Relevance of drinking water as a source of human exposure to bisphenol A

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A comprehensive search of studies describing bisphenol A (BPA) concentrations in drinking water and source waters (i.e., surface water and groundwater) was conducted to evaluate the relevance of drinking water as a source of human exposure and risk. Data from 65 papers were evaluated from North America (31), Europe (17), and Asia (17). The fraction of drinking water measurements reported as less than the detection limit is high; 95%, 48%, and 41%, for North America, Europe, and Asia, respectively. The maximum quantified (in excess of the detection limit) BPA concentrations from North America, Europe, and Asia are 0.099 μg/l, 0.014 μg/l, and 0.317 μg/l. The highest quantified median and 95th percentile concentrations of BPA in Asian drinking water are 0.026 μg/l and 0.19 μg/l, while high detection limits restricted the determination of representative median and 95th percentile concentrations in North America and Europe. BPA in drinking water represents a minor component of overall human exposure, and compared with the lowest available oral toxicity benchmark of 16 μg/kg-bw/day (includes an uncertainty factor of 300) gives margins of safety > 1100. Human biomonitoring data indicate that ingestion of drinking water represents < 2.8% of the total intake of BPA.

INTRODUCTION

Bisphenol A (BPA, 4,4’-isopropylidene diphenol, CAS Registry No. 80-05-7) is a commercially important industrial chemical with an estimated worldwide production capacity of approximately 5.2 million metric tonnes in 2008.1 BPA is primarily used as an intermediate in the production of polycarbonate plastic and epoxy and other specialty resins.2–4 Major end-use applications for polycarbonate include glazing and sheeting, electrical and electronic goods, electronic storage media, and household equipment, including bottles, utensils and containers. Epoxy resins are used for protective coatings for architectural structures, marine and car coatings, container coatings, and printed circuit boards. BPA is also used in the production of phenoplast, phenolic and unsaturated polyester resins, polyvinylchloride, and thermal paper. The presence of BPA in the environment and consumer products has been the subject of public and regulatory attention, primarily due to concerns about its weak endocrine activity. The environmental fate and ecotoxicological properties of BPA have been extensively evaluated5–8 and a number of risk assessments have been conducted by regulatory authorities around the world.5,9,10 Small amounts of BPA may enter the environment from production and processing facilities, which often discharge to sewage treatment plants.1,6 Once introduced to the environment, BPA primarily partitions to the aquatic compartment.5 Extensive monitoring of BPA in various environmental media has been conducted over the last 10 years. Klecka et al.11 recently published the results of a statistical analysis of environmental concentrations in North America and Europe. Median BPA concentrations for fresh surface waters for North America and Europe were 0.081 μg/l and 0.01 μg/l, while 95th percentiles were 0.47 μg/l and 0.35 μg/l, respectively. In contrast to fresh surface waters, only limited data are available for sediments and less for marine ecosystems. Many of these studies characterized the sample locations as being downstream of wastewater discharges, receiving waters for industrial facilities, areas susceptible to contamination, urban waterways, or industrial ports.

Measurements of BPA in drinking water and its source waters have been reported in numerous studies by government agencies and other researchers.12–15 Several of the studies are described as national monitoring programs. For many of these studies, BPA is one of a long list of analytes, whereas other studies have focused on measurements of BPA only. To date, the available data have not been summarized, analyzed statistically, nor has the relevance to human exposures been assessed. Globally, the source of drinking water is more or less equally divided between surface water and groundwater (48.22% and 48.23%, respectively), with the balance (3.55%) obtained from desalination of saltwater.16 In 2006, 54% of the world’s population had a piped connection providing drinking water, compared with 33% who used other improved drinking water sources. The remaining 13% of the population relied on unimproved sources.16 Drinking water treatment typically involves mixing surface water with a coagulant to assist with flocculation of finely divided suspended matter, which may be removed by sedimentation and filtration, and then the filtered water is disinfected by chemical methods, predominantly chlorine-based, or by physical methods such as ultraviolet radiation.17 Depending upon the surface water,

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additional processes may be used, including activated carbon treatment for the removal of dissolved organic material, demineralization for the reduction of dissolved ions (usually through advanced membrane treatment), and hydrogen sulphide/iron/manganese removal.

