-nitrosodimethylamine (NDMA), and halogenated disinfection byproducts (DBPs) are a key

concern for potable reuse treatment trains, because their concentrations exhibit the lowest margins of safety relative to health risk-based action levels across different reuse scenarios (National Research Council, 2012). The U.S. Environmental Protection Agency's (USEPA's) Integrated Risk Information System (IRIS) indicates that NDMA is a probable human carcinogen with a 0.7 ng/L concentration in drinking water associated with a 10^{-6} lifetime excess cancer risk (US EPA, 1993). NDMA itself (Sedlak et al., 2005) and precursors for its formation during chloramination (Sedlak et al., 2005; Shah and Mitch, 2012) and ozonation (Gerrity et al., 2013; Dai et al., 2015) are largely associated with wastewater effluents. Apart from NDMA, an array of unregulated halogenated DBPs (e.g., haloacetonitriles, haloacetamides, haloacetaldehydes, and halonitromethanes) exhibit cytotoxicity or genotoxicity orders of magnitude higher than regulated trihalomethanes and haloacetic acids (Richardson et al., 2007; Plewa and Wagner, 2011). Along with halogenated DBPs, NDMA in particular has become a major driver for the design and operation of potable reuse treatment trains (Gerrity et al., 2013). For instance, many UV systems were originally installed to remove NDMA from the RO permeate but subsequently converted to UV/H₂O₂ AOP systems to control other contaminants (Mitch et al., 2013).

Previous studies have measured the concentrations of either *N*-nitrosamines or halogenated DBPs across potable reuse treatment trains, but their relative importance is difficult to gauge as they have not been evaluated simultaneously within the same study. Information regarding *N*-nitrosamines derives mainly from U.S. treatment trains. Plumlee *et al.* (2008) determined that ~70% of NDMA was removed across a full-scale treatment train. Similarly, Gerrity *et al.* (2015) found that NDMA, along with *N*-nitrosomorpholine (NMOR), remained the most prevalent of six *N*-nitrosamines at two full-scale treatment trains, but both were effectively removed by the combined RO/AOP treatment. Sgroi *et al.* (2015) observed that NDMA re-formed after

UV/H₂O₂ AOP within a full-scale treatment train, presumably due to reactions of residual precursors with chloramines. These studies largely focused on NDMA, with NMOR concentrations reported for only one treatment train. Recently, we showed that NDMA, NMOR and *N*-nitrosodiethanolamine were among the most prevalent of total *N*-nitrosamines at three full-scale and a pilot-scale treatment train, but that the combined RO/AOP treatment achieved significant removal of these and total *N*-nitrosamines (Dai et al., 2015). Information regarding halogenated DBPs derives mainly from Australian treatment trains. Farré *et al.* (2012) showed that the relative abundances of five halogenated DBP classes at a full-scale treatment train followed the trend of trihalomethanes > haloacetonitriles > haloketones > iodinated trihalomethanes > trichloronitromethane, but no specific DBP concentrations were reported. Linge *et al.* (2013) showed that the concentrations of halogenated DBPs followed the trend of haloacetic acids > trihalomethanes > haloketones > haloacetonitriles > haloacetaldehydes across MF and RO at a full-scale and a pilot-scale treatment trains. To date, assessment of exposures to DBPs associated with potable reuse is hampered by the lack of simultaneous evaluations of a full suite of DBPs within and across treatment trains.

The main goal of the current study was to quantitatively compare the concentrations of *N*-nitrosamines to halogenated DBPs within representative U.S. potable reuse treatment trains. A second goal was to evaluate the extent to which DBP concentrations are common across different treatment trains. While the loads of industrial contaminants of concern to potable reuse (e.g., solvents) are anticipated to vary widely depending on specific industries in the sewershed, it is possible that the loads of DBPs are somewhat consistent due to DBP formation from organic matter precursors deriving from domestic sewage (Zeng and Mitch, 2015). A third goal was to provide a preliminary evaluation of the relative importance of different DBP classes with respect

to the DBP-associated toxicity of potable reuse waters. Although the contribution of a DBP species to the toxicity of a water is driven by both the innate toxicity of the DBP and its concentration, previous research has addressed these issues separately with only a few exceptions (Farré et al., 2013; Neale et al., 2012). While toxicological assays indicate that the toxicity of *N*-nitrosamines and unregulated halogenated DBPs are orders of magnitude higher than that of regulated trihalomethanes and haloacetic acids, they tend to occur at lower concentrations, such that their contribution to toxicity is unclear. Unfortunately, assays that can directly quantify the contribution of different DBP classes to the DBP-associated toxicity of disinfected waters are not available, due to the lack of concentration protocols capable of fully capturing the volatile halogenated DBPs that are the focus of current research. To evaluate the significance of DBPs with regard to their potential contribution to toxicity, we divided the concentrations of DBPs by their toxicity index values to construct theoretical toxicity profiles along the treatment trains. While toxicological assays are needed, particularly to account for mixture effects, these estimates can highlight DBP classes for future toxicological research.

2. Materials and Methods

Chemicals and reagents used are described in the supplementary material (Text S1).

