

Article

# Exposure to BPA in Children—Media-Based and Biomonitoring-Based Approaches

Krista L.Y. Christensen \* and Matthew Lorber

National Center for Environmental Assessment, Office of Research and Development, United States Environmental Protection Agency, Washington, DC 20460, USA; E-Mail: lorber.matthew@epa.gov

\* Author to whom correspondence should be addressed; E-Mail: christensen.krista@epa.gov; Tel.: +1-703-347-0185; Fax: +1-703-347-8622.

Received: 25 February 2014; in revised form: 27 March 2014 / Accepted: 3 April 2014 / Published: 17 April 2014

Abstract: Bisphenol A (BPA) is used in numerous industrial and consumer product applications resulting in ubiquitous exposure. Children's exposure is of particular concern because of evidence of developmental effects. Childhood exposure is estimated for different age groups in two ways. The "forward" approach uses information on BPA concentrations in food and other environmental media (air, water, etc.) combined with average contact rates for each medium. The "backward" approach relies on urinary biomonitoring, extrapolating backward to the intake which would have led to the observed biomarker level. The forward analysis shows that BPA intakes are dominated by canned food consumption, and that intakes are higher for younger ages. Mean intake estimates ranged from ~125 ng/kg-day for 1 year-olds to ~73 ng/kg-day among 16-20 years olds. Biomonitoring-based intakes show the same trend of lower intakes for older children, with an estimate of 121 (median) to 153 (mean) ng/kg-day for 2-6 years, compared with 33 (median) to 53-66 (mean) ng/kg-day for 16-20 years. Infant intakes were estimated to range from ~46 to 137 ng/kg-day. Recognizing uncertainties and limitations, this analysis suggests that the "forward" and "backward" methods provide comparable results and identify canned foods as a potentially important source of BPA exposure for children.

Keywords: biomonitoring; BPA; exposure; children

#### 1. Introduction

Bisphenol A (BPA) is a high production volume chemical [1] which is used in numerous industrial and consumer product applications [2]. Exposure is nearly ubiquitous; in the United States (US), the 2009–2010 National Health and Nutrition Examination Survey (NHANES) found that nearly 90% of individuals aged 6 years and older had detectable BPA in their urine [3]. Urine levels have declined over time in the NHANES surveys (2003–2010), but levels in children aged 6–11 years remain comparable to or higher than those in adolescents and adults [4]. The near-ubiquitous exposure to BPA is of concern because animal and human studies have identified potential health effects associated with BPA exposure, and many of these focused on adverse effects of exposure during fetal development. For example, a 2007 review of rodent studies found convincing evidence of developmental exposure that affected the brain, male reproductive system, metabolism, and potentially also the female reproductive system [5]. Thus, it is important to characterize children's exposure to BPA.

Exposure to contaminants such as BPA can be estimated in two different ways. The first ("forward") approach uses information on BPA concentrations in food and other environmental media (air, water, *etc.*) combined with average contact rates for each medium. The second ("backward") approach relies on urinary biomonitoring data and dosimetry information to "back-calculate" the intake which would have led to the observed biomarker level. Diet has been cited as the primary source of non-occupational BPA exposure [2,6,7]; thus when using the forward approach, it is particularly important to capture dietary sources of BPA. In this study we survey the literature on BPA exposure for children, focusing on data from the United States. We focus on data on BPA levels in food and environmental media, as well as biomonitoring data on urinary levels among children.

Previous studies using the forward approach to study BPA exposure in the general population have reported estimated BPA intakes of 30 to 60 ng/kg-day [8,9] to 1400 ng/kg-day for adults consuming canned foods (a high exposure scenario) [10]. These and other studies have also concluded that the major route of exposure is dietary [7–11]. However, other studies have also identified the following as potential sources of BPA exposure: some dental sealants [12], thermal paper products (e.g., receipts) [13,14], cosmetics [2,15,16], dust [11,17,18], medical interventions [19–21], and indoor air [8,11].

For BPA, the most common biomarker is its presence in urine. Backward approaches for estimating dose extrapolate from urine measurements of BPA to estimate the amount of total BPA exposure (from all routes) to which individuals were exposed. Studies which have used this method to estimate BPA exposure reported average (mean, median, or other central tendency) intakes ranging from ~20 to 70 ng/kg-day among adults in the US and Japan [7,22–25], 40 ng/kg-day among students (aged 20–29 years) in Germany [26], 55 ng/kg-day among children ages 2–14 years in Germany [27], and 70 ng/kg-day among US girls aged 6–8 years [7,28].

In this paper, we derive both forward and backward based intake estimates for the following age groups: 1 year, 2 years, 3–5 years, 6–10 years, 11–15 years, and 16–20 years. Much of the core data used in this assessment was previously gathered for a recent and comprehensive European Food Safety Authority (EFSA) report [16], and in this paper we focus on the studies identified in this report from the U.S. and North America. Finally, we summarize data available to characterize infant (0–1 year) exposures including intake estimates derived by others.

#### 2. Experimental Section

I. Body weight (kg), BW

II. Surface area (m<sup>2</sup>), SA

11.4

0.53

13.8

0.61

### 2.1. Forward Based Intake Estimation

BPA exposure from non-food media was determined by combining published information on BPA concentrations in each media type (dust, air, and drinking water) with age-group specific contact rates for each medium [29]. Other exposure pathways that have been identified for BPA (such as cosmetics, thermal paper and dental sealants) are not included in this analysis, as we assume that these pathways are not expected to be a major contribution for children's exposure to BPA; the implications of this assumption are discussed later in this paper. BPA exposure to dust was included while exposure to soil was not considered. This is because BPA concentrations are expected to be much lower if at all present in soil as compared to dust. For example, Wilson et al. [11], who provided results from environmental sampling at the North Carolina and Ohio daycare locations where BPA urine data was obtained (discussed below), did not report BPA in soil as it was found in less than 5% of soil samples, while BPA was quantified in 40% of the dust samples taken. Similarly, EFSA [16] considered dust exposures only, and not exposures to outdoor soils. As noted above, studies included were identified from the EFSA report [16], and are specific to the U.S. Table A1 provides an overview of the air, dust, and drinking water concentrations from various studies. Table 1 provides the final concentrations and the contact rates used for non-food exposures. The values in Table 1 represent the approximate midpoint of values from the relevant studies provided in Table A1.

<b>T T T T T T T T T T</b>	r , 1 , ·	1		C 1 1	· / 1 · ·		1
Ighle I	ntake equation	on and naram	eters for non	-tood media	with media	contact rates	by age group.
<b>I</b> avic 1.1	mane equain	on and param		-ioou moula	, while incura	contact rates	UV age group.

		Int	ake Equation						
$I_{\rm m} = CR_{\rm m} \times CONC_{\rm m}/BW$ for dust and water ingestion, and inhalation									
	$I_{dc} = (SA \times FR \times ADH \times ABS \times CONC_m)/BW$ for dermal contact								
		]	Definitions						
	$I_{\rm m} = {\rm Tot}$	al BPA intal	te from medium	"m" ng/kg-day					
	$I_{\rm dc} = { m Tota}$	l BPA intake	e from dermal co	ntact, ng/kg-day					
$CR_m = Contact rate$	e for medium "m"; m	ng/day for du	st ingestion; mL	/day for water ing	gestion; m <sup>3</sup> /day for	inhalation			
CONC	$C_{\rm m} = \text{Concentration fi}$	om medium	"m", ng/g for du	ıst; ng/mL for wa	ter; ng/m <sup>3</sup> for air				
	SA	= Surface are	ea that contacts t	he skin, m <sup>2</sup>					
FR = 1	Fraction of surface a	rea which is	exposed for derr	nal contact. 0.40	for all scenarios				
ADH =	Mass of dust which	adheres to sk	cin upon contact.	$mg/cm^2$ -day, 0.0	7 for all scenarios				
ABS = Of total mass of B	PA which is in dust	that contacts	the skin, the fra	ction which pene	trates the skin, 0.30	for all scenarios			
		BW=	Body weight, kg	7					
			osure Parameter						
				Value					
Description	Age 1 Year	Age 2	Ages 3 to 5	Ages 6 to 10	Ages 11 to 15	Ages 16 to 20			

18.6

0.76

31.8

1.08

56.8

1.59

71.6

1.84

	II. Co	ncentration	s and Contac	t Rates, Mean			
Description	Concentration	Age 1 Year	Age 2 Years	Ages 3 to 5 Years	Ages 6 to 10 Years	Ages 11 to 15 Years	0
Dust Ingestion (mg/day) <sup>a</sup>	50 ng/g	60	60	60	60	60	60
Dust Dermal Absorption (mg/day) <sup>b</sup>	50 ng/g	44.5	51.2	63.8	90.7	133.6	154.6
Inhalation (m <sup>3</sup> /day)	1 ng/m <sup>3</sup>	8.0	8.9	10.1	12.0	15.2	16.3
Water Ingestion (mL/day)	0.1 ng/mL	271	317	327	414	520	638
	III. B	PA Exposu	re by Pathwa	ıy, ng/kg-day			
Description	Age 1 Veen <sup>c</sup>	Age 2	Ages 3 to 5	5 Ages 6 to 1	Ages 1	1 to 15	Ages 16 to 20
Description	Age 1 Year <sup>c</sup>	Years <sup>c</sup>	Years	Years	Yea	ars	Years
Dust Ingestion	0.26	0.22	0.16	0.09	0.0	)5	0.04
Dust Dermal Absorption	0.20	0.19	0.17	0.14	0.1	2	0.11
Inhalation	0.70	0.64	0.54	0.38	0.2	27	0.23
Water Ingestion	2.38	2.30	1.76	1.30	0.9	02	0.89
IV. Total BPA Exposure from air, dust and drinking water (ng/kg-day)	3.54	3.35	2.63	1.92	1.3	35	1.27

 Table 1. Cont.