Drinking water treatment technologies typically remove 76–99% of the amount of BPA present in source waters.\textsuperscript{16,17} For example, Kleywegt et al.\textsuperscript{18} determined that drinking water treatment plants using granulated activated carbon or granulated activated carbon followed by ultraviolet radiation removed 80–99% of the BPA detected in river source water. Stackelberg et al.\textsuperscript{19} measured a 76% decrease in BPA from source water to finished water for a drinking water treatment plant consisting of clarification with feric chloride, primary disinfection with sodium hypochlorite, sand/granulated activated carbon filtration, and secondary disinfection. Snyder et al.\textsuperscript{15} evaluated 20 drinking water treatment plants where the frequency of BPA detection (detection limit = 0.005 μg/l) decreased from 44% in source water to 16% in raw water intake, 6% in finished drinking water, and 0% in water within the distribution system. The maximum concentration detected was 0.120 μg/l. Benotti et al.\textsuperscript{12} evaluated BPA removal in 19 drinking water treatment plants. BPA was detected in 17% of the surface water-source waters, with a maximum measured concentration of 0.014 μg/l, and the concentration was <0.005 μg/l in all finished waters. BPA was not detected in the groundwater-source water; however, the measured concentration in finished water was 0.025 μg/l.

Human exposure to BPA has been evaluated by characterizing the concentration of BPA in media such as diet, dust, and air.\textsuperscript{9,20–22} Willhite et al.\textsuperscript{21} and AIST\textsuperscript{9} have suggested that ingestion of water is a minor source of exposure compared with food intake. Snyder et al.\textsuperscript{15} recently evaluated a relatively small dataset of drinking water samples from the United States and determined a margin of safety of 72,000.

The objectives of this study were to conduct a comprehensive review of BPA measurements in drinking water and source waters (surface water and groundwater), and to determine the relative contributions of drinking water to overall exposure and potential human health risk. The investigation included an exhaustive review of studies reporting monitoring data for BPA in North America, Europe, and Asia. Data for Japan were excluded because a comprehensive review was recently completed,\textsuperscript{8} and the results of the review are compared here. Estimated intakes from drinking water were then compared with overall exposure from all sources, and margin of safety determinations were made using established oral toxicity benchmarks. Finally, BPA exposures were evaluated in the context of recently reported human urinary biomonitoring data. It was beyond the scope of this paper to identify the underlying sources or mechanism of BPA entry into drinking water or source waters (i.e., surface water and groundwater).

**METHODS**

Identification and Evaluation of Studies

A literature search was conducted to identify environmental monitoring studies published between 1990 and 2010, which reported measurements of BPA in drinking water and its source waters. A two-stage data evaluation process was used similar to Klecka et al.\textsuperscript{11} Studies were initially scored for completeness in the description of sampling location, date, and procedures, analytical/laboratory methodology, analytical reporting limits, analytical results, quality assurance and quality control sample procedures, and quality assurance/quality control results. Each paper was then carefully reviewed by an analytical chemist with expertise in the analysis of BPA. Studies categorized as "reliable" or "very reliable" in both reviews were used in the subsequent evaluation (see Klecka et al.\textsuperscript{11} for criteria). There were two studies that lacked sufficient information in English for classification of reliability (i.e., a Norwegian government study\textsuperscript{23} and a study of a Chinese drinking water treatment plant\textsuperscript{24}); therefore, absent information for rejection they were retained for further analysis. All studies are listed in the Supplementary Information available online.

**Statistical Treatment of Data**

Data from the studies that passed the reliability review described above were then summarized using basic descriptive statistics such as the range, median, and 95th percentile. However, there were three issues that confounded this analysis: depending upon the medium, up to 95% of measured concentrations were reported as less than the detection limit; the detection limits differed between studies by four orders of magnitude; and for some studies, only summary statistics were available limiting our ability to combine studies and perform the statistical analysis. There are a number of available methods to characterize non-detected concentrations.\textsuperscript{25,26} In a previous analysis of BPA in surface water and sediment, Klecka et al.\textsuperscript{11} used the non-parametric Kaplan–Meier method\textsuperscript{25,26} whereby, distributions of datasets with minimal non-detected concentrations were applied to datasets having limited detected concentrations to enable statistical analysis of data. However, in the present study, BPA was quantified in excess of the detection limit in only 5% of samples of drinking water in North America, and this was considered to be too small a fraction to apply the Kaplan–Meier method. Instead, the distribution of concentrations for each medium is described by grouping or binning the data according to detection limit in the case of samples reported as less than the detection limit, and according to measured concentration, in the case of samples for which concentrations exceed the detection limit. These groupings are used to identify the median and 95th percentile concentrations in addition to the overall minimum and maximum concentrations. One advantage of this

