Estimation of Daily Bisphenol A Intake of Japanese Individuals with Emphasis on Uncertainty and Variability

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(Received June 27, 2005; accepted December 22, 2005)

Key words: bisphenol A, daily intake, risk assessment, uncertainty, Monte Carlo simulation

The purpose of this study was to comprehensively assess the exposure of Japanese individuals to bisphenol A (BPA) with emphasis on uncertainty and variability in available information. The uncertainty and variability in parameters were numerically analyzed using Monte Carlo simulation. The uncertainty in the functional relationship between sources and exposure was treated by comparing two approaches: one was to aggregate ingestion and inhalation through all possible exposure pathways and the other was to estimate the intake from urinary excretion by backward calculation. For individuals aged 6 months or above, food was the most significant source of intake. The alteration of the method used in inactivating the inside surface of drink cans slightly contributed to the decrease in daily intake. By the backward calculation approach based on urinary excretion, 95% confidence intervals for the daily intake for high-exposure populations were estimated to be 0.037–0.064 μg/kg/day for males and 0.043–0.075 μg/kg/day for females. Even conservatively estimated daily intakes were lower than the EU’s temporary tolerable daily intake (TDI) of 10 μg/kg/day as well as the U.S. Environmental Protection Agency (US EPA)’s reference dose (RfD) of 50 μg/kg/day. Thus, it is unlikely that humans, including infants and young children, are at unacceptable risk from possible BPA exposure.

1. Introduction

Bisphenol A (BPA) is a chemical that is primarily used in the production of polycarbonate (PC) plastic and epoxy resins (EXRs). These plastics are used in a variety of consumer products, including food and drink packaging and a large number of non-food-related

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articles. Recently, against the backdrop of both public and scientific concerns regarding the low-dose effects of BPA, scientific panels have been convened to evaluate the weight of evidence for potential developmental and reproductive toxicity of BPA at low doses; however, no consistent, conclusive evidence has been found.\(^1\,^2\) The European Commission Scientific Committee on Food (SCF) proposed a temporary tolerable daily intake (TDI) of 10 \(\mu g/kg/day\) on the basis of a 3-generation dietary rat study with reproductive- and endocrine-related endpoints in 2002,\(^3\) while the U.S. Environmental Protection Agency (US EPA) suggested a reference dose (RfD) of 50 \(\mu g/kg/day\).\(^4\)

To assess the risk posed by BPA to humans, exposure levels for the concerned populations as well as toxicity information are necessary. In Japan, duplicate diet studies identified 0.19–3.7 \(\mu g/day\) BPA in meals served by 2 hospitals\(^5\) and <0.5–1.9 \(\mu g/kg\) of BPA in the meals of 50 families.\(^6\) A total diet study that collected approximately 200 food items in Tokyo indicated that the daily BPA intakes were 0.00475 \(\mu g/kg/day\) for children aged 2–6 years and 0.00195 \(\mu g/kg/day\) for adults.\(^7\) Arakawa et al.\(^8\) observed that the daily urinary excretion of BPA ranged from <0.003 to 0.23 \(\mu g/kg/day\) in 24-h urine samples collected from 36 male university students aged 24.7 ± 3.0 years. These studies provide valuable information on the exposure of Japanese individuals to BPA. However, since their estimates were based on limited data, they may represent intakes for subpopulations at a certain time rather than being representative intakes for Japanese individuals.

Outside Japan, the SCF has published realistic worst case estimates of consumer exposure to BPA via foodstuffs as ranging from 0.48 \(\mu g/kg/day\) for adults to 1.6 \(\mu g/kg/day\) for infants.\(^3\) In the USA, Wilson et al.\(^9\) reported that the daily BPA intakes for 9 preschool children aged 2–5 years were between 0.018 and 0.071 \(\mu g/kg/day\); these values were estimated from the actual measurements of BPA levels in the air, play area soil, floor dust, duplicate diets, and hand surface wipes in day care centers and homes. In New Zealand, Thomson and Grounds\(^10\) estimated the daily intake from canned food based on the measurement of BPA concentration in 80 canned foods and 24-h dietary recall information from 4399 individual consumers and obtained average and maximum intakes of 0.008 and 0.29 \(\mu g/kg/day\), respectively.