All exposure parameters were central tendency recommendations in the Exposure Factors Handbook (EPA, 2011); <sup>a</sup> Dust ingestion rates are used, rather than soil + dust, since we are only considering childhood contact with indoor dust. BPA concentrations are for dust; <sup>b</sup> The Dust Dermal Absorption , in mg/day, encompasses the first several parameters of the dermal contact equation provided above, plus conversion factors, and is calculated as: surface area (m<sup>2</sup>) \* fraction exposed for dermal contact (0.40) \* amount adhering to skin (0.07 mg/cm<sup>2</sup>-day) \* fraction absorbed through skin (0.30) \* 10,000 cm<sup>2</sup>/m<sup>2</sup>. The FR of 0.40, or 40%, corresponds approximately to the surface area of the head + arms + hands + legs + feet (feet are included to be conservative assuming that young children spend more indoor time barefoot). Amount of dust adhering to the skin is set to 0.07 mg/cm<sup>2</sup>-day, which is the average over body parts and activities for the following: residential indoors, daycare (indoor and outdoor), outdoor sports, indoor sports, activities with soil (Table 7-4 of (EPA, 2011) [29]). Fraction absorbed through the skin is set at 0.30, or 30%, based on recommendations in EFSA document (Section 4.5.2 of (EFSA 2013) [16]); <sup>c</sup>The "1 year" age group includes children aged 12–23 months, while the "2 year" age group includes children aged 24–35 months, and so on.

The food datasets include three localized market basket surveys in the US [30–33] and a total diet study for a city in Canada [34]. One of the US studies included two rounds of sampling of Dallas, Texas supermarkets in 2010 for canned and non-canned food items. The first round of sampling was reported in Schecter *et al.* [30], and the second round was reported in Schecter *et al.* [32] which also included an assessment of adult exposures to BPA combining both rounds of food sampling. The combined data set included 204 samples, 112 of which were canned and the remaining 92 representing fresh or frozen foods. Detectable BPA concentrations were present in 73% of the canned samples compared to only 7% for non-canned foods. A second regional US study focused on canned foods, with 78 canned food samples and 2 frozen food samples obtained from the Washington DC and surrounding metropolitan areas in Maryland in 2010 [31]. BPA was present in 91% of the canned food samples, and these Washington DC samples were generally higher in BPA concentration than the samples from Texas by up to an order of magnitude, with the exception of canned vegetable concentrations, which were comparable for the two locations. A third study in the US

included 267 samples from grocery stores in Albany, NY that were measured for bisphenol analogs including BPA and seven other analogs such as bisphenol F (BPF) and bisphenol S (BPS) [33]. Thirty-one of the samples were canned, and BPA was present in 27 of these (87%). Concentrations found were generally higher than those found in Texas but lower than those found in Washington DC. The final study was from Canada, and entailed collection of 154 composite food samples in Quebec City as part of a total diet study conducted by Health Canada [34]. Only the composites containing canned samples were used in this assessment, and some of these composites had both canned and non-canned foods, so a direct comparison of percent positives in canned foods is not possible with these data. Concentrations found were comparable to the US studies. A tabular summary of the canned food group concentrations from the three studies is provided in Table A2.

In order to estimate BPA intake from food, we first estimated the fraction of food (by mass) which was consumed in canned form for each age group (1 year, 2 years, 3–5 years, 6–10 years, 11–15 years, and 16–20 years of age). These fractions were developed from the 2003–2008 What We Eat in America—Food Commodity Intake Database (WWEIA-FCID) maintained by the U.S. EPA [35]. This database utilizes information from the dietary recall completed by NHANES participants (2003–2008) and the EPA "recipe" database to translate reported food consumption into consumption of agricultural food commodities, including descriptions of cooked status and food form (e.g., canned or other form). The full details of the procedure used to determine a fraction canned for our food groups is outlined in the Appendix, following Table A2 and including Tables A3 and A4.

The fraction canned ranged narrowly from 0.14 to 0.34, with a slight tendency towards higher canned fractions for higher age ranges, particularly for the 16–20 years, as compared to all other age ranges. The canned fractions were used with canned and non-canned food concentrations (shown in Table 2) to determine overall weighted food group concentrations. These were combined with age-group specific contact rates for each food group drawn from the Environmental Protection Agency's Exposure Factors Handbook (EFH) [29], to generate dietary BPA intake estimates.

**Table 2.** Bisphenol A (BPA) intake from food, recalculated using three studies for canned food concentrations. Concentrations in canned food are an average of the following studies: [32], US; [31], US; [34], Canada.

	Intake Equation							
	$I_{t} = \sum \left[ CR_{f} \times FC_{f} \times CONC_{f,c} + CR_{f} \times (1 - FC_{f}) \times \right]$	CONC <sub>f,o</sub> ]						
	$I_{\rm t}$ = Total BPA intake from all foods, ng/kg	day						
	$CR_f = contact rate for food type "f" g/kg-c$	lay						
	$FC_f =$ fraction of food type "f" that comes from ca	nned food						
$CONC_{f,c/o} =$	concentration of food type "f" from "c" canned, or	"o" other sources, ng/g						
	I. Average Concentration in Food Type, ng/g W	et Weight						
Description	Canned (from Table A2)	Other (from [32])						
Vegetables	40.5	0.04						
Fruit	2.3	0.02						
Meat	18.3	0.02						
Fish	31.5	0						
Dairy	7.5	0						

Description Vegetables

<b>ble 2.</b> <i>Cont.</i>										
Rate, Per Capita Mean										
2 1/	Ages 3 to	Ages 6 to	Ages 11 to 15	Ages 16 to						
2 Years	5 Years	10 Years	Years	20 Years						
6.7	5.4	3.7	2.3	2.3						
7.8	4.6	2.3	0.9	0.9						

Ta

II. Contact

Age

Age 1 Year

6.7

#### 7.8 Fruit 4.0 4.0 3.9 2.8 2.0 2.0 Meat 0.3 0.2 0.2 Fish 0.3 0.1 0.1 Dairy 43.2 43.2 24.0 12.9 5.5 5.5 III. Fraction of Food Eaten in Canned/Jarred form by Age Group and Food Type Ages 3 to Ages 6 to Ages 11 to 15 Ages 16 to Age 2 Years Description Age 1 Year 5 Years **10 Years** Years 20 Years 0.18 0.23 0.27 0.31 Vegetables 0.18 0.17 Fruit 0.18 0.16 0.17 0.21 0.24 0.26 Meat 0.21 0.18 0.18 0.23 0.37 0.32 Fish 0.28 0.16 0.26 0.26 0.39 0.34 0.14 0.24 0.28 Milk 0.16 0.17 0.21 IV. BPA Exposure From Food Type Results are Expressed as Canned/Other, ng/kg-day Ages 3 to Ages 6 to Ages 11 to 15 Ages 16 to Description Age 1 Year Age 2 Years **5** Years **10 Years** Years 20 Years Vegetables 48.8/0.2 46.1/0.2 39.4/0.2 34.5/0.1 25.2/0.1 28.9/0.1 2.8/0.1 2.7/0.1 2.0/0.11.4/0.03 1.7/0.03 Fruit 2.3/0.1Meat 22.0/0.1 20.8/0.1 17.7/0.1 15.5/0.1 11.3/0.04 13.0/0.04 Fish 38.0/0 35.9/0 30.6/0 26.8/0 19.6/0 22.5/0 4.7/09.1/0 8.5/0 7.3/0 6.4/05.4/0Dairy V. Total BPA Exposure From 121.8/0.5 114.4/0.5 97.7/0.4 85.5/0.2 62.6/0.1 71.8/0.1 Food, Canned/Other, ng/kg-day

# 2.2. Backward Based Intake Estimation

Two biomonitoring datasets were used to determine BPA exposure using the "backward approach" The first biomonitoring dataset is the Children's Total (Aggregate) Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study [36], conducted among 257 children aged 23 to 64 months in North Carolina and Ohio (details of the sampling procedure are found in [11]). In brief, urine samples characterized as representing a 48 h period were collected for each child during a 2-day period in 2000–2001. These samples were constructed by pooling 6 spot samples (3 per day, collected in the morning, afternoon, and evening). These samples were then analyzed for total (free plus conjugated) BPA. Total BPA excretion for the 48 h period is estimated by multiplying the BPA urine concentration (ng/mL) by an estimated urine output of 400 mL/day, the average output for children aged 1-4 years [37]. BPA excretion, corrected for body weight, was also estimated, assuming an average weight of 17.1 kg (weighted average for 23-64 months of age [29]). BPA toxicokinetic studies have shown that essentially 100% of BPA oral exposure is excreted within 48 h in urine [38], so assuming ongoing steady state exposure, daily excretion will approximately equal daily intake.