2.1. Water sample collection

Water samples were collected between November 2014 and June 2015 from five potable reuse treatment trains in the U.S. Treatment train A treats secondary wastewater effluent with MF (with upstream chloramine addition), RO, and UV/H₂O₂ AOP. Treatment train B treats secondary effluent with ozonation (O₃), MF (with upstream chloramine addition), RO, and UV/H₂O₂ AOP. Treatment train C treats tertiary effluent with O₃, biological activated carbon (BAC), MF (with upstream chloramine addition), RO, and UV/H₂O₂ AOP. Treatment train D treats secondary effluent with MF (with upstream chloramine addition), RO, and UV/H₂O₂ AOP.

Treatment train E treats secondary effluent with MF (with upstream chloramine addition), RO, and UV alone. The secondary or tertiary wastewater effluents serving as influents to treatment trains B-E were impacted by industrial discharges. Treatment train A was sampled once. Treatment trains B, C, and D were sampled twice, separated by several months, while treatment train E was sampled twice on two consecutive days.

Grab samples were taken at multiple locations along each treatment train, including secondary or tertiary effluent, O₃ effluent (for treatment trains B and C), BAC effluent (for treatment train C only), MF filtrate, RO permeate, and UV-based AOP effluent. At each location, samples were collected into high-density polyethylene jars (for *N*-nitrosamine analysis) and headspace-free glass vials (for halogenated DBP analysis) and transported on ice to Stanford University as soon as practicably possible (within 24 h or less). Water quality data for each treatment train are summarized in the supplementary material (see Tables S1-S5). L-Ascorbic acid (~31 mg/L) was used to quench residual chloramines onsite and 1 N sulfuric acid was used to acidify samples for analyte preservation (Lee et al., 2007). The UV-based AOP effluent samples were treated under simulated distribution system (SDS) conditions (Koch et al., 1991) to evaluate levels of residual DBP precursors potentially entering distribution systems for potential future direct potable reuse scenarios; the SDS assay involved adjusting the pH to 8 with borate buffer and application of 2.5 mgCl₂/L preformed monochloramine for 3 days. At full-scale, treatment train E employed UV without advanced oxidation; RO permeate samples of treatment train E were also treated in the laboratory to evaluate levels of DBPs formed under alternative AOP treatment conditions. Samples were treated with 3 mg/L H₂O₂ or 1 mg/L free chlorine (Cl₂) and exposed to UV irradiation produced at a fixed germicidal fluence of 750 mJ/cm² in a bench-scale semi-collimated beam UV apparatus (equipped with four 12 W LP General Electric low pressure

mercury germicidal bulbs emitting predominantly at 254 nm). The procedures for quantifying UV germicidal fluence were described previously (Jin et al., 2006; Shah et al., 2011).

2.2. Analysis of N-nitrosamines and halogenated DBPs

Duplicate samples, along with laboratory and field blanks, were extracted for DBP analysis. Nine *N*-nitrosamines (NAs), including NDMA, NMOR, *N*-nitrosomethylethylamine (NMEA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodi-*n*-propylamine (NDPA), *N*-nitrosodi-*n*-butylamine (NDBA), *N*-nitrosopyrrolidine (NPYR), *N*-nitrosopiperidine (NPIP), and *N*-nitrosodiphenylamine (NDPhA), were extracted following a modified USEPA Method 521 (Dai et al., 2015). Thirty-five halogenated DBPs, including four trihalomethanes (THMs: chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM), bromoform (TBM)), six iodinated trihalomethanes (I-THMs: iodoform (TIM), bromodiiodomethane (BDIM), bromochloriodomethane (BCIM), chlorodiiodomethane (CDIM), dibromiodomethane (DBIM), and dichloriodomethane (DCIM)), ten haloacetic acids (HAAs: bromoacetic acid (BAA), bromochloroacetic acid (BCAA), bromodichloroacetic acid (BDCAA), chloroacetic acid (CAA), dibromochloroacetic acid (DBCAA), dibromoacetic acid (DBAA), dichloroacetic acid (DCAA), tribromoacetic acid (TBAA), trichloroacetic acid (TCAA), and iodoacetic acid (IAA)), four haloacetonitriles (HANs: bromochloroacetonitrile (BCAN), dibromoacetonitrile (DBAN), dichloroacetonitrile (DCAN), and trichloroacetonitrile (TCAN)), four haloacetaldehydes (HALs: trichloroacetaldehyde (chloral hydrate; TCAL), bromodichloroacetaldehyde (BDCAL), dibromochloroacetaldehyde (DBCAL), and tribromoacetaldehyde (TBAL)), four haloacetamides (HAMs: dichloroacetamide (DCAM), dibromoacetamide (DBAM), bromochloroacetamide (BCAM), and trichloroacetamide (TCAM)), two haloketones (HKs: 1,1-dichloropropanone (1,1-DCP) and 1,1,1-trichloropropanone (1,1,1-TCP)), and one halonitromethane (HNM:

trichloronitromethane (chloropicrin; TCNM)), were extracted following modified USEPA Methods 551.1 and 552.3 (Lee et al., 2007; Zeng and Arnold, 2014). Note that brominated halonitromethanes degraded in the presence of L-ascorbic acid and were not analyzed in this study (Lee et al., 2007). The final DBP extracts were analyzed by gas chromatography-mass spectrometry (GC-MS). Further details on DBP extraction protocols, GC-MS instrument parameters, and method reporting limits are provided in the supplementary material (Tables S6 and S7). Further details on DBP extraction protocols, GC-MS instrument parameters, and method reporting limits have been described elsewhere (Zeng and Mitch, 2016).