The purpose of this study was to comprehensively assess the exposure of Japanese individuals to BPA with emphasis on uncertainty and variability regarding the available information. The uncertainty arises from a lack of knowledge regarding the true value of a required parameter and/or the structure of a model, namely, the functional relationship between sources and exposure.\(^11\) The uncertainty and variability in the parameters were numerically analyzed using Monte Carlo simulation. The uncertainty in the functional relationship between sources and BPA exposure was treated by comparing two approaches: one was to aggregate ingestion and inhalation through all possible exposure pathways and the other was to estimate the intake from urinary excretion by backward calculation.

2. Methods

2.1 Overall intake from various exposure pathways

Since the parameters required to estimate BPA intake, such as amount of food consumption, breathing volume, and frequency of PC tableware use, are dependent on age, the daily BPA intake was separately estimated for 6 age groups: infants aged 0–5 months, infants aged 6–11 months, children aged 1–6 years, students aged 7–14 years, young persons aged 15–19
years, and adults aged >19 years. Conceptual models that express possible exposure pathways for each age group are shown in Fig. 1. Apart from typical exposure sources such as air, water, and food items, which will be included in standard exposure assessment, BPA-specific sources such as toys and tableware were also considered. Furthermore, the intake from food items was characterized in detail by categorizing these items as canned food, canned drinks, non-canned food, and non-canned drinks.

The intake from air, water, soil, and food items was basically estimated as

$$I_i = IG_i \times C_i \div BW,$$

(1)

where $I_i$ is the BPA intake from the media $i$, $IG_i$ is the ingestion of media $i$, $C_i$ is the BPA concentration in media $i$, and $BW$ is the body weight. The subscript $i$ denotes the exposure media such as air, water, soil, or food items.

The intake from consumer articles such as infant feeding bottles, tableware, and toys was estimated as

$$I_j = M_j \times CT_j \div BW,$$

(2)

where $I_j$ is the BPA intake from media $j$, $M_j$ is the migration rate from the media $j$, and $CT_j$...
is the contact time with the media $j$. The subscript $j$ denotes exposure media such as infant feeding bottles, tableware, or toys. Monte Carlo simulations were performed in order to account for variabilities in $IG_i$, $C_i$, $BW$, $M_j$, and $CT_j$. The distributions of parameters required for the Monte Carlo simulations are described in the following sections.

2.2 Intake from food

Infants aged 0–5 months and 6–11 months are ordinarily fed with breast milk and/or formula. Makino et al.\(^{(12)}\) reported that the BPA concentrations in the breast milk of 15 women were below the detection limit of 0.6 µg/L. We assumed that the intake from breast milk was negligible. The BPA intake from formula was estimated by considering BPA concentration in water and BPA migration from baby feeding bottles made of PC, which are described in the following sections.

For infants aged 6–11 months, the BPA intake from baby food as well as from formula was considered. BPA concentrations in more than 60 types of baby food have been reported.\(^{(13,14)}\) BPA was detected in 6 types of baby food. The maximum concentration was 5.0 µg/kg, which was detected in boiled vegetables packed in a retort pouch.\(^{(13)}\) We assumed that the concentration in baby food followed a uniform distribution in the range of 0 to 5.0 µg/kg. This assumption would result in the overestimation of the frequency of higher concentrations because BPA was not detected in most baby foods. However, since adequate information was not available on a more realistic distribution shape for this parameter, we followed this assumption considering the possible overestimation of BPA intake.