The second biomonitoring dataset is the 2009/2010 cycle of the National Health and Nutrition Examination Survey (NHANES, total number of participants = 10,537). The NHANES is a sample survey which is designed to be representative of the general (*i.e.*, civilian, non-institutionalized) U.S. population when applying the included survey weights [39]. We applied the recommended survey weighting methodology to obtain nationally representative estimates of BPA in urine, focusing on children and adolescents aged 6-20 years. BPA concentration was measured in a single urine spot sample for a random 1/3 of NHANES participants aged 6 years and older [3]. Total BPA excretion was estimated in two ways; in both cases, excretion was corrected for individual body weight as reported for each NHANES participant. First, total daily BPA excretion was estimated by multiplying BPA urine concentration (ng/mL) for each individual by assumed daily urine output (mL/day). Assumed urine output values were determined based on age as follows: 5-9 years: 500 mL, 10-14 years: 700 mL, 15-20 years: 1200 mL [37]. Second, total BPA excretion was estimated using the creatinine-correction approach [40], which necessitates individual information on both BPA and creatinine concentrations in urine (provided in the NHANES) as well as demographic characteristics. This method assumes that the ratio of creatinine to the substance of interest (i.e., BPA) is constant over the course of a day, for a given individual. By estimating total daily creatinine excretion, the total daily BPA excretion can be inferred. For the NHANES data, total daily creatinine excretion was estimated using the equations of Mage et al., which incorporate demographic characteristics such as sex, age, and height [41]. Again, it was assumed that all ingested BPA was excreted in urine, and that daily excretion equals daily intake.

### 2.3. Infant Exposures

There are few studies providing data on BPA exposure in infants. We used information from the EFSA report [16] which provided forward-based intake estimates, and data from three published studies on BPA urine concentration among US infants [42–44], to characterize BPA exposure in this age group. One study was conducted among very young infants aged 7–44 days [44], while the other two were conducted among older infants aged 2–15 months [43] or 12 months [42]. Total daily BPA excretion was estimated by multiplying BPA urine concentration ( $\mu$ g/L) reported in each study, by estimated daily urine output (L/day), and normalizing for body weight (age-appropriate values taken from the EFH [29]). Urine output values were as follows: <1 year: 300 mL (0.3 L), 1 year: 400 mL (0.4 L) [37].

#### 3. Results and Discussion

#### 3.1. BPA Intakes from Non-Food Media

U.S. studies on BPA concentration in non-food media are summarized in Table A1. Media examined include indoor air (central tendency levels ranging from <LOD (0.8 to 0.9) to 1.8 ng/m<sup>3</sup>), outdoor air (central tendency levels ranging from <LOD (0.8 to 0.9) to 1.0 ng/m<sup>3</sup>), dust (central tendency levels of  $\sim$ 40 and 422 ng/g in two studies), and drinking water (maximum reported concentration of 0.2 ng/mL in one study). The final values selected were combined with age-specific media contact rates, as provided in Table 1. Intakes from these non-food pathways was very low; dust ingestion and dermal absorption, and inhalation, each contributed <1 ng/kg-day for all the age groups. The largest contribution was from water ingestion, and these intakes were inversely related to age (1 year olds:

average water ingestion intake of 2.38 ng/kg-day, compared to 0.89 ng/kg-day for 16–20 year olds). Similarly, total BPA intake from these non-food pathways was highest for the youngest children (3.54 ng/kg-day for 1 year olds and 3.35 for 2 year olds) and thereafter decreased with age.

#### 3.2. BPA Intakes from Food

BPA concentrations measured in food ranged from 2.3 ng/g for fruit to 40.5 ng/g for vegetables. Fish concentrations were comparable to vegetables at 31.5 ng/g, followed by meat concentrations at 18.3 ng/g and dairy at 7.5 ng/g. These food concentrations were combined with average intakes to derive age-specific food intakes, as shown in Table 2. Estimated BPA intakes varied by age group, with the highest estimated intakes for ages 1 year and 2 years, at 121.8 and 114.4 ng/kg-day respectively, and the lowest for older children and adolescents aged 11–15 years and 16–20 years, at 62.6 and 71.8 ng/kg-day, respectively. In each age group, the largest contributor was vegetables, with fish intake the second highest, and fruit the lowest. Food intakes were overwhelmingly dominated by canned foods, with foods in "other" packaging explaining <1% of food intakes.

#### 3.3. BPA Intakes Derived from Biomonitoring Data

As outlined in the Methods section, BPA biomonitoring data for children were available for two datasets: the CTEPP study of children aged 23 to 64 months conducted in 2000–2001, and the 2009/2010 NHANES data for children and adolescents aged 6–20 years.

In the CTEPP data, there was one outlier (a sample from North Carolina daycare) with a very high urine BPA concentration of 211 ng/mL, in comparison to a median of 5.15 ng/mL in the remaining 142 samples. This outlier was excluded from further analysis. The median total BPA daily excretion was 121 ng/kg-day, with a 95th percentile of 453 ng/kg-day for the age range 2–6 years (Table 3, with additional details in Table A5).

In the 2009/2010 NHANES data, the youngest ages included in the sample of individuals with urine BPA concentrations measured was 6 years. In the NHANES, there were notable differences in urine concentration by age group (Table 3, with additional details in Table A6).

Higher urine concentrations were seen for older children (medians of 2.2 ng/mL for 11–15 and 16–20 years), with slightly lower concentrations for children aged 6–10 years old (median of 1.7 ng/mL). However, on a body weight basis, the central tendency of intakes characterized by the median were comparable among the three age ranges: 31 (volume-based) and 43 (creatinine based) ng/kg-day for ages 6–10 years, 29 (volume) and 33 (creatinine) ng/kg-day for day for ages 11–15 years, and 34 (volume) and 33 (creatinine) ng/kg-day for ages 16–20 years. The 95th percentiles were highest for ages 6–10 years, 87 (volume) and 97 (creatinine) ng/kg-day, compared to 66 (volume) and 53 (creatinine) ng/kg-day for ages 16–20 years.

Age Range	Central Tendency, Mean and/or Median	95th	Description
0–1	46 (mean) [44] 64 (mean) [43] 137 (median) [42]	772 [42], 1796 [43]	[42–44] Also see Table A7
1–5	mean = 153; median = 121	453	[36]; Table A5 Children's study in OH and NC, ages 23 to 64 months, $n = 142$
6–10	mean = 87–97; median = 31–43	185–187	[39]; Table A6 NHANES 2009–2010 cycle. Range provided because of different calculation methods: lower value based on urine volume, higher based on creatinine.
11–15	mean = 50–65; median = 29–33	160–162	[39]; Table A6 NHANES 2009–2010 cycle. Ranges provided because of different calculation methods: lower value based on urine volume, higher based on creatinine.
16–20	mean= 53–66; median = 33–34	135–193	[39]; Table A6 NHANES 2009–2010 cycle. Ranges provided because of different calculation methods: lower value based on urine volume, higher based on creatinine.

Table 3. Summary of intakes derived from biomonitoring data (intakes in ng BPA/kg-day).

#### 3.4. Infant Data

Specifically for infants and young children, BPA concentrations in breast milk, colostrum and formula are also of interest when estimating dietary exposure (Table A8). Only one U.S. study reported colostrum levels of BPA, from mothers of premature infants [21]. The geometric mean level was 0.7  $\mu$ g/L in this study, considerably lower than an overall average calculated from multiple studies in the EFSA report of 3.0  $\mu$ g/L [16]. For mature breast milk (*i.e.*, not colostrum), two U.S. studies reported median values of 1.1 [45] and 1.3 [21]  $\mu$ g/L; notably, one of these excluded two very high values (>200  $\mu$ g/L) from the analysis. A third study reported a range of 0.73–1.62  $\mu$ g/L among four samples, but noted that these samples may have been contaminated [46]. These values are similar to but slightly higher than, the EFSA average of 0.9  $\mu$ g/L [16]. Regarding formula, two North American studies reported rather high mean BPA concentrations of just under 6  $\mu$ g/L in canned liquid formula [47,48], and one study reported a lower median of 1  $\mu$ g/L [30]. The one U.S. study examining powdered formula detected BPA in only one of fourteen samples analyzed [47]; the EFSA document estimated an average of 0.3 ng/g for the combination of canned and powdered formula [16].

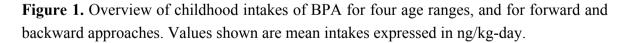
The EFSA document provided estimates of BPA intakes for infants. Using concentrations from around the world, not just the U.S., they assigned a concentration of 0.9 ng/g in breast milk. Assuming a breast milk intake of 150 g/kg-day for infants aged 0–3 months and 132 g/kg-day for infants aged 4–6 months, they found an average BPA intake estimate of 135 ng BPA/kg-day for infants aged 0–3 months, and 119 ng BPA/kg-day for infants aged 4–6 months. There was relatively little information on BPA concentrations in formula, but for canned powdered formula, data were available to estimate an average dietary exposure of 36 ng/kg-day for infants aged 0–3 months (based on BPA concentrations in formula and water of 0.3 ng/g and 0.2 ng/g, respectively).