| Table 1. Geographic distribution of bisphenol A monitoring data. |
|----------------|----------------|----------------|
| Country       | Drinking water | Surface water-source water | Groundwater-source water |
| North America | 3 (130+)       | 4 (130+)                 | 1 (5)                     |
| Canada        | 3 (130+)       | 4 (130+)                 | 1 (5)                     |
| Mexico        | 0              | 0                        | 1 (2)                     |
| USA           | 10 (288+)      | 14 (612+)                | 10 (451)                  |
| Total         | 13 (418+)      | 18 (742+)                | 12 (458)                  |
| Europe        | 1 (164)\textsuperscript{b} | 1 (164)\textsuperscript{b} | 0                         |
| France        | 1 (2)          | 1 (2)                    | 0                         |
| Germany       | 1 (10)         | 0                        | 0                         |
| Italy         | 1 (6)          | 1 (8)                    | 1 (2)                     |
| Norway        | 0              | 1 (12)                   | 0                         |
| Spain         | 1 (7)          | 7 (46+)                  | 1 (3)                     |
| Sweden        | 1 (34)\textsuperscript{g} | 0                        | 0                         |
| UK            | 1 (4)          | 2 (70+)                  | 0                         |
| Total         | 6 (63)         | 12 (138+)                | 3 (169)                   |
| Asia          |                |                          |                           |
| China         | 9 (25)         | 4 (80)                   | 0                         |
| Iran          | 1 (1)          | 0                        | 0                         |
| Singapore     | 1 (1)          | 0                        | 0                         |
| South         | 0              | 2 (486)                  | 0                         |
| Korea         | 0              | 1 (120)                  | 0                         |
| Taiwan        | 0              | 1 (120)                  | 0                         |
| Total         | 11 (27)        | 7 (686)                  | 0                         |
| Overall total | 30 (508+)      | 37 (1566+)               | 15 (627)                  |

\textsuperscript{a}The values shown represent the total number of studies followed by the number of samples. The actual number of samples is larger than reported here as some studies do not report the number of samples.\textsuperscript{b}23 countries are represented.\textsuperscript{c}The data are for raw, not finished drinking water as reported by\textsuperscript{27} and are not included in subsequent analysis of drinking water.
RESULTS
Summary of Environmental Monitoring Studies Utilized in the Analysis
A total of 76 papers or reports, published between 1990 and 2010, were identified that contained data for BPA in North America, Europe, or Asia (excluding Japan) in drinking water and/or source waters. Following the data quality and analytical reviews, 11 papers received a low-reliability ranking or were eliminated because they contained duplicate data, had unreliable analytical methods (e.g., contamination of blanks), or the data were presented in a format that could not be used for further analysis. The 65 papers retained for analysis include 31 papers from North America, 17 from Europe, and 17 from Asia. A summary of each study is presented in the Supplementary Information available online.

Drinking water is divided according to source, that is, surface water, groundwater, or mixed/unspecified source. Source waters were identified based on the descriptions provided by the study authors and, therefore, there may be additional data for source waters that could not be identified.

Table 1 summarizes the geographical distribution of available monitoring data listing the number of studies and samples for each country. For some studies, the actual number of samples was not reported; therefore, a “+” is placed after the number of samples to indicate the data are representative of a number of samples greater than reported. Tables 2–4 present summary statistics and the distribution of sample concentrations (detected and not detected) within the pre-defined ranges (e.g., <0.001 μg/l, 0.01 μg/l to <0.01 μg/l, 0.1 μg/l to <1 μg/l, and ≥1 μg/l) for drinking water, surface water-source water, and groundwater-source water. As individual data points were not always available, the sum of the number of samples may be less than the total number of samples at the top of the table when individual data points are not available. Details of individual studies are provided in the Supplementary Material available online.

Drinking Water
BPA concentrations in drinking water collected from Canada, USA, six European countries, and three Asian countries are presented in Table 2. The data for finished drinking water (includes effluent from drinking water treatment plants i.e., finished drinking water ready for distribution) as well as distribution water and tap water) are further categorized according to source as described for each study. The North American data include national monitoring studies of drinking water3,13 and two other large studies (54–128 samples).13,14 The European and Asian studies of drinking water are all much smaller studies (1–12 samples). Summary statistics for each drinking water study are provided in the Supplementary Information available online.