For the 4 regulated THMs (THM4), the bromine incorporation factor (BIF) was calculated according to equation 1, where the concentrations are on a molar basis.

$$\text{BIF} = \frac{\text{BDCM} + 2\text{DBCM} + 3[\text{TBM}]\text{TCM}}{\text{BDCM} + \text{DBCM} + [\text{TBM}]}$$
 (Eq. 1)

3. Results and Discussion

3.1. Trends in DBP concentrations across treatment trains

Figures 1-5 (upper panels) illustrate the mean concentrations of different classes of DBPs (on a nanomolar basis) across individual potable reuse treatment trains, as well as their relative proportions. For trains B-D, the mean concentrations measured over the 2014 and 2015 sampling episodes are portrayed. Tables S6-S16 provide the individual DBP concentrations in $\mu\text{g/L}$ or ng/L measured for each sampling episode for all trains, as well as the average concentrations measured over the two sampling episodes for trains B-D. Within the secondary or tertiary effluents serving as influents to the treatment trains, chloroform (TCM) dominated among THMs with the concentration ranging from 3.4-8.6 $\mu\text{g/L}$ over all sampling events, while the bromine incorporation factor for THM4 ranged from 0.50 to 0.74 among the five treatment trains sampled during 2015. Dichloro- and trichloroacetic acids dominated among HAAs with a summed

concentration of 1.1-5.2 µg/L. Dichloroacetonitrile and dichloroacetamide, with concentrations ranging from 0.53-1.6 µg/L, and from <0.14-1.2 µg/L, respectively, were the only two other halogenated DBPs detected in the influents. Among *N*-nitrosamines, NDMA and NMOR were frequently detected in the influents, with NDMA concentrations ranging from <2.0 ng/L at train C to 320 ng/L at train B and NMOR concentrations ranging from 5.4 ng/L at train A to 53 ng/L at train B. The only other *N*-nitrosamine detected was NPYR, with a concentration of 2.6 ng/L at train D and 11 ng/L at train B.

Both trains B and C employed ozonation as the first process unit. Ozonation significantly increased the concentrations of NDMA, trichloroacetaldehyde (from <0.15 to 1.0 or 0.7 µg/L, respectively, as the average for the 2014 and 2015 sampling episodes), and dichloroacetamide (2-3 folds), but did not affect the concentrations of other DBPs. At trains B and C, ozonation increased the concentration of NDMA from 247 to 466 ng/L and from <2.0 to 21 ng/L, respectively. Train C also employed biological activated carbon (BAC) downstream of ozonation. BAC effectively reduced the concentrations of NDMA, trichloroacetaldehyde, and dichloroacetonitrile to below their method reporting limits, the concentrations of HAAs (i.e., dichloro- and trichloroacetic acids) by ~50%, and the concentration of dichloroacetamide by ~70%, but did not affect the concentrations of THMs.

Chloramines applied upstream of microfiltration (MF) for biofouling control promoted the formation of DBPs. For all treatment trains, the concentrations of DBPs in the MF filtrate were consistently the highest. Chloramination upstream of MF typically increased the concentrations of those halogenated DBPs detected in the treatment train influents by factors of 2-12. Several DBP classes, including iodinated THMs, halo ketones, and chloropicrin, were first measurable in the MF filtrate. For instance, moniodinated THMs, such as dichloriodomethane,

bromochloroiodomethane, and dibromiodomethane, were detected in the MF filtrate at trains A, B, and D, with the concentration of dichloriodomethane reaching 1.1 $\mu\text{g/L}$ at train B. Similarly, several brominated analogues of halogenated DBPs were first measurable in the MF filtrate. For instance, dichloroacetonitrile was the only HAN detected in the treatment train influents, but dibromoacetonitrile was also detected in the MF filtrate at all treatment trains with concentrations ranging from 0.49-1.1 $\mu\text{g/L}$. Note that the detection of brominated analogues was more likely associated with the increase in DBP concentrations rather than the increase in bromine incorporation. For instance, the average BIF for THM4 in the MF filtrates sampled during 2015 was 0.69 (± 0.15 standard deviation), which was not statistically different from that in the treatment train influents (i.e., 0.60 ± 0.10). Chloramination upstream of MF also increased the concentration of NDMA. For trains A, B, D, and E, where NDMA was detected in the influents, the concentration of NDMA in the MF filtrate increased by a factor of 1.4-8.5. Notably, the highest concentration of NDMA reached up to 1020 ng/L in the MF filtrate at train B sampled during 2014.

Reverse osmosis (RO) removed HAAs, chloropicrin, halo ketones, and haloacetaldehydes to below their method reporting limits. The removal efficiencies for haloacetamides generally were $>70\%$. The removal efficiencies for THMs, including iodinated THMs, were $\sim 50\%$, but lower removal efficiencies frequently were observed for the lower molecular weight analogues, particularly chloroform. Similarly, the removal efficiencies for HANs were only $\sim 50\%$, consistent with prior bench-scale (Doederer et al., 2014) and field studies (Farré et al., 2013; Linge et al., 2013). The removal efficiency for NMOR was typically $>80\%$, although 3 ng/L was detected in the RO permeate at train D. The removal efficiency for NDMA varied with the treatment train, ranging from $\sim 65\%$ at trains B and E to 100% at train C.