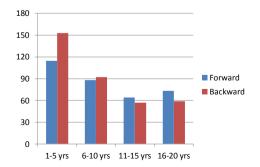
Biomonitoring data for U.S. infants is summarized in Table A7. From the three studies of urine BPA concentrations in US infants, the median daily excretions, assumed as noted earlier to be equal to intakes, ranged from 63.5 ng/kg-day [43] to 137 [42] among the older infants; the 95th percentile of excretion was notably higher at 772 [42] and 1796 ng/kg-day [43]. Excretion was somewhat lower for the youngest infants, with a geometric mean of 45.8 ng/kg-day [44], although this was based on a relatively small sample of 12 infants.

#### 4. Conclusions

BPA exposure is ubiquitous in the general population, due to its presence in consumer products and environmental media. We used information from published studies and biomonitoring datasets to estimate BPA exposure from food and non-food media among children, focusing on studies conducted in the U.S. In forward-based intake estimates, we found that in general, intake was dominated by food sources, as has also been reported in previous studies [2,6,7]. Intake from environmental media including dust, air and drinking water were minimal (~1 to 3 ng/kg-day, depending on age group). Food accounted for ~60–120 ng/kg-day of BPA intake, and BPA intake was highest for the youngest age groups. For these food estimates, canned food explained essentially the entire exposure, with only <1% of food exposures coming from non-canned foods.

A similar pattern of higher intakes for younger ages was seen when estimating BPA intake from biomonitoring (urine concentration) data. Median intakes of about 120 ng/kg-day were determined for an experimental cohort of children aged 2–6. In the nationally representative NHANES study population, median intakes were fairly comparable for children between 6 and 20 years of age, but average daily BPA intake was highest for children aged 6–10 years, and decreased for older children and adolescents. Finally, although data on infants is limited, three studies supported estimated average BPA intake estimates ranging from 46 to 137 ng/kg-day, substantially higher than seen in older children in the NHANES study. It is not surprising that younger children may have higher BPA exposure compared to older children or adults, given that they consume more food and drink on a per body weight basis. For example, children aged 1–2 years consume on average 113 g/kg-day of food, compared with 28 g/kg-day for adolescents aged 16–20 years [29]. Given that the main source of BPA exposure appears to be dietary, this naturally leads to the possibility of higher BPA exposure for younger children.





Mean biomonitoring-based intakes from Table 3 were used in Figure 1 because they were most comparable to the forward based intakes. For the forward based approach, the contact factors in EPA's Exposure Factors Handbook [29] are mean values for the age groups, not medians. In addition, the concentrations used in the forward analysis were based on the means from three studies rather than the medians from these studies. While the forward based intakes for the age range of 1–5 years was presented as a mean, in fact there was a declining trend in the analysis with the highest intake calculated at 1 year at 122 ng/kg-day, declining to 115 ng/kg-day for age 2, to 98 ng/kg-day for the 3–5 age range.

In any case, Figure 1 shows that the forward and backward-based analyses are quite consistent. Obviously, there are uncertainties in both the forward and backward-based estimates. The backward estimate for the youngest age range was based on a limited sample size (n = 142) from two geographic locations. As well, the procedure to estimate each child's intake used constant values for a daily volume of urine excretion, which clearly varies by individual. Three of the four North American food surveys used to determine a representative food concentration were local grab samples from supermarkets. As seen in Table A2, there was generally about an order of magnitude difference in the highest and lowest average survey concentration found within each food category. For example, the average BPA concentration in canned meat from one survey was 2 ng/g (sample size n = 38) while it was 58 ng/g (n = 17) in another. The assignment of the canned fraction parameter is uncertain as well. In the WWEIA-FCID database, canned is defined as follows, "a canned food is one preserved by application of heat and formation of an hermetic or airtight seal on the container in which the food is stored. Generally foods treated in this manner are available to consumers in cans, bottles and jars." By this definition, there may be some overestimation of the "canned fraction", which is strictly canned foods. Some discrepancies can be seen with other independently derived canned fractions. For example, the USDA [49] derived a canned fraction for fruit of 0.06 based on their Economic Research Service (ERS) Food Availability data base. This compares to the range of 0.16 to 0.24 derived in this study. The USDA [49] estimate for canned vegetables of 0.24 was consistent with the range of 0.17 to 0.31 found in this study. Schecter et al. [32] used the ERS database further to determine a canned fraction of 0.24 for fish for their BPA exposure assessment, and this is similar to the 0.16 to 0.34 range derived in this assessment. In addition, we did not consider some food items/groups such as canned soda—this could lead to an underestimate of BPA dietary intake, particularly for older age groups.

Nonetheless, the consistency between the backward and forward estimates does suggest general validity of the approach and the results for BPA exposure among children in the US. Given that, this analysis shows the importance of canned food consumption for childhood exposures to BPA. Non-food exposures accounted for only about 1.4% to 2% of the total intakes for the various age ranges, and non-canned foods accounted for <1%, suggesting that around 97% to 98% of all exposures of children to BPA are due to consumption of canned foods (data not shown). Other exposure pathways that have been identified for BPA, such as cosmetics, thermal paper and dental sealants. Using data from around the world, EFSA estimated an average exposure of 18 ng/kg-day for thermal paper contact (credit card receipts, *etc*) and 1.2 ng/kg-day for cosmetics [16]. Thus, these exposures (particularly cosmetics) are relatively low compared to those estimated from food pathways.

For context, EFSA estimated an average dietary exposure (form food and beverages) of 290 ng/kg-day for children aged 3-10 years, and 159 ng/kg-day for teenagers aged 10-18 years (the two older age groups most likely to have contact with cosmetics and thermal paper) [16]. Of course, there are individuals for whom these pathways may play a much larger role-for example, teenagers working in retail may have very high exposure to thermal paper. However, on the population level, the contribution of non-food pathways to total exposure appears to be relatively low. It is important to note that in terms of toxicity, dermal exposures may be particularly important in that, while comprising a smaller proportion of total BPA exposure, such exposures may result in a higher proportion of unconjugated BPA compared to non-dermal exposure routes [50], leading to different toxicity. Dental sealants are another potential source of exposure, as reviewed in [2]. However, the studies reviewed here generally focused on short-term exposure potential (*i.e.*, one to several hours following the dental procedure). One study which followed patients for a longer period of time found BPA in saliva at 1 and 3 h post-application, but did not detect any BPA in saliva collected 1, 3 or 5 days post-application [51]. However, the short-term exposures could be quite high depending on the type of sealant used; one study found urine levels of up to 27.3 ng/mL in treated patients [12], compared to a median BPA concentration of 2.0 ng/mL in 2009–2010 NHANES participants aged 6–20 years (Table A6).

Overall, in the US, exposure of adults to BPA is lower than that of children. Assessing intakes using the same NHANES cycle of October 2009 as was used for children, we estimate a mean BPA intake of 83 (creatinine-based) to 88 (urine volume based) ng/kg-day, and a median BPA intake of 33 (creatinine-based) to 32 (urine volume based) ng/kg-day for all individuals over the age of 20 years. This is very similar to the intakes for the age range of 16–20 years, which had a mean of 53 (creatinine based) and 66 (urine volume based) ng/kg-day and a median of 33 ng/kg-day, but it is lower than all other age ranges. While similar pathways for BPA exposure may come into play for adults as for children, the importance of the food pathway may be less for adults. We continued the assessment of canned fractions using the WWEIA-FCID database (Table A4) and found that the fraction of food consumed as canned declines by about 0.1 from the 16-20 years age group to the adult category, across all food groups. One can surmise that proportionally, BPA exposures from food decline while other pathways for BPA exposure become more prominent for adults. In addition to differences by age, there may also be important differences in exposure pathways and levels according to demographic factors such as socio-economic status or race/ethnicity (e.g., biomonitoring data from Mexican-American children presented in [52,53]). However, due to lack of data on exposure sources and pathways according to these factors, we were not able to examine them in this analysis.

BPA is a ubiquitous exposure, and this analysis shows that exposures may be substantially higher among younger children compared older children. Moreover, the relative importance of different sources of exposure may depend on age; among children, the vast majority of BPA exposure appears to be from canned food. Given the concerns over potential adverse health effects related to BPA exposure, it is important to continue to monitor BPA exposure levels and identify potentially mitigatable sources.

### Acknowledgments

The authors would like to acknowledge Linda Phillips for valuable technical advice.

### **Author Contributions**

Both authors (KYC and ML) worked collaboratively on all aspects of the manuscript.

#### Abbreviations

BPA, bisphenol A; CTEPP, Children's Total (Aggregate) Exposure to Persistent Pesticides and Other Persistent Organic Pollutants; EFSA, European Food Safety Authority; EPA, Environmental Protection Agency; LOD, limit of detection; NHANES, National Health and Nutrition Examination Survey; WWEIA-FCID, What We Eat in America—Food Commodity Intake Database.

#### Appendix

The studies described in Table A1 come from the European Food Safety Authority (EFSA) draft Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs—Part: exposure assessment [16]. The studies included here report media BPA concentrations in the U.S.