The detection limits for drinking water vary by four orders of magnitude across all studies, and the frequency of detection was 5%, 52%, and 59%, for North America, Europe, and Asia respectively. The greater detection frequency in Asia and Europe is a function of lower detection limits, not higher concentrations of BPA. The limited detection frequency makes it difficult to compare BPA concentrations between regions, as most of the summary statistics are reported as less than the detection limit. In North America, the median for all sources of drinking water ranged from <0.002 μg/l to <1 μg/l, and the 95th percentile ranged from <0.099 μg/l to <1.6 μg/l. The maximum reported detected concentration of BPA in North American drinking water was 0.099 μg/l. In a few studies with detection limits of 1 μg/l or more

| Table 2. Bisphenol A concentrations in drinking water reported for North America, Europe, and Asia. |
|---|---|---|---|---|---|
| Source | North America | Europe | Asia |
| | Surface water | Groundwater | Mixed/unspecified | Surface water | Groundwater | Mixed/unspecified |
| Number of samples | 171 | 9 | 12 | 87 | 18 | 4 |
| Percent samples with detection limit | 2% | 2% | 3% | 19% | 1% | 2% |
| Concentration (μg/l) | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Minimum | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Maximum | 0.007 | 0.014 | 0.026 | 0.001 | 0.002 | 0.002 |
| Abbreviation: DL, detection limit. |
| aThe number of samples quantified at a concentration equal to or exceeding the detection limit. |
| bTwo data points with a mean value of 0.0019 μg/l. |
| cIndividual data points were not available to provide breakdown within defined concentration ranges; results ranged from 0.002 μg/l to 0.009 μg/l. |
| eE denotes a reported estimated value that is less than detection limit. |

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The number of samples quantified at a concentration equal or exceeding the detection limit.\(^b\)
The predominately lower detection limits in Europe yielded medians ranging from \(0.0002 \mu g/l\) to \(0.002 \mu g/l\), and the 95th percentile ranged from \(0.014 \mu g/l\) to \(5.1 \mu g/l\) depending on the source. Asia had the highest BPA concentration quantified (0.317 \(\mu g/l\)).

Surface Water Sources
BPA concentrations in surface water-source water collected from Canada, USA, five European countries, and three Asian countries are presented in Table 3. The North American data include national monitoring studies described above for drinking water.\(^{13,15}\) and two other large studies.\(^{12,14}\) In Asia, several large studies of surface water-source water are available (52–480 samples),\(^{29–31}\) while the European studies of surface water-source water are smaller in scope (most have 2–12 samples). Summary statistics for each of the studies are provided in the Supplementary Information available online.

(e.g. Carter et al.\(^{13}\)) BPA was present in several samples and estimates of values less than the detection limit are reported for those samples; the maximum of these estimated concentrations is 0.45 \(\mu g/l\). The predominately lower detection limits in Europe yielded medians ranging from \(0.0002 \mu g/l\) to \(0.002 \mu g/l\), and the 95th percentile ranged from \(0.014 \mu g/l\) to \(5.1 \mu g/l\) depending on the source. Asia had the highest BPA concentration quantified (0.317 \(\mu g/l\)).

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### Table 3. Bisphenol A concentrations in surface water (identified as a drinking source) reported for North America, Europe, and Asia.

|                       | North America | Europe | Asia |
|-----------------------|---------------|--------|------|
| Total number of samples | >742          | >138   | 686  |
| Number of samples > detection limit | 43            | 78     | 586  |
| Percent samples > detection limit | <6%           | <57%   | 85%  |
| Number of samples within concentration range (\(\mu g/l\)) | < DL Quantified\(^b\) | < DL Quantified\(^b\) | < DL Quantified\(^b\) |
| <0.001                | >2            | 1      | 3    | 2    | 0    |
| 0.001 to <0.01        | 148           | 40\(^c\) | 26   | 15   | 0    | 501\(^d\) |
| 0.01 to <0.1          | 109           | 15     | 51   | 49   |     |
| 0.1 to <1             | 0             | 1      | 6    | 9    | 51   | 14   |
| 1 or >1               | 440           | 1      | 10   | 1    | 0    | >1\(^e\) |

Concentration (\(\mu g/l\))

|                   | North America | Europe | Asia |
|--------------------|---------------|--------|------|
| Minimum            | <0.0001       | <0.0002 | 0.0022 |
| Median             | <1            | <0.006 | <0.0155 |
| 95th percentile    | <1            | <5.1   |      |
| Maximum            | 1.9           | <5.1 (2.97\(^g\)) | 4.23 |