The UV-based advanced oxidation process (UV-AOP) removed *N*-nitrosamines to below their method reporting limits, even at train B, where the concentration of NDMA measured in the RO permeate was 320 ng/L. AOP further reduced the concentrations of remaining THMs by ~20% and of dichloroacetamide by ~30-50%. The removal efficiencies for HANs increased with bromine incorporation, following the trend of dichloroacetonitrile (~10%) < bromochloroacetonitrile (~60%) < dibromoacetonitrile (100%). Train E employed UV alone. While UV/H₂O₂ AOP treatment of the Train E RO permeate in the laboratory further reduced the concentrations of THMs, dichloroacetamide, and dichloroacetonitrile compared to standalone UV, UV/Cl₂ AOP treatment increased the concentrations of THMs, HAAs, trichloroacetaldehyde, and dichloroacetamide, but reduced that of dichloroacetonitrile.

When chloramines were applied to the AOP effluent for a simulated distribution system (SDS) analysis for potential future direct potable reuse scenarios, the formation of several classes of DBPs resumed, including THMs, HAAs, NDMA, trichloroacetaldehyde, and, in fewer cases, HANs and dichloroacetamide. While potable reuse treatment trains significantly reduced dissolved organic carbon (see Tables S1-S5), and likely the loads of pathogens and other contaminants of emerging concern (e.g., pharmaceuticals), SDS chloramination sometimes increased the concentrations of several classes of DBPs to levels as high as or even higher than those in the influents to these facilities. For instance, the concentrations of HAAs, trichloroacetaldehyde, and HANs in the chloraminated AOP effluent frequently were up to two-fold higher than those in the treatment train influents. Similarly, the concentration of NDMA in the chloraminated AOP effluent was 2.6-9.7 ng/L, which was higher than that in the influent to train C, similar to those in the influents to trains A and D, and lower than those in the influents to trains B and E. The concentration of NDMA in the chloraminated AOP effluent reached 9.0 ng/L

at train B, approaching the 10 ng/L notification level in California (California Department of Public Health, 2013), but was far below the concentration of 247 ng/L in the influent.

3.2. Consistency of DBP concentrations within and across treatment trains

For most DBPs, the concentrations were fairly consistent both for sampling campaigns separated by months within the same individual treatment trains (B, C and D) and for sampling campaigns within the same time window across all five treatment trains. For trains B, C, and D, the average relative standard deviation for concentrations of all DBP classes measured during the 2014 and 2015 sampling campaigns ranged from 2.9 to 12.7% (average 5.7%) in the MF filtrate, 3.1 to 8.4% (average 6.7%) in the RO permeate, and 4.3 to 11.1% (average 6.9%) in the AOP effluent (see Table S13 for relative standard deviations for individual DBP classes). Across all treatment trains, the relative standard deviations for concentrations of different halogenated DBP classes measured during the 2015 sampling campaign ranged from 27 to 124% (average 55%) in the MF filtrate, 29 to 133% (average 77%) in the RO permeate, 32 to 96% (average 53%) in the AOP effluent, and 33 to 155% (average 70%) in the SDS chloraminated AOP effluent (see Table S14 for relative standard deviations for individual DBP classes). Note that many of the highest relative standard deviations were associated with scenarios where certain DBP classes were below their method reporting limits in one or more treatment trains. To be conservative, the concentrations of non-detectable DBP classes were mathematically treated as 0 µg/L, which maximized the relative standard deviation of concentrations across the treatment trains. Compared to halogenated DBPs, the relative standard deviations for NDMA concentrations were more variable. For instance, the concentration of NDMA in the MF filtrate varied from 4.5 to 1020 ng/L. However, the concentration of NDMA was <2 ng/L in the RO permeate at all treatment trains, and only ranged from 2.6 to 9.7 ng/L in the SDS chloraminated AOP effluent.

Studies reporting specific concentrations of halogenated DBPs, particularly unregulated classes, along potable reuse treatment trains, are scarce in the literature. One study reported comparable concentrations of HAAs after MF and RO treatment at a full-scale treatment train in Australia (see Table 1). However, the concentrations of THMs, haloketones, and particularly HANs were much lower than those observed in the U.S. treatment trains investigated in this study. Furthermore, the concentrations of chloropicrin, iodinated THMs, and haloacetamides were not evaluated. The median concentrations of NDMA and NMOR measured in this study were comparable to the concentration ranges in the MF filtrate, RO permeate, and AOP effluent reported in earlier work (Table 1). However, the concentrations of NDMA measured in the MF filtrate and RO permeate at train B were higher than the previously measured ranges by an order of magnitude. Regardless, the effective removal of *N*-nitrosamines achieved by AOP was similar to previous observations.