Media (Units)	Results	Reference and Details			
		[11]; USA (NC, OH); 2000–2001			
	Median: <lod (0.9)-1.8;<="" td=""><td>CTEPP study of 257 preschool children and their primary adult</td></lod>	CTEPP study of 257 preschool children and their primary adult			
	Range: <lod (0.9)–1.8,<="" td=""><td>caregivers; 295 samples collected over 48 h period in 4 groups: NC,</td></lod>	caregivers; 295 samples collected over 48 h period in 4 groups: NC,			
	Range. $<$ LOD (0.9)–193	home; NC, daycare; OH, home; OH, daycare. Percent detections ranged			
		from 45%–73% depending on sampling site.			
Indoor air	Median: <lod (0.8)<="" td=""><td>[54]; USA (CA)</td></lod>	[54]; USA (CA)			
$(ng/m^3)$	Max: 22	Study of 50 non-smoking homes in two CA cities; number of samples and			
(lig/iii )	WIUX, 22	LOD not reported.			
	Geometric Mean: 1.5 (home),	[36]; USA (OH)			
	1.1 (daycare);	Subset of participants in the CTEPP study; 81 preschool children a			
	Range: <lod (0.6)–30.3="" (home),<br=""><lod (0.6)–7.4="" (daycare)<="" td=""><td>their primary adult caregivers; 103 samples collected over</td></lod></lod>	their primary adult caregivers; 103 samples collected over			
		48 h period in 2 groups: home and daycare. Percent detections ranged			
		from 68%–73% depending on sampling site.			
		[11]; USA (NC, OH); 2000–2001			
	Median: <lod (0.9);<br="">Range: LOD (0.9)–51.5</lod>	CTEPP study of 257 preschool children and their primary adult			
		caregivers; 257 samples collected over 48-h period in 4 groups: NC,			
	Kuige. EOD (0.9) 51.5	home; NC, daycare; OH, home; OH, daycare. Percent detections rate			
		from 31%-44% depending on sampling site.			
Outdoor air	Geometric Mean: 1.0 (home),	[36]; USA (OH)			
$(ng/m^3)$	0.8 (daycare);	Subset of participants in the CTEPP study; 81 preschool children and			
(ing/inf)	Range: <lod (0.6)–19.0="" (home),<="" td=""><td>their primary adult caregivers; 97 samples collected over 48 h period in 2</td></lod>	their primary adult caregivers; 97 samples collected over 48 h period in 2			
	<pre><lod (0.6)-6.9="" (daycare)<="" pre=""></lod></pre>	groups: home and daycare. Percent detections ranged from $40\%$ – $44\%$			
		depending on sampling site.			
	Median: <lod (0.8)<="" td=""><td>[54]; USA (CA)</td></lod>	[54]; USA (CA)			
	Maximum: 1.7	Study of 50 non-smoking homes in two CA cities; number of samples and			
		LOD not reported.			

Table A1. U.S. studies reporting BPA concentrations in non-food media.

Media (Units)	Results	Reference and Details			
	Median: 422; Range: <0.5–10,200	[55]; USA (KY, NY); 2006, 2010 Study of 48 houses in KY and NY, and 6 laboratories in KY; 50 indoor dust samples, along with 4 clothes dryer lint samples and 2 refrigerator dust samples collected (total $n = 56$ ). Percent detection was 95%			
Dust (ng/g)	Median: <lod (4)–30.8<br="">Range: <lod (4)–707<="" td=""><td colspan="3">[11]; USA (NC, OH); 2000–2001 CTEPP study of 257 preschool children and their primary adult caregivers; 267 samples collected over 48 h period in 4 groups: NC home; NC, daycare; OH, home; OH, daycare. Percent detections rang from 25%–70% depending on sampling site.</td></lod></lod>	[11]; USA (NC, OH); 2000–2001 CTEPP study of 257 preschool children and their primary adult caregivers; 267 samples collected over 48 h period in 4 groups: NC home; NC, daycare; OH, home; OH, daycare. Percent detections rang from 25%–70% depending on sampling site.			
	Geometric Mean: 40.4 (home), 38.9 (daycare); Range: 19.6–589 (home), 20.0–124 (daycare)	[36]; USA (OH) Subset of participants in the CTEPP study; 81 preschool children and their primary adult caregivers; 99 samples collected over 48 h period in 2 groups: home and daycare. Percent detections ranged from 43%–70% depending on sampling site.			
Drinking water (ng/g)	Maximum: 0.2	[56]; USA (NJ); 2003 Samples collected from a drinking water treatment plant, over a 3-week period. Twelve samples collected at each of 6 sites in the plant. Detection rate was 100% in source water and 17% in treated (finished) water.			

 Table A1. Cont.

The studies described in Table A2 are Canadian and U.S. studies reporting on BPA concentrations in canned food items (means calculated assuming non-detected concentrations = 0).

Food	Final Selected	Literature Other Data		Location and Specific Foods <sup>2</sup>		
Category	Value, ng/g Whole <sup>1</sup>	% Pos (n) Mean		-		
		100 (6)	23	Canadian, beans, beets, peas, tomatoes		
Vagatablag	12 7	92 (39)	20	U.S. (1), green beans, corn, peas, tomatoes, mixed		
Vegetables	43.7	96 (25)	88	U.S. (2), green beans, corn, tomatoes, peas, misc Veg (wax beans, spinach, stir fry, oyster mushrooms, almond jelly)		
		50 (4)	1	Canadian, cherries, pineapple		
Fruit	2.1	22 (9)	0.3	U.S. (1), cling peaches, oranges, pineapple		
		57 (14)	5	U.S. (2), fruit cocktail, pineapple, sliced peaches		
		100 (1)	10	Canadian, luncheon meats		
Meat	23.3	82 (38)	2	U.S. (1), chicken (soup, chunk), beef (chili, corned), Spam, ham spread		
		100 (17)	58	U.S. (2), pork & beans, chili		
		100 (1)	106	Canadian, unspecified		
Fish	39.7	58 (12)	1	U.S. (1), tuna, sardines		
		100 (6)	100 (6) 12 U.S. (2), tuna, albacore, mad			
Deim	7.5	100 (1)	15	Canadian; evaporated milk		
Dairy	7.5	0 (8)	ND (0.4)	U.S. (1), snacking cheese		

Table A2. U.S. and Canada studies \* reporting BPA concentrations in canned food.

<sup>1</sup> The final selected values were calculated as the mean of mean study values, <sup>2</sup> Canadian study: [34] U.S. study (1): [32] U.S. study (2): [31].

The following is a description of how fractions of food groups consumed as canned, were derived. As noted in the Methods section, the "food form" information field specifies which of these six food forms best describes the given food item: (1) not applicable; (2) fresh or not specified; (3) frozen; (4) dried; (5) canned; and (6) cured, pickled, smoked, or salted. The procedure to determine a fraction canned for our food groups followed this four-step procedure:

- 1 Every individual record in the WWEIA-FCID file "Commodity\_CSFFM\_Intake\_0308.cvs" contains information on participant ID, and reported consumption (by mass) for a single food item, categorized according to a numerical "agricultural food commodity" code. The remaining variables specify the day on which the food was consumed, the food form as described above, the cooking method, and the cooked status. There are a total of 558 commodity codes in the database, which are linked to a text description in the "FCID\_Code\_Description.csv" file. We grouped these codes into the following food groups to correspond to the BPA food concentration data: vegetables, fruit, meat, fish, and dairy.
- 2 With this categorization, each record included a consumption rate for a given individual and given food item, a food group, and a food form. The records were collapsed across specific food items within each food form and food group, yielding a total consumption (by mass, for each individual) of food consumed in each form, for each food group.
- 3 Next, records were again collapsed, this time over all food forms within a food group. This yielded a total consumption (by mass, for each individual) for each food group. The total canned form of each food group (calculated in Step 2) was divided by the total amount of food in each food group (calculated in Step 3) for each individual, to calculate the fraction of food (by mass) within each group, consumed in canned form. Table A3 provides the (unweighted) number of individuals in each age group, and the number consuming any food in a given food group; note that not all individuals consumed food within each group, thus the number of individuals represented by the canned fractions is different across groups.
- 4 Finally, the median fraction of foods eaten in the canned form by surveyed individuals was summarized according to food groups and age groups (detailed results in Table A4).

Tables A3 and A4 describe data used to derive the fraction of food consumed in canned form; Table A3 shows the (unweighted) number of individuals in each age group who had any consumption of each food group. Table A4 shows the fraction of food in each food group (by mass) consumed as canned, by age group.

Table A5 shows results from the CTEPP study for BPA urine concentration and estimated BPA excretion.

Food Group	Infant (<1 Year)	Age 1 Year	Age 2 Years	Ages 3 to 5 Years	Ages 6 to 10 Years	Ages 11 to 15 Years	Ages 16 to 20 Years	Ages 21+ Years
Total Number in Age Group	1387	895	860	1642	2523	3202	2994	14,135
Eggs	427	808	802	1549	2414	3017	2798	13,298
Fish	39	130	157	283	470	587	582	4325
Fruit	1279	891	852	1626	2492	3101	2838	13,489
Grain	844	888	853	1640	2519	3195	2980	14,073
Meat	418	777	799	1535	2399	3049	2806	13,087
Milk	1218	895	860	1641	2522	3195	2982	14,071
Poultry	480	719	695	1315	2004	2429	2248	10,443
Rice	858	778	744	1421	2211	2718	2495	12,247
Vegetables	1084	895	859	1642	2523	3202	2993	14,131

**Table A3.** Number of individuals in each age group, who had any (non-zero) consumption from each food group (NHANES 2003–2008).