Abbreviation: DL, detection limit.
\(^a\)The number of samples quantified at a concentration equal to or exceeding the detection limit.
\(^b\)Individual data points were not available to provide breakdown within defined concentration ranges; results ranged from 0.002 \(\mu g/l\) to 0.12 \(\mu g/l\).
\(^c\)Individual data points were not available to provide breakdown within defined concentration ranges; results ranged from 0.002 \(\mu g/l\) to 0.12 \(\mu g/l\).
\(^d\)Individual data points were not available to provide breakdown within defined concentration ranges; results ranged from 0.0025 \(\mu g/l\) to 0.0965 \(\mu g/l\).
\(^e\)The 95\(^{th}\) percentile could not be calculated as individual data points were not available for all studies.
\(^f\)The maximum detected value.

### Table 4. Bisphenol A concentrations in groundwater (identified as a drinking source) reported for North America and Europe.

|                       | North America | Europe |
|-----------------------|---------------|--------|
| Total number of samples | 458           | 169    |
| Number of samples > detection limit | 13            | 67     |
| Percent samples > detection limit | 3%           | 40%    |
| Number of samples within concentration range (\(\mu g/l\)) | < DL Quantified\(^b\) | < DL Quantified\(^b\) |
| <0.001                | 0             | 2      | 2    | 0    |
| 0.001 to <0.01        | 28            | 0      | 100  | >2   |
| 0.01 to <0.1          | 3             | 6      | 0    | 16\(^e\) |
| 0.1 to <1             | 3             | 0      | 0    |      |
| 1 or >1               | 411           | 5      | 0    |      |

Concentration (\(\mu g/l\))

|                   | North America | Europe |
|--------------------|---------------|--------|
| Minimum            | 0.0004        | <0.0002 |
| Median             | <1            | <0.001 |
| 95th percentile    | <1            | <0.073 (90\(^{th}\) percentile) |
| Maximum            | 6.4           | 2.299  |

Abbreviation: DL, detection limit.
\(^a\)The number of samples quantified at a concentration equal to or exceeding the detection limit.
\(^b\)Individual data points were not available to provide breakdown within defined concentration ranges; results ranged from 0.073 \(\mu g/l\) to 2.299 \(\mu g/l\).
Similar to the drinking water data, the detection limits for surface water vary by four orders of magnitude across all studies, and the frequency of detection was 6%, 57%, and 85% for North America, Europe, and Asia respectively. Again, the difference between regions is primarily a function of detection limit sensitivity.

For surface water-source water in North America, the median and 95th percentile concentrations are equal to the predominant detection limit of 1 µg/l. For Europe, the median and 95th percentile concentrations are <0.006 µg/l and <5.1 µg/l, and the median concentration for Asia is <0.0155 µg/l. The maximum concentration quantified in surface water-source water was 4.23 µg/l.

Groundwater Sources
BPA concentrations in groundwater-source water collected from Canada, Mexico, USA, and 23 European countries are presented in Table 4. No data are available for Asia. The USA data include two national monitoring studies of source waters. The European dataset includes a study of groundwater-source water in 23 countries. Summary statistics for each of the studies are provided in the Supplementary Information available online.

Again, there was a wide range of detection limits that varied by four orders of magnitude across all studies, and the frequency of detection was 3% and 40% for North America and Europe, respectively. Similar to the other sampled media, the detection limits for the European studies are generally much lower.

For groundwater-source water, the median concentrations are equal to the detection limits; the median concentrations for North America and Europe are <1 and <0.001 µg/l, respectively. In North America, the 95th percentile of the concentrations is <1 µg/l. In Europe, the 90th percentile is <0.073 µg/l (the 95th percentile could not be calculated because we do not have individual data points for all studies). The maximum concentrations quantified for North America and Europe are 6.4 µg/l and 2.299 µg/l, respectively.

DISCUSSION
A systematic evaluation of the data base of BPA drinking water and source water (surface water and groundwater) concentrations was conducted to determine the relative contributions of drinking water to overall exposure and potential human health risk.