The relatively consistent concentration profiles of DBPs, particularly halogenated DBPs, observed across all five treatment trains, despite differences in influent water qualities (i.e., secondary or tertiary effluents) and treatment process units (with or without O₃ and BAC) bears important implications for future exposure assessments. In the U.S., concerns have been raised regarding exposure to discharges of industrial compounds (e.g., solvents) that are poorly rejected by RO, particularly for direct potable reuse scenarios where there might only be limited time to detect the discharge and enable diversion of the waste stream from the treatment train. However, chronic exposures to chemical contaminants may be of higher concern than episodic exposures, such as those attributed to industrial solvents, for potable reuse scenarios. Our results indicate that DBPs represent a class of chemical contaminants that not only are poorly removed by RO

and, for halogenated DBPs, by AOP, but also occur at concentrations that are relatively consistent across time and space.

3.3. Toxicological significance of DBP classes across treatment trains

THMs and, to a lesser degree, HAAs dominated the DBP mixtures in terms of concentrations across each treatment train, generally accounting for >60% of the total DBP concentration in the MF filtrate and >80% of the total DBP concentration in all other samples. *N*-Nitrosamines were minor components in the DBP mixture, contributing <1% of the total DBP concentration throughout most treatment trains, and <4% throughout train B. However, there has been a significant focus on *N*-nitrosamines within potable reuse treatment trains (National Research Council, 2012) due to their high cancer potencies (US EPA, 1993). Although the contribution of chemical contaminants to the toxicity of a water is a function of both their concentrations and toxic potencies, previous research has not evaluated this balance to highlight DBP classes of potential concern in potable reuse waters.

We estimated the potential contributions of DBPs to toxicity by dividing their concentrations within potable reuse treatment trains by concentrations determined in toxicological assays to be associated with adverse health outcomes. This approach is similar to the margin of safety calculations performed by the National Research Council for different potable reuse scenarios, wherein contaminant concentrations were divided by health risk-based action levels (National Research Council, 2012). Unfortunately, health risk-based action levels are not available for most of the unregulated, halogenated DBPs measured in our study. For all DBPs except *N*-nitrosamines (discussed further below), *in vitro*, chronic cell cytotoxicity was selected as a quantitative biological endpoint because it is among the most general of adverse biological endpoints (the reduction in growth compared to an untreated control), capturing a wide array of

toxic modes of action (Plewa and Wagner, 2011). Furthermore, cytotoxicity has been commonly applied for assessing the total toxicity of drinking water (Jeong et al., 2012) and recycled wastewater (Escher et al., 2013; Tang et al., 2014; Leusch and Snyder, 2015). For most of the halogenated DBP classes targeted in this study, DBP concentrations associated with a 50% reduction in cell viability or cell growth of Chinese hamster ovary (CHO) cells compared to untreated controls (i.e., LC₅₀ cytotoxicity index values in molar units; see Table S15) have been derived using the same 72-h *in vitro* assay, by the same research group, facilitating quantitative comparison. The CHO cell LC₅₀ values for the following DBP classes were available from existing literature: THMs (Plewa and Wagner, 2009), HAAs (Plewa et al., 2010), iodinated THMs (Richardson et al., 2008a), HANs (Muellner et al., 2007), haloacetamides (Plewa et al., 2008), halonitromethanes (Plewa et al., 2004), and haloacetaldehydes (Jeong et al., 2015). DBP concentrations were divided by their CHO cell LC₅₀ values. Since the LC₅₀ value corresponds to a DBP concentration that induces killing in 50% of a population of treated cells, it represents a far higher concentration than would be considered protective of human health. Recognizing the difficulty of extrapolating from *in vitro* assays to human health risk assessments, we *did not* seek to calculate the absolute risk levels associated with ingestion of potable reuse waters. Accordingly, we weighted the concentrations of DBPs by their LC₅₀ values to estimate the relative contributions to the DBP-associated toxicity.

For *N*-nitrosamines, the CHO cell LC₅₀ values were either not available (NPYR), insignificant (NDMA), or extremely high (1.1×10^{-2} M for NMOR (Wagner et al., 2014)); a high value indicates low apparent toxicity. To be more conservative regarding the potential contribution of *N*-nitrosamines to toxicity, we employed cancer risk as the biological endpoint. The USEPA recently released age-adjusted drinking water concentrations associated with 10⁻⁶ lifetime excess

cancer risk for NDMA and NPYR as 0.6 ng/L and 2 ng/L, respectively, in Federal Register 2014-24582 (US EPA, 2014). The California Office of Environmental Health Hazard Assessment derived a drinking water concentration associated with 10^{-6} lifetime excess cancer risk for NMOR as 5 ng/L based on California 27 CCR §25705 (California Department of Public Health, 2013). Again, because our focus was on the relative risk associated with different DBP classes rather than the absolute risk, we converted these drinking water concentrations to those associated with a 50% lifetime excess cancer risk (i.e., $LECR_{50}$ in molar units; see Table S16) to place them on a common risk basis to the LC_{50} values for halogenated DBPs. For instance, we calculated a $LECR_{50}$ value of 4.04×10^{-6} M for NDMA, 9.99×10^{-6} M for NPYR, and 2.15×10^{-5} M for NMOR, respectively. For the two haloketones, 1,1-dichloropropanone and 1,1,1-trichloropropanone, because neither 10^{-6} lifetime excess cancer risk data nor CHO cell LC_{50} values were available, they were excluded from these calculations.