**Table A4.** Fraction of food group consumed canned by mass (not adjusted for body weight), by age group and food group (NHANES 2003–2008). Value in cell is median (interquartile range).

Food	Age 1 Veen	Age 2 Veens	Ages 3 to 5	Ages 6 to 10	Ages 11 to	Ages 16 to 20	Ages 21+
Group	Age 1 Year	Age 2 Years	Years	Years	15 Years	Years	Years
<b>F</b>	0.09	0.11	0.14	0.18	0.23	0.27	0.11
Eggs	(0.02–0.3)	(0.02–0.3)	(0.04–0.3)	(0.1–0.3)	(0.1–0.4)	(0.1–0.5)	(0.02–0.3)
<b>F</b> '.1	0.28	0.16	0.26	0.26	0.29	0.34	0.20
Fish	(0.1–0.7)	(0.1–0.4)	(0.1–0.5)	(0.1–0.6)	(0.2–0.5)	(0.2–0.6)	(0.2–0.5)
F :4	0.18	0.16	0.17	0.21	0.24	0.26	0.13
Fruit	(0.1–0.4)	(0.1–0.3)	(0.1–0.3)	(0.1–0.4)	(0.1–0.4)	(0.1–0.5)	(0.03–0.3)
<u> </u>	0.17	0.15	0.17	0.20	0.24	0.28	0.13
Grain	(0.1–0.4)	(0.04–0.3)	(0.1–0.3)	(0.1–0.4)	(0.1–0.4)	(0.1–0.5)	(0.02–0.3)
	0.21	0.18	0.18	0.23	0.27	0.32	0.17
Meat	(0.1–0.4)	(0.1–0.4)	(0.1–0.3)	(0.1–0.4)	(0.2-0.4)	(0.2–0.5)	(0.04–0.3)
N (* 11	0.16	0.14	0.17	0.21	0.24	0.28	0.14
Milk	(0.03-0.4)	(0.03-0.3)	(0.1–0.3)	(0.1–0.4)	(0.1–0.4)	(0.1–0.5)	(0.03–0.3)
	0.19	0.17	0.19	0.22	0.25	0.31	0.15
Poultry	(0.1–0.4)	(0.1–0.4)	(0.1–0.4)	(0.1–0.4)	(0.1–0.4)	(0.2–0.5)	(0.04-0.7)
D.'	0.19	0.17	0.17	0.22	0.27	0.29	0.15
Rice	(0.04–0.4)	(0.04–0.4)	(0.1–0.3)	(0.1–0.4)	(0.1–0.5)	(0.1–0.5)	(0.03-0.7)
¥7 . 11	0.18	0.17	0.18	0.23	0.27	0.31	0.17
Vegetables	(0.1–0.4)	(0.1–0.3)	(0.1–0.3)	(0.1–0.4)	(0.2-0.4)	(0.2–0.5)	(0.1–0.6)

**Table A5.** BPA urine concentrations and estimated daily excretions based on Children's Total (Aggregate) Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) data, North Carolina and Ohio, 2000–2001.

Group ( <i>n</i> )	Measure	Mean (SD)	Median (25th, 75th Percentiles)	95th Percentile
	BPA concentration (ng/mL)	6.5 (6.4)	5.2 (2.6, 7.7)	19.3
Total (142)	BPA excretion based on urine volume (ng/kg-day)	152.5 (149.6)	120.8 (61.0, 180.6)	452.6
	BPA concentration (ng/mL)	6.9 (6.4)	5.2 (3.8–7.9)	16.6
North Carolina, daycare (46)	BPA excretion based on urine volume (ng/kg-day)	162.1 (150.7)	120.8 (89.1–185.3)	389.3
North Carolina, daycare,	BPA concentration (ng/mL)	4.1 (2.6)	4.1 (1.6–5.7)	10.2
collected at daycare (19)	BPA excretion based on urine volume (ng/kg-day)	94.9 (61.8)	96.2 (37.5–133.7)	239.2
Newly Constinue document	BPA concentration (ng/mL)	8.9 (7.5)	7.5 (4.5–11.1)	21.2
North Carolina, daycare, collected at home (27)	BPA excretion based on urine volume (ng/kg-day)	209.3 (179.2)	175.9 (105.5– 260.3)	497.2
	BPA concentration (ng/mL)	6.6 (6.4)	5.2 (2.4–7.4)	19.8
Ohio, all (96)	BPA excretion based on urine volume (ng/kg-day)	147.9 (149.7)	120.8 (56.3–173.5)	464.3
	BPA concentration (ng/mL)	6.7 (7.4)	5.2 (2.4–7.8)	19.8
Ohio, daycare (56)	BPA excretion based on urine volume (ng/kg-day)	158.0 (173.3)	120.8 (56.3–181.7)	464.3
	BPA concentration (ng/mL)	4.3 (3.1)	3.2 (1.9-6.9)	8.8
Ohio, daycare, collected at daycare (22)	BPA excretion based on urine volume (ng/kg-day)	99.8 (72.5)	75.0 (44.6–161.8)	206.4
	BPA concentration (ng/mL)	8.4 (8.8)	5.5 (3.0–9.4)	36.2
Ohio, daycare, collected at home (34)	BPA excretion based on urine volume (ng/kg-day)	195.7 (207.3)	129.0 (70.4–220.4)	848.9
	BPA concentration (ng/mL)	5.7 (4.6)	4.8 (2.5-6.9)	16.4
Ohio, home (40)	BPA excretion based on urine volume (ng/kg-day)	133.6 (108.8)	111.4 (58.6–160.6)	383.4

Table A6 shows results from the NHANES 2009–2010 study for BPA urine concentration and estimated BPA excretion.

The studies described in Table A8 come from the EFSA draft Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs—Part: exposure assessment [16]. The studies included here report breast milk, colostrum and formula BPA concentrations in the U.S.

The studies described in Table A7 come from the EFSA draft Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs—Part: exposure assessment [16]. The studies included here report BPA urine concentrations and estimated BPA excretion among infants in the U.S.

Group ( <i>n</i> , unweighted)	Measure	Mean (SD)	Median (25th, 75th Percentiles)	95th Percentile
Total 6-20 years (870)	BPA concentration (ng/mL)	3.9 (12.4)	2.0 (1.1-3.8)	10.2
(571)	BPA excretion based on creatinine correction (ng/kg)	71.9 (270.8)	35.6 (23.1–63.0)	162.8
(863)	63) BPA excretion based on urine volume (ng/kg) 67.3 (257.6)		31.9 (16.2–57.7)	181.5
Aged 6-10 years (341)	BPA concentration (ng/mL)	4.5 (19.8)	1.7 (1.0–3.4)	9.7
(339)	BPA excretion based on creatinine correction (ng/kg)	97.2 (415.1)	42.5 (28.2–71.2)	185.3
(340)	BPA excretion based on urine volume (ng/kg)	87.0 (423.0)	30.5 (18.8–60.8)	186.6
Aged 11–15 years (281)	BPA concentration (ng/mL)		2.2 (1.0–3.5)	9.3
(232)	BPA excretion based on creatinine correction (ng/kg)	65.4 (205.1)	32.5 (17.8–56.8)	161.5
(279)	BPA excretion based on urine volume (ng/kg)	49.7 (87.8)	28.7 (13.9–51.8)	159.6
Aged 16–20 years (248)	BPA concentration (ng/mL)		2.2 (1.2–4.3)	10.9
(248)	BPA excretion based on creatinine correction (ng/kg)	53.3 (74.7)	33.2 (23.2–57.9)	134.6
(244)	BPA excretion based on urine volume (ng/kg)	65.9 (118.0)	33.8 (17.0–75.0)	193.4

**Table A6.** BPA urine concentrations and estimated daily excretions based on National Health and Nutrition Examination Survey (NHANES) data, U.S., 2009–2010. All values except n (group size) are weighted for survey sampling.