The BPA concentrations in 929 types of food items were available for individuals aged 1 year or above.\(^{(5,15–19)}\) In general, the concentrations in canned food and drinks were higher than those in non-canned food and drinks. This was due to the migration of BPA from the EXR coating that was applied to the inside of the cans. Kawamura et al.\(^{(15)}\) observed that a higher BPA concentration occurred in canned coffee and tea, which were heated for the purpose of sterilization after packing in comparison with other beverages that were not heated. We categorized the food items into 13 groups (Table 1), each of which consisted of 4 subgroups: canned food, canned drinks, non-canned food, and non-canned drinks. The

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Parameters of uniform distributions that characterize the BPA concentration in food [µg/kg].(^{(5,15–19)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>food group</td>
<td>canned food</td>
</tr>
<tr>
<td></td>
<td>min</td>
</tr>
<tr>
<td>1</td>
<td>rice</td>
</tr>
<tr>
<td>2</td>
<td>grain crops other than rice, seeds, and potatoes</td>
</tr>
<tr>
<td>3</td>
<td>sugar, sweets, and snacks</td>
</tr>
<tr>
<td>4</td>
<td>fats</td>
</tr>
<tr>
<td>5</td>
<td>beans</td>
</tr>
<tr>
<td>6</td>
<td>fruits</td>
</tr>
<tr>
<td>7</td>
<td>green vegetables</td>
</tr>
<tr>
<td>8</td>
<td>other vegetables, mushrooms, and seaweeds</td>
</tr>
<tr>
<td>9</td>
<td>seasoning and beverages</td>
</tr>
<tr>
<td>10</td>
<td>fish and shellfish</td>
</tr>
<tr>
<td>11</td>
<td>meat and eggs</td>
</tr>
<tr>
<td>12</td>
<td>milk and dairy products</td>
</tr>
<tr>
<td>13</td>
<td>other</td>
</tr>
</tbody>
</table>

\(^{a)}\) There is no drink for this food group.
distribution of BPA concentrations was individually considered for each subgroup. Each distribution was assumed to follow a uniform distribution, the range of which extended from the lowest concentration to the highest one among the concentrations reported in published studies (Table 1). The distributions of amounts of food items consumed by each age class were obtained from the results of the National Nutrition Survey in Japan.\(^{(20)}\)

2.3 Migration from baby feeding bottles

For infants aged 0–5 months and 6–11 months, BPA migration from baby feeding bottles into formula was considered as one of the possible exposure pathways. As described by the SCF,\(^{(3)}\) published migration studies indicated that no significant effect was observed from repeated use, abrasion, heating, or chemical sterilization of PC feeding bottles. The highest BPA release from commercially available feeding bottles was 3.9 $\mu$g/L for a new unwashed bottle when extraction was performed with water at 95°C for 30 min.\(^{(21)}\) However, most bottles did not elute a detectable amount of BPA (<0.5 $\mu$g/L). We assumed that the migration from PC feeding bottles followed a uniform distribution with minimum and maximum values of 0 $\mu$g/L and 3.9 $\mu$g/L, respectively. This assumption would result in the overestimation of the frequency of higher migration.

It was assumed that 6.3% of infants used PC feeding bottles. This percentage was the same as that observed among nursery school children in 1998.\(^{(22)}\) The percentages in recent years appeared to be lower than 6.3% because PC feeding bottles began to be replaced with those made of other materials around 1998 due to public anxiety over endocrine disrupting chemicals in Japan. However, since recent data were unavailable, we did not estimate BPA intake due to migration from feeding bottles in years other than 1998.

2.4 Migration from PC tableware and EXR-coated chopsticks

For individuals aged 6 months and above, BPA migrations from PC tableware and/or from EXR-coated chopsticks into food were considered. To evaluate the exposure from those sources, parameters such as migration rate, population that uses them, and the frequency of use are required. The migration rates were derived from the published results of migration tests,\(^{(21,23,24)}\) namely, the BPA concentration in extraction solvents at a specific temperature and for a certain extraction period. Typical solvents and conditions used in the migration tests were as follows: water at 60°C or 95°C for 30 min, 20% ethanol at 60°C for 30 min, 4% acetic acid at 60°C or 95°C for 30 min, or n-heptane at 25°C for 60 min. An obvious relationship was not observed between migration concentration and extraction conditions. We assumed that the migration amount under extraction conditions of 95°C water for 30 min was equivalent to the amount of intake per meal because this set of test conditions was the most commonly used and appeared to be moderately conservative compared with the others.

Empirical distributions were applied to BPA migration from PC tableware or from EXR-coated chopsticks used in