Figures 1-5 (lower panels) illustrate the additive toxicity associated with DBPs as well as the relative proportions contributed by different DBP classes, assuming that the DBP-associated toxicity is additive (Stork et al., 2007; Yeatts et al., 2010). This assumption has been used for predicting the toxicity of complex mixtures of trace organic contaminants (Tang et al., 2013). For all five treatment trains, the magnitude of additive toxicity increased significantly in the MF filtrate due to upstream chloramination. RO reduced the additive toxicity by >50%, while UV-based AOP achieved further reductions. SDS chloramination increased the additive toxicity of the AOP effluent, typically to levels above that in the secondary or tertiary effluent. Despite their dominance in terms of concentrations, THMs and HAAs were minor contributors to the additive toxicity across different treatment trains, except after BAC at train C, where the additive toxicity was low overall.

N-Nitrosamines contributed between ~5-95% of the additive toxicity in the secondary or tertiary effluent. Ozonation at trains B and C and BAC at train C increased the contribution of *N*-nitrosamines. However, due to significant formation of halogenated DBPs upon chloramination upstream of MF, the contribution of *N*-nitrosamines to the additive toxicity became relatively unimportant in the MF filtrate. Even at train B, which featured up to 1020 ng/L NDMA in the MF filtrate, the contribution of *N*-nitrosamines to the additive toxicity was considerably lower than that of halogenated DBPs.

HANs and haloacetamides, and to a lesser degree, haloacetaldehydes, dominated the additive toxicity in the MF filtrate, while HANs dominated the additive toxicity in the RO permeate as a result of the significant removal of haloacetamides and haloacetaldehydes by RO. The dominance of toxicity associated with HANs persisted through UV-based AOP, and after SDS chloramination, where additional HANs formed. Dichloroacetonitrile and bromochloroacetonitrile contributed almost equally to the HAN-associated toxicity. As with other halogenated DBP classes, the concentrations of dichloroacetonitrile and bromochloroacetonitrile were remarkably consistent across all treatment trains. For instance, the concentrations of dichloroacetonitrile were ~2.5 (± 0.6 $\mu\text{g/L}$ standard deviation) across trains A, B, D and E, with the exception at train C (i.e., ~0.9 $\mu\text{g/L}$), while the concentrations of bromochloroacetonitrile were 0.33 ± 0.06 $\mu\text{g/L}$ across all five treatment trains. While the concentrations of dichloroacetonitrile were roughly 7-fold higher than those of bromochloroacetonitrile, the CHO cell LC_{50} value for bromochloroacetonitrile is approximately 7-fold lower (i.e., 8.5×10^{-6} M) than for dichloroacetonitrile (i.e., 5.7×10^{-5} M) (see Table S15). Unregulated halogenated DBPs, and HANs in particular, have received less attention than *N*-nitrosamines for their potential contributions to the toxicity of potable reuse waters. Our

assessment suggests that HANs warrant further attention, particularly given that they are poorly removed by the RO and AOP treatment units that are central to existing potable reuse FAT trains.

4. Conclusions

This study evaluated the concentrations of *N*-nitrosamines as well as regulated and unregulated halogenated DBPs across five U.S. potable reuse facilities employing Full Advanced Treatment trains. The concentrations of THMs, HAAs, dichloroacetonitrile, and dichloroacetamide were largely in the low $\mu\text{g/L}$ range in the secondary or tertiary municipal wastewater effluents serving as influents to the treatment trains, while the concentrations of NDMA ($<2\text{--}320\text{ ng/L}$) and NMOR ($5.4\text{--}53\text{ ng/L}$) were more variable. Ozonation at two treatment trains increased the concentrations of trichloroacetaldehyde, dichloroacetamide, and NDMA, but BAC at one of the treatment trains reduced the concentrations of NDMA, HAAs, trichloroacetaldehyde, dichloroacetonitrile, and dichloroacetamide. Application of chloramines upstream of MF increased the concentrations of all DBP classes evaluated, including *N*-nitrosamines, THMs (including iodinated THMs), HAAs, chloropicrin, haloketones, HANs, haloacetamides, and haloacetaldehydes, to their highest levels observed along the treatment trains. RO effectively reduced the concentrations of HAAs, chloropicrin, haloketones, and haloacetaldehydes, but only partially removed THMs, haloacetamides, HANs, and *N*-nitrosamines. UV-based AOP eliminated NDMA, but only poorly removed THMs, haloacetamides, HANs, particularly the less brominated analogues. Although residual DBPs may be partially removed within the environmental buffers employed for indirect potable reuse (e.g., aquifer recharge), removal may be limited under direct potable reuse scenarios of increasing interest to water utilities. Application of chloramines to the AOP effluents under simulated distribution system conditions for future DPR scenarios resulted in the additional formation of NDMA, THMs, HAAs, trichloroacetaldehyde, and, in fewer cases, HANs and dichloroacetamide,

indicating the presence of DBP precursors in the AOP effluent. While potable reuse treatment trains likely removed a wide array of other contaminants of emerging concern (e.g., pharmaceuticals), the concentrations of DBPs measured after SDS chloramination were similar or somewhat greater than those measured in the influents to these facilities.