**Table A7.** BPA urine concentrations and estimated daily excretions based on published studies among infants.

Study Population	Measure	Mean (SD)	Median (25th, 75th Percentiles)	95th Percentile
[42]	BPA concentration (µg/L)		3.9 (1.8, 7.6)	22
Cincinnati, OH Mother-child pairs participating in the	BPA concentration (µg/g creatinine)		18 (9.9, 34)	91
HOMES study; data shown are for 1	Creatinine concentration (mg/dL)		19 (12, 34)	75
year olds ( $n = 213$ ) Urine samples collected during 2004–2009 at clinic or home visits	Estimated BPA daily BPA intake (ng/kg-day) *		137 (63, 267)	772

Study Population	Measure	Mean (SD)	Median (25th, 75th Percentiles)	95th Percentile
[43] Boston, MA	Total BPA concentration (µg/L)	6.0 (16.2)	1.8 (1.2, 4.4)	50.9
Mother-child pairs participating in the EARtH study; data shown are for	Free BPA concentration (µg/L)	0.5 (0.4)	<lod (<lod,<br=""><lod)< td=""><td>19.4</td></lod)<></lod>	19.4
infants 2–15 months old ( $n = 29$ ). Includes 4 sets of twins. Urine samples collected during 2006–2008 from diapers [43]	Estimated total BPA daily BPA intake (ng/kg-day) *	1800	63.5 (42, 155)	1796
F441	Glucoronidated BPA concentration (µg/L)	Geometric mean: 0.74		
[44] Baltimore, MD	Unconjugated BPA concentration (µg/L)	0.4 (95% CI: 0.3, 0.6)		
Infants 7–44 days old ( $n = 12$ )	Estimated glucuronidated BPA intake (ng/kg-day) *	46.3		

# Table A7. Cont.

\* Daily urine excretion assumed to be 300 mL/day for infants <1 year old, and 400 mL/day for children 1 year old [37]. Body weights are assumed to be 4.8 kg for infants 7–44 days old (value for birth to 1 month), 11.4 kg for 12 month olds (value for 1 to <2 years), and 8.5 kg for 2–15 month olds (average of values for 1 to <3, 3 to <6, 6 to <12, and 12 to <24 month olds) [29].

Media (Units)	Results	Reference and Details	
Colostrum (µg/L)	Average: 3.0 High: 6.6	EFSA document calculated from multiple studies ((Table 30) in [16]).	
		[21]	
	Geometric Mean: 0.7	USA; Study of mothers and their premature infants in a NICU;	
		2 samples collected at 3–5 days post partum.	
	Median: 1.1;	[45]	
	Maximum: 7.3	USA; 20 samples, BPA detected in 90%.	
	Median: 1.1;	[45]	
Mature milk (µg/L) -	Range: <lod (0.3)—<="" td=""><td>USA; Pooled milk samples from anonymous donors, <math>n = 20</math> samples with 90%</td></lod>	USA; Pooled milk samples from anonymous donors, $n = 20$ samples with 90%	
	6.3	detection rate for total BPA.	
		[21]	
	Median: 1.3	USA; Study of mothers and their premature infants in a NICU;	
		26 but two outliers of 222 and 296 removed from analysis.	
-	Average: 0.9; High: 2.6	EFSA document calculated from multiple studies (Table 30 in [16]).	
Formula—canned, liquid (μg/L )	Mean, 2007: 5.0 (milk-based), 5.8 (soy-based) Mean, 2008: 6.8 (milk-based), 5.3 (soy-based)	[48] USA and Canada; 2007–2008; Study of 21 samples stored at room temperature for 10 months (2008), in comparison with samples from same lot (but different cans) evaluate at baseline (2007). BPA increases from baseline were between 29.8% and 110%.	
	Mean: 5.74; Range: 0.56–11	[47] USA; Study of 104 formula containers representing 36 products, from across the USA. [30]	
	Median: 1.1	USA (TX); Study of 9 samples, detection rate of 33% (LOD of 0.2 $\mu$ g/L).	

Table A8. BPA concentrations in breast milk, colostrum and formula.

# **Conflicts of Interest**

The authors declare no conflict of interest.

# Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Environmental Protection Agency.

# References

- 1. Environmental Protection Agency (EPA). *Bisphenol A Action Plan*; U.S. Environmental Protection Agency: Washington, DC, USA, 2010.
- Vandenberg, L.N.; Hauser, R.; Marcus, M.; Olea, N.; Welshons, W.V. Human exposure to bisphenol A (BPA). *Reprod. Toxicol.* 2007, 24, 139–177.
- CDC Laboratory Documentation for environmental phenols, 2009–2010 NHANES. Available online: http://www.cdc.gov/nchs/nhanes/nhanes2009–2010/EPH\_F.htm (accessed on 24 October 2013).
- 4. CDC. Fourth National Report on Human Exposure to Environmental Chemicals—Updated Tables September 2012. Available online: http://www.cdc.gov/exposurereport/pdf/FourthReport\_ UpdatedTables\_Sep2012.pdf (accessed on 24 October 2013).
- Richter, C.A.; Birnbaum, L.S.; Farabollini, F.; Newbold, R.R.; Rubin, B.S.; Talsness, C.E.; Vandenbergh, J.G.; Walser-Kuntz, D.R.; vom Saal, F.S. *In vivo* Effects of bisphenol A in laboratory rodent studies. *Reprod. Toxicol.* 2007, 24, 199–224.
- 6. Kang, J.H.; Kondo, F.; Katayama, Y. Human exposure to bisphenol A. *Toxicology* **2006**, *226*, 79–89.
- 7. World Health Organization (WHO). Joint FAO/WHO Expert Meeting to Review Toxicological and Health Aspects of Bisphenol A: Summary Report including Report of Stakeholder Meeting on Bisphenol A; World Health Organization: Ottawa, Canada, 2010.
- 8. Miyamoto, K.; Kotake, M. Estimation of daily bisphenol A intake of Japanese individuals with emphasis on uncertainty and variability. *Environ. Sci.* **2006**, *13*, 15–29.
- Von Goetz, N.; Wormuth, M.; Scheringer, M.; Hungerbuhler, K. Bisphenol A: How the Most Relevant Exposure Sources Contribute to Total Consumer Exposure. *Risk Anal.* 2010, 30, 473–487.
- European Union (EU). European Union Risk Assessment Report: 4,4' ISOPROPYLIDENEDIPHENOL (BISPHENOL-A); CAS No: 80-05-7, EINECS No: 201-245-8; European Union: Luxembourg, 2003.
- 11. Wilson, N.K.; Chuang, J.C.; Morgan, M.K.; Lordo, R.A.; Sheldon, L.S. An observational study of the potential exposures of preschool children to pentachlorophenol, bisphenol-A, and nonylphenol at home and daycare. *Environ. Res.* **2007**, *103*, 9–20.
- Joskow, R.; Barr, D.B.; Barr, J.R.; Calafat, A.M.; Needham, L.L.; Rubin, C. Exposure to bisphenol A from bis-glycidyl dimethacrylate-based dental sealants. J. Am. Dent. Assoc. 2006, 137, 353–362.

- 13. Geens, T.; Goeyens, L.; Kannan, K.; Neels, H.; Covaci, A. Levels of bisphenol-A in thermal paper receipts from Belgium and estimation of human exposure. *Sci. Total Environ.* **2012**, *435–436*, 30–33.
- 14. Liao, C.; Kannan, K. Widespread occurrence of bisphenol A in paper and paper products: Implications for human exposure. *Environ. Sci. Technol.* **2011**, *45*, 9372–9379.
- Dodson, R.E.; Nishioka, M.; Standley, L.J.; Perovich, L.J.; Brody, J.G.; Rudel, R.A. Endocrine disruptors and asthma-associated chemicals in consumer products. *Environ. Health Perspect.* 2012, *120*, 935–943.
- 16. EFSA. DRAFT Scientific Opinion on the Risks to Public Health Related to the Presence of Bisphenol A (BPA) in Foodstuffs—Part: Exposure Assessment; EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); European Food Safety Authority (EFSA): Parma, Italy, 2013.
- Rudel, R.A.; Brody, J.G.; Spengler, J.D.; Vallarino, J.; Geno, P.W.; Sun, G.; Yau, A. Identification of selected hormonally active agents and animal mammary carcinogens in commercial and residential air and dust samples. *J. Air Waste Manag. Assoc.* 2001, *51*, 499–513.
- 18. Rudel, R.A.; Camann, D.E.; Spengler, J.D.; Korn, L.R.; Brody, J.G. Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. *Environ. Sci. Technol.* **2003**, *37*, 4543–4553.
- Calafat, A.M.; Weuve, J.; Ye, X.; Jia, L.T.; Hu, H.; Ringer, S.; Huttner, K.; Hauser, R. Exposure to bisphenol A and other phenols in neonatal intensive care unit premature infants. *Environ. Health Perspect.* 2009, 117, 639–644.
- Vandentorren, S.; Zeman, F.; Morin, L.; Sarter, H.; Bidondo, M.L.; Oleko, A.; Leridon, H. Bisphenol-A and phthalates contamination of urine samples by catheters in the Elfe pilot study: Implications for large-scale biomonitoring studies. *Environ. Res.* 2011, *111*, 761–764.
- Duty, S.M.; Mendonca, K.; Hauser, R.; Calafat, A.M.; Ye, X.; Meeker, J.D.; Ackerman, R.; Cullinane, J.; Faller, J.; Ringer, S. Potential sources of bisphenol A in the neonatal intensive care unit. *Pediatrics* 2013, *131*, 483–489.
- Calafat, A.M.; Kuklenyik, Z.; Reidy, J.A.; Caudill, S.P.; Ekong, J.; Needham, L.L. Urinary concentrations of bisphenol A and 4-nonylphenol in a human reference population. *Environ. Health Perspect.* 2005, 113, 391–395.
- Lakind, J.S.; Naiman, D.Q. Daily intake of bisphenol A and potential sources of exposure: 2005–2006 National Health and Nutrition Examination Survey. J. Expo. Sci. Environ. Epidemiol. 2011, 21, 272–279.
- CERHR NTP-CERHR Expert Panel Report on the Reproductive and Developmental Toxicity of Bisphenol A; National Toxicology Program, U.S. Department of Health and Human Services: Research Triangle Park, NC, USA, 2007.
- 25. Lakind, J.S.; Naiman, D.Q. Bisphenol A (BPA) daily intakes in the United States: Estimates from the 2003–2004 NHANES urinary BPA data. *J. Exp. Sci. Environ. Epidemiol.* **2008**, *18*, 608–615.
- Koch, H.M.; Kolossa-Gehring, M.; Schroter-Kermani, C.; Angerer, J.; Bruning, T. Bisphenol A in 24 h urine and plasma samples of the German Environmental Specimen Bank from 1995 to 2009: A retrospective exposure evaluation. *J. Exp. Sci. Environ. Epidemiol.* 2012, 22, 610–616.