An accepted procedure as outlined in Klecka et al. was used to categorize available studies for acceptability and inclusion into our evaluation. Studies that were included demonstrated standard, validated methodology; however, some studies were designed to detect multiple related analytes in a sample (e.g., several studies were part of a nationwide reconnaissance program), which likely sacrificed some of the analytical sensitivity. Given that the median and 95th percentile values are not detectable for most source categories, it is difficult to compare BPA concentrations across sources and regions. A comparison of the maximum drinking water concentrations across regions and sources, while not ideal, indicates relatively similar values within each source category. A better indicator of the upper-limit concentrations is the 95th percentile value as maximum values may be influenced by single samples and potential outliers. Nonetheless, across regions, maximum drinking water concentrations ranged from 0.014 µg/l to <5.1 µg/l, surface water-source water from 1.9 µg/l to <5.1 µg/l, and groundwater-source water from 2.299 µg/l to 6.4 µg/l (Tables 2–4). In general, it would be expected that finished drinking water concentrations of BPA would be 10-fold to 100-fold lower than source waters as the efficiency of drinking water treatment plants indicate a removal efficiency in the range of 76–99%.

A recent comprehensive review (n = 182) of source water (the source of the water is not specified), finished drinking water, and tap water was conducted in Japan by the Research Center for Chemical Risk Management. BPA was detected in 38% of the 74 source water samples, with a maximum concentration of 0.06 µg/l (the most frequent quantitation limit was 0.01 µg/l). BPA was detected in 4% of the 74 finished drinking water samples with a maximum measured concentration of 0.01 µg/l, and BPA was detected in 8% of the 34 tap water samples with a maximum concentration of 0.007 µg/l (detection limit of 0.003 µg/l and quantitation limit of 0.01 µg/l). A recent study of drinking water in Chicago and its source water (Lake Michigan) found that of the 146 samples tested, BPA was detected in 4 drinking water samples, with a maximum concentration of 0.051 µg/l, and in 7 source water samples, with a maximum concentration of 0.054 µg/l.

Overall, a vast amount of drinking water and source water data for BPA is available across North America, Europe, and Asia. Our assessment evaluated 65 studies and >2700 samples and AIST10 evaluated 182 samples. The entirety of the data indicate that BPA concentrations in treated drinking water are not likely to be greater than about 0.317 µg/l (i.e., the maximum quantified concentration in our study).

Human Exposure to BPA
For the purposes of evaluating human exposure to BPA via drinking water, the highest quantified median and 95th percentile BPA concentration in drinking water (i.e., 0.026 µg/l and 0.19 µg/l, detected in Asia) were used to estimate potential drinking water intakes of BPA for children aged 3 months to <6 months, 3 years to <6 years, 6 years to <11 years, and adults. Drinking water intakes were then compared with estimates of overall BPA exposure and recent human biomonitoring data for similar age groups presented by WHO. Margin of safety determinations were made using the lowest of available oral toxicity benchmarks (i.e., oral reference doses, tolerable daily intake values, etc.). Here, margin of safety is defined as the oral toxicity benchmark divided by the potential exposure. The target margin of safety is ≥1 as the associated uncertainty factors (e.g., inter- and intra-species variability) are already included within the derivation of the oral toxicity benchmark.

Oral toxicity benchmarks are available for BPA from several sources and range from 16 µg/kg bw/day to 50 µg/kg bw/day. The US Environmental Protection Agency’s oral reference dose of 50 µg/kg bw/day is based upon the lowest observed adverse effect (reduced body weight) level of 50 mg/kg/day from a chronic dietary rat study and an uncertainty factor of 100. The European Food Safety Authority’s tolerable daily intake of 50 µg/kg bw/day (which was recently reaffirmed) is based upon a no observed adverse effect level of 5 mg/kg bw/day established from a multi-generation reproductive toxicity study in rats and an uncertainty factor of 100. Additionally, Health Canada’s provisional tolerable daily intake of 25 µg/kg bw/day is based on a no observed effect level of 25 mg/kg bw/day from a 90-day rat study and an uncertainty factor of 100. Finally, Willhite et al. recently derived an oral toxicity benchmark of 16 µg/kg bw/day based on no observed adverse effect levels of 5 mg/kg bw/day for systemic toxicity in rats and mice and an uncertainty factor of 300.