The concentrations of DBPs measured in the MF filtrate, RO permeate, AOP effluent, and chloraminated AOP effluent were relatively similar both within individual treatment trains sampled several months apart, and across all five treatment trains. The consistency of DBP concentrations suggests the potential for DBPs to exhibit a stable profile for future chronic exposure assessment. However, weighting individual DBP concentrations by their toxic potencies suggested that HANs, which are poorly removed by the combined RO/AOP treatment, may be important contributors to the DBP-associated toxicity of the final product water. The high importance attributed to HANs relative to *N*-nitrosamines and regulated THMs and HAAs occurred despite the more sensitive toxicological endpoint (i.e., cancer potency) employed for *N*-nitrosamines and the far greater concentrations of THMs and HAAs. While these calculations are suggestive, further research employing whole water toxicity assays is needed to quantify the contribution of HANs to the toxicity of potable reuse product waters. Based on the DBP concentrations measured in this study, we estimate that a high degree of sample concentration is needed to observe significant effects in current *in vitro* toxicity assays. Unfortunately, the low molecular weight, uncharged DBPs that are the focus of current research are also volatile, rendering them particularly susceptible to losses during sample concentration (Richardson et al., 2008b; Yeh et al., 2014).

Recently, there has been growing interest in the development of RO-free treatment trains (e.g., O₃/BAC combination) for potable reuse, particularly for inland communities for which

brine disposal is challenging. Our results suggest that HANs, haloacetamides, and to a lesser degree haloacetaldehydes may drive the DBP-associated toxicity of O₃/BAC effluents. Furthermore, while the ability to remove *N*-nitrosamines is an important advantage of UV-based AOP, our results suggest that alternative processes capable of achieving more efficient removal of halogenated DBPs, such as HANs, may be attractive. For instance, activated carbon may enable removal of halogenated DBPs, and potentially some of the residual organic matter serving as precursors for the formation of additional DBPs in chloraminated distribution systems.

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Appendix A. Supplementary material Supplementary material related to this article can be found at <http://dx.doi.org/10.1016/j.watres>.

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Table 1

	Post MF		Post RO		Post AOP		Dist Sys
	This work ^a	Literature ^b	This work ^a	Literature ^b	This work ^a	Literature ^b	This work ^a
<i>N</i>-Nitrosamines (ng/L)							
NDMA	56 (4.5-1020)	18-57	11 (<2.0-490)	14-41	<2.0	<2.5-14	6.9 (2.6-9.7)
NPYR	3.2 (<2.0-17)	NA ^c	<2.0	NA ^c	<2.0	NA ^c	<2.0
NMOR	17 (2.7-39)	7.5	<2.4 (<2.4-3.1)	<5.0	<2.4	<5.0	<2.4
THMs (µg/L)							
TCM	12 (7.6-15)	0.15-8.9	7.9 (5.2-12)	0.10-0.14	5.6 (4.0-8.7)	NA ^c	7.5 (5.1-11)
BDCM	8.5 (5.4-13)	0.070-0.75	4.7 (3.6-8.3)	0.040-0.060	2.2 (1.5-5.1)	NA ^c	3.3 (2.2-6.0)
DBCM	4.5 (3.1-8.6)	0.25-0.43	2.2 (1.4-5.0)	<0.24	0.76 (0.35-2.3)	NA ^c	1.4 (0.48-3.1)
TBM	1.7 (1.0-4.8)	0.040-0.19	0.82 (0.35-2.4)	<0.010	<0.21(<0.21-1.2)	NA ^c	<0.21 (<0.21-1.4)
HAAs (µg/L)							
CAA	0.52 (0.30-1.0)	0.43-0.58	<0.22	NA ^c	<0.22	NA ^c	<0.22
DCAA	8.8 (5.9-11)	1.5-13	<0.17	<0.16	<0.17	NA ^c	4.1 (2.4-4.9)
TCAA	6.2 (4.1-8.4)	0.31-19	<0.18	NA ^c	<0.18	NA ^c	1.9 (<0.18-3.1)
BCAA	1.6 (0.74-2.6)	1.8-5.2	<0.16	NA ^c	<0.16	NA ^c	0.39 (<0.16-1.0)
DBAA	1.5 (0.63-2.8)	0.40-0.53	<0.18	NA ^c	<0.18	NA ^c	0.28 (<0.18-0.56)
BDCAA	0.84 (0.36-1.5)	0.27-0.28	<0.22	NA ^c	<0.22	NA ^c	<0.22
DBCAA	0.33 (<0.22-0.56)	0.42-0.56	<0.22	NA ^c	<0.22	NA ^c	<0.22
TBAA	<0.24 (<0.24-0.40)	NA ^c	<0.24	NA ^c	<0.24	NA ^c	<0.24
I-THMs (µg/L)							
DCIM	0.78 (<0.20-2.0)	NA ^c	0.28 (<0.20-0.95)	NA ^c	<0.20	NA ^c	<0.20
BCIM	0.33 (<0.21-1.1)	NA ^c	<0.21 (<0.21-0.46)	NA ^c	<0.21	NA ^c	<0.21
DBIM	<0.17 (<0.17-0.65)	NA ^c	<0.17	NA ^c	<0.17	NA ^c	<0.17
HNMs (µg/L)							
TCNM	0.31 (<0.16-0.55)	NA ^c	<0.16	NA ^c	<0.16	NA ^c	<0.16
HKs (µg/L)							
1,1-DCP	2.6 (<0.18-3.2)	0.41-1.3	<0.18	<0.23	<0.18	NA ^c	<0.18 (<0.18-0.54)
1,1,1-TCP	0.92 (<0.22-1.7)	<0.11	<0.22	<0.060	<0.22	NA ^c	<0.22
HALs (µg/L)							
TCAL	3.2 (2.1-4.2)	<0.17	<0.15	NA ^c	<0.15	NA ^c	0.42 (<0.15-0.79)
BDCAL	1.2 (<0.14-1.8)	NA ^c	<0.14	NA ^c	<0.14	NA ^c	<0.14
DBCAL	0.50 (<0.20-0.86)	NA ^c	<0.20	NA ^c	<0.20	NA ^c	<0.20
HANs (µg/L)							
DCAN	5.0 (2.8-6.8)	0.020-0.44	2.2 (0.78-2.7)	0.050-0.12	1.9 (0.69-2.3)	NA ^c	2.0 (0.89-3.3)
BCAN	2.1 (1.1-3.0)	0.050-0.070	0.86 (0.49-1.6)	0.020-0.040	0.31 (0.25-0.43)	NA ^c	0.33 (0.26-0.43)
DBAN	0.79 (0.49-1.2)	NA ^c	0.37 (0.25-0.61)	NA ^c	<0.20	NA ^c	<0.20
HAMs (µg/L)							
DCAM	3.8 (2.0-8.2)	NA ^c	0.67 (<0.14-2.3)	NA ^c	0.42 (<0.14-1.2)	NA ^c	0.76 (0.26-2.2)
BCAM	1.2 (0.52-1.7)	NA ^c	<0.17	NA ^c	<0.17	NA ^c	<0.17
DBAM	0.47 (<0.17-0.76)	NA ^c	<0.22	NA ^c	<0.22	NA ^c	<0.22
TCAM	<0.24 (<0.24-0.61)	NA ^c	<0.24	NA ^c	<0.24	NA ^c	<0.24