- Becker, K.; Goen, T.; Seiwert, M.; Conrad, A.; Pick-Fuss, H.; Muller, J.; Wittassek, M.; Schulz, C.; Kolossa-Gehring, M. GerES IV: Phthalate metabolites and bisphenol A in urine of German children. *Int. J. Hyg. Environ. Health* 2009, *212*, 685–692.
- Wolff, M.S.; Teitelbaum, S.L.; Windham, G.; Pinney, S.M.; Britton, J.A.; Chelimo, C.; Godbold, J.; Biro, F.; Kushi, L.H.; Pfeiffer, C.M.; *et al.* Pilot study of urinary biomarkers of phytoestrogens, phthalates, and phenols in girls. *Environ. Health Perspect.* 2007, *115*, 116–121.
- 29. Environmental Protection Agency (EPA). *Exposure Factors Handbook, 2011 Edition. EPA/600/R-090/052F*; U.S. Environmental Protection Agency: Washington, DC, USA, 2011.
- Schecter, A.; Malik, N.; Haffner, D.; Smith, S.; Harris, T.R.; Paepke, O.; Birnbaum, L. Bisphenol A (BPA) in U.S. Food. *Environ. Sci. Technol.* 2010, 44, 9425–9430.
- 31. Noonan, G.O.; Ackerman, L.K.; Begley, T.H. Concentration of bisphenol A in highly consumed canned foods on the U.S. market. *J. Agric. Food Chem.* **2011**, *59*, 7178–7185.
- 32. Schecter, A.; Lorber, M.; Paepke, O.; Waqar, M.; Birnbaum, L.S. Exposure to Bisphenol A (BPA) in fresh, frozen and canned food from Texas, USA. *Environ. Sci. Tech.* **2013**, in press.
- Liao, C.; Kannan, K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. J. Agric. Food Chem. 2013, 61, 4655–4662.
- Cao, X.L.; Perez-Locas, C.; Dufresne, G.; Clement, G.; Popovic, S.; Beraldin, F.; Dabeka, R.W.; Feeley, M. Concentrations of bisphenol A in the composite food samples from the 2008 Canadian total diet study in Quebec City and dietary intake estimates. *Food Addit. Contam. Part A* 2011, 28, 791–798.
- Environmental Protection Agency (EPA). 2003–2008 What We Eat In America—Food Commodity Intake Database Documentation. U.S. Available online: http://fcid.foodrisk.org/docs/ WWEIA-FCID\_0308\_Background-Codebooks-ControlStats.pdf. (accessed on 1 November 2013).
- Morgan, M.K.; Jones, P.A.; Calafat, A.M.; Ye, X.Y.; Croghan, C.W.; Chuang, J.C.; Wilson, N.K.; Clifton, M.S.; Figueroa, Z.; Sheldon, L.S. Assessing the Quantitative Relationships between Preschool Children's Exposures to Bisphenol A by Route and Urinary Biomonitoring. *Environ. Sci. Technol.* 2011, 45, 5309–5316.
- 37. The International Commission on Radiological Protection (ICRP). ICRP Publication 89. Basic Anatomical and Physiological Data for Use in Radiological Protection: Reference Values; The International Commission on Radiological Protection: Ottawa, Canada, 2002.
- Volkel, W.; Colnot, T.; Csanady, G.A.; Filser, J.G.; Dekant, W. Metabolism and kinetics of bisphenol A in humans at low doses following oral administration. *Chem. Res. Toxicol.* 2002, 15, 1281–1287.
- Centers for Disease Control and Prevention (CDC); National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Available online: http://www.cdc.gov/ nchs/nhanes/nhanes\_questionnaires.htm (accessed on 24 October 2013).
- 40. David, R.M. Exposure to phthalate esters. Environ. Health Perspect. 2000, 108, A440.
- Mage, D.T.; Allen, R.H.; Kodali, A. Creatinine corrections for estimating children's and adult's pesticide intake doses in equilibrium with urinary pesticide and creatinine concentrations. *J. Exp. Sci. Environ. Epidemiol.* 2008, 18, 360–368.

- 42. Braun, J.M.; Kalkbrenner, A.E.; Calafat, A.M.; Yolton, K.; Ye, X.; Dietrich, K.N.; Lanphear, B.P. Impact of early-life bisphenol A exposure on behavior and executive function in children. *Pediatrics* **2011**, *128*, 873–882.
- 43. Mendonca, K.; Hauser, R.; Calafat, A.M.; Arbuckle, T.E.; Duty, S.M. Bisphenol a concentrations in maternal breast milk and infant urine. *Int. Arch. Occup. Environ. Health* **2014**, *87*, 13–20.
- Nachman, R.M.; Fox, S.D.; Golden, W.C.; Sibinga, E.; Veenstra, T.D.; Groopman, J.D.; Lees, P.S. Urinary free bisphenol A and bisphenol A-glucuronide concentrations in newborns. *J. Pediatr.* 2013, *162*, 870–872.
- 45. Ye, X.; Kuklenyik, Z.; Needham, L.L.; Calafat, A.M. Measuring environmental phenols and chlorinated organic chemicals in breast milk using automated on-line column-switching-high performance liquid chromatography-isotope dilution tandem mass spectrometry. *J. Chromatogr. B* **2006**, *831*, 110–115.
- 46. Ye, X.; Bishop, A.M.; Needham, L.L.; Calafat, A.M. Automated on-line column-switching HPLC-MS/MS method with peak focusing for measuring parabens, triclosan, and other environmental phenols in human milk. *Anal. Chimica Acta* **2008**, *622*, 150–156.
- Ackerman, L.K.; Noonan, G.O.; Heiserman, W.M.; Roach, J.A.; Limm, W.; Begley, T.H. Determination of bisphenol A in U.S. infant formulas: Updated methods and concentrations. *J. Agric. Food Chem.* 2010, 58, 2307–2313.
- 48. Cao, X.L.; Corriveau, J.; Popovic, S. Migration of bisphenol A from can coatings to liquid infant formula during storage at room temperature. *J. Food Prot.* **2009**, *72*, 2571–2574.
- 49. USDA. Economic Research Service (ERS) Website with data on food availability. Available online: http://www.ers.usda.gov/data-products/food-availability-(per-capita)-datasystem.aspx#.UdxLRzvVDTo (accessed on 20 December 2013).
- 50. Mielke, H.; Partosch, F.; Gundert-Remy, U. The contribution of dermal exposure to the internal exposure of bisphenol A in man. *Toxicol. Lett.* **2011**, *204*, 190–198.
- Fung, E.Y.; Ewoldsen, N.O.; St Germain, H.A., Jr.; Marx, D.B.; Miaw, C.L.; Siew, C.; Chou, H.N.; Gruninger, S.E.; Meyer, D.M. Pharmacokinetics of bisphenol A released from a dental sealant. J. Am. Dent. Assoc. 2000, 131, 51–58.
- Harley, K.G.; Aguilar Schall, R.; Chevrier, J.; Tyler, K.; Aguirre, H.; Bradman, A.; Holland, N.T.; Lustig, R.H.; Calafat, A.M.; Eskenazi, B. Prenatal and postnatal bisphenol A exposure and body mass index in childhood in the CHAMACOS cohort. *Environ. Health Perspect.* 2013, *121*, 514–520.
- Volberg, V.; Harley, K.; Calafat, A.M.; Dave, V.; McFadden, J.; Eskenazi, B.; Holland, N. Maternal bisphenol a exposure during pregnancy and its association with adipokines in Mexican-American children. *Environ. Mol. Mutagen.* 2013, 54, 621–628.
- Rudel, R.A.; Dodson, R.E.; Perovich, L.J.; Morello-Frosch, R.; Camann, D.E.; Zuniga, M.M.; Yau, A.Y.; Just, A.C.; Brody, J.G. Semivolatile endocrine-disrupting compounds in paired indoor and outdoor air in two northern california communities. *Environ. Sci. Technol.* 2010, 44, 6583–6590.
- Loganathan, S.N.; Kannan, K. Occurrence of bisphenol a in indoor dust from two locations in the eastern united states and implications for human exposures. *Arch. Environ. Contam. Toxicol.* 2011, *61*, 68–73.

56. Stackelberg, P.E.; Gibs, J.; Furlong, E.T.; Meyer, M.T.; Zaugg, S.D.; Lippincott, R.L. Efficiency of conventional drinking-water-treatment processes in removal of pharmaceuticals and other organic compounds. *Sci. Total Environ.* **2007**, *377*, 255–272.

 $\bigcirc$  2014 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/3.0/).