Potential drinking water intake was determined using the following equation:

\[ \text{Dose (µg/kg - bw/day)} = \frac{\text{Concentration in drinking water (µg/l)}}{\text{Ingestion rate (l/day)}} \times \text{Absorption factor (unitless)} \times \text{Body weight (kg)} \]

The US Environmental Protection Agency provides mean estimates of drinking water ingestion of 0.56 l/day, 0.38 l/day, 0.51 l/day, and 1.2 l/day for children aged 3 to <6 months, 3 years to <6 years, 6 years to <11 years, and adults, respectively. The
body weights for these age groups are 7.4 kg, 18.6 kg, 31.8 kg, and 70 kg [25]; although 80 kg is cited by US Environmental Protection Agency, the generally accepted value used in risk assessment of 70 kg is used here). Based upon a median concentration of BPA of 0.026 µg/l and 100% absorption, the estimated median BPA drinking water intake is 0.0020 µg/kg-bw/day, 0.00053 µg/kg-bw/day, 0.00042 µg/kg-bw/day, and 0.00045 µg/kg-bw/day for children aged 3 to <6 months, 3 years to <6 years, 6 years to <11 years, and adults, respectively. Using the 95th percentile concentration of 0.19 µg/l, the corresponding potential BPA drinking water intake values are 0.014 µg/kg-bw/day, 0.0039 µg/kg-bw/day, 0.0031 µg/kg-bw/day, and 0.0033 µg/kg-bw/day. The margin of safety for the median water intake compared with the lowest oral toxicity benchmark of 16 µg/kg-bw/day (which includes an uncertainty factor of 300) ranges from 8200 to 38,000 (Table 5). The margin of safety for the 95th percentile ranges from 1100 to 5200 (Table 5). These findings are in agreement with the work of Snyder et al. who determined a margin of safety of 72,000 based upon a maximum detected drinking water concentration of 0.025 µg/l and an oral toxicity benchmark of 50 µg/kg-bw/day.

To understand the relative contribution of drinking water to overall exposure, a comparison is made to estimated BPA intakes recently reported by the World Health Organization (Table 5). The primary source of BPA exposure is the diet. Other sources of exposure such as inhalation of airborne BPA or indirect ingestion of BPA from soil/dust are at least one order of magnitude less than exposure from the diet. The WHO presented ranges of dietary intake for children aged 0 to 6 months, 6 months to 3 years, children aged >3 years to adult, and adults, similar to the age range presented above for drinking water. The average of the ranges reported by WHO for each age group is presented in Table 5. For children aged 0 to 6 months and 6 months to 3 years, three potential diets were presented. The highest estimated dietary intake of 2.2 µg/kg-bw/day (i.e., represented by the use of polycarbonate bottles and formula only) and 0.55 µg/kg-bw/day (i.e., represented by a diet using polycarbonate bottles and formula and solid food), respectively, was used. Drinking water contributes very little to overall BPA exposure: the 95th percentile drinking water intake (0.0031 µg/kg-bw/day to 0.014 µg/kg-bw/day) is only 0.13–0.40% of the 95th percentile total dietary intake for similar age ranges (Table 5). As expected, the margin of safety for total dietary intake is lower compared with drinking water, but acceptable (>1) using the most conservative oral toxicity benchmark of 16 µg/kg-bw/day that includes an uncertainty factor of 300. The margin of safety for the average dietary intake ranges from 7.2 to 36 and from 4.4 to 13 for the 95th percentile ranges (Table 5).

To estimate dietary exposure to a particular chemical, a sufficiently large database of chemical concentrations in food along with dietary consumption patterns is needed. This often requires an evaluation of numerous studies to determine exposure. Biomonitoring data on the other hand provide direct estimates of internal dose that represent all potential sources and routes of exposure. The WHO recently evaluated BPA biomonitoring data from North America, Europe, and Southeast Asia. The WHO reported that average urinary BPA concentrations (representing free and conjugated BPA) were similar across regions and in the range of approximately 1–3.7 µg/l. They estimated daily exposure by back-calculating from urinary BPA concentrations by multiplying by age-specific urinary output and dividing by body weight giving median exposure estimates of 0.07 µg/kg-bw/day, 0.12 µg/kg-bw/day, 0.07 µg/kg-bw/day for children aged 1–5 months, 3–5 years, and 6–11 years, respectively, and 0.05 µg/kg-bw/day for the general population aged 6–60+ years. The 95th percentile values were 1.61 µg/kg-bw/day, 0.78 µg/kg-bw/day, 0.31 µg/kg-bw/day, and 0.27 µg/kg-bw/day for the same age groups, respectively. These exposure estimates are 2–31-fold lower than the estimates based on dietary exposure. The margin of safety for BPA intake, back-calculated from the biomonitoring data, ranges from 130 to 320 for the median values and 10 to 59 for the 95th percentile values (Table 5). Compared with the intakes calculated from the biomonitoring data, drinking water contributes very little to overall exposure. The 50th percentile drinking water intake is only 0.4–2.8% of the 50th percentile intake based upon biomonitoring data, and the 95th percentile drinking water intake is only 0.5%–1.2% of the 95th percentile intake based upon biomonitoring data, for similar age ranges (Table 5).