^a Median and range of concentrations measured in this study; ^b Range of concentrations reported in previous studies (Gerrity et al. 2015, Plumlee et al. 2008, Sgroi et al. 2015, Farré et al. 2012, Linge et al. 2013); ^c NA = Not available.

Figure 1. Concentration and toxicity profiles of disinfection byproducts along the potable reuse treatment train A. “Sec Eff” = Secondary effluent sample; “Post MF” = Microfiltration filtrate sample; “Post RO” = Reverse osmosis permeate sample; “Post AOP” = UV/H₂O₂ AOP effluent water sample; “Dist Sys” = Simulated distribution system sample. Treatment train A was sampled once in 2015. Data represent the mean and standard deviation ($n = 2$) of DBP concentrations measured during the 2015 sampling campaign (data from Table S6).

Figure 2. Concentration and toxicity profiles of disinfection byproducts along the potable reuse treatment train B. “Sec Eff” = Secondary effluent sample; “Post O₃” = Ozonation effluent sample; “Post MF” = Microfiltration filtrate sample; “Post RO” = Reverse osmosis permeate sample; “Post AOP” = UV/H₂O₂ AOP effluent sample; “Dist Sys” = Simulated distribution system sample. Treatment train B was sampled twice in 2014 and 2015. Data represent the mean and standard deviation ($n = 2-4$) of DBP concentrations measured during the 2014 and 2015 sampling campaigns (data from Table S9).

Figure 3. Concentration and toxicity profiles of disinfection byproducts along the potable reuse treatment train C. “Tert Eff” = Tertiary effluent sample; “Post O₃” = Ozonation effluent sample; “Post BAC” = Biological activated carbon effluent sample; “Post MF” = Microfiltration filtrate sample; “Post RO” = Reverse osmosis permeate sample; “Post AOP” = UV/H₂O₂ AOP effluent sample; “Dist Sys” = Simulated distribution system sample. Treatment train C was sampled twice in 2014 and 2015. Data represent the mean and standard deviation ($n = 2-4$) of DBP concentrations measured during the 2014 and 2015 sampling campaigns (data from Table S12).

Figure 4. Concentration and toxicity profiles of disinfection byproducts along the potable reuse treatment train D. “Sec Eff” = Secondary effluent sample; “Post MF” = Microfiltration filtrate sample; “Post RO” = Reverse osmosis permeate sample; “Post AOP” = UV/H₂O₂ AOP effluent sample; “Dist Sys” = Simulated distribution system sample. Treatment train D was sampled twice in 2014 and 2015. Data represent the mean and standard deviation ($n = 2-4$) of DBP concentrations measured during the 2014 and 2015 sampling campaigns (data from Table S15).

Figure 5. Concentration and toxicity profiles of disinfection byproducts along the potable reuse treatment train E. “Sec Eff” = Secondary effluent sample; “Post MF” = Microfiltration filtrate sample; “Post RO” = Reverse osmosis permeate sample; “Post UV” = UV effluent sample sample; “Post AOP” = pilot-scale UV/H₂O₂ AOP effluent sample; “Post UV/Cl₂” = pilot-scale UV/Cl₂ AOP effluent sample; “Dist Sys” = Simulated distribution system sample (corresponding to the “Post UV” sample). Treatment train E was sampled twice in 2015. Data represent the mean and standard deviation ($n = 2$) of DBP concentrations measured during the two 2015 sampling campaigns (data from Table S16).