Krishnan et al. recently developed a biomonitoring guidance value for BPA termed the biomonitoring equivalent. The

### Table 5. Estimated intakes of bisphenol A and margins of safety.

| Drinking water intake | Calculated intakes of BPA µg/kg-bw/day | Margin of Safetya |
|-----------------------|----------------------------------------|-------------------|
|                       | 50th percentile | 95th percentile | 50th percentile | 95th percentile |
| 3 to <6 months        | 0.0020         | 0.0039          | 8200           | 1100            |
| 3- to 6-year olds     | 0.00053        | 0.0031          | 30,000         | 4100            |
| 6- to 11-year olds    | 0.00042        | 0.0033          | 38,000         | 5200            |
| Adult                 | 0.00045        | 0.0033          | 36,000         | 4900            |

| Total intake estimated from dietary exposureb |                  |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|------------------|
| 0 to 6-month old                            | 2.2c             | 3.6              | 7.2              | 4.4              |
| 6-month to 3-year olds                      | 0.55d            | 2.3              | 29               | 7.0              |
| 3-year olds to adult                        | 0.45d            | 1.2              | 36               | 13               |
| adults                                      | 0.9f             | 2.6              | 18               | 6.2              |

| Total intake estimated from biomonitoring dab |                  |                  |                  |                  |
|----------------------------------------------|------------------|------------------|------------------|------------------|
| 1- to 5-month olds                           | 0.07d            | 1.61d            | 230              | 10               |
| 3- to 5-year olds                            | 0.12             | 0.78             | 130              | 21               |
| 6- to 11-year olds                           | 0.07             | 0.31             | 230              | 52               |
| 6- to >60-year olds                          | 0.05             | 0.27             | 320              | 59               |

aThe toxicological benchmark of 16 µg/kg-bw/day was used for margin of safety (MOS) determinations. The target MOS is 1 as the associated uncertainty factors (e.g., inter- and intra-species variability) are included within the derivation of benchmark.
bSource, WHO.\[22\]
cThe mean values reported by WHO were used.
dTwo values were given based on differences in urine volume; the greater value is used here.\[22\]
biomonitoring equivalent is defined as “as the concentration or range of concentrations of chemical in a biological medium (blood, urine, or other medium) that is consistent with an existing health-based exposure guidance value such as a reference dose or tolerable daily intake”. The biomonitoring equivalent is derived using chemical-specific pharmacokinetic data to translate the existing toxicological benchmark (used as the basis for the guideline value) to an internal dose in humans. The advantage of this approach is that the biomonitoring equivalent can be compared directly with the biomonitoring data without having to back-calculate to an exposure dose using urinary output and body weight. For BPA, Krishnan et al. determined urinary-based biomonitoring equivalent values of 1–2 mg/l derived from Health Canada’s provisional tolerable daily intake and US Environmental Protection Agency’s reference dose/European Food Safety Authority’s tolerable daily intake, respectively. Based upon the urinary BPA concentrations presented by the WHO that ranged from <0.45 µg/l to 3.7 µg/l for the median and from 10.13 µg/l to 22.9 µg/l for the 95th percentile and using the lower biomonitoring equivalent value of 1 mg/l, margin of safety values range from 22.9 to 1 mg/l and 22.9 to 0.19 mg/l for the 95th percentile concentration was 0.19 mg/l (i.e., the maximum concentration quantified in our study). In Asia, where the data were not limited by elevated detection limits, the highest concentration in drinking water was 0.026 µg/l and the 95th percentile concentration was 0.19 µg/l. A comparison of the calculated intake of BPA via ingestion of drinking water with the intake back-calculated from urinary biomonitoring data shows that drinking water represents 2.8% of the total intake with a margin of safety (using the lowest available oral toxicity benchmark) >1100 for all age groups.

CONFLICT OF INTEREST

The authors are either employed by or have provided consulting services for companies that produce and sell BPA as well as certain other products that contain BPA. KEC and CAS are independent contractors who have worked for government and industry. SGH is employed by ACC and represents the Polycarbonate/BPA Global Group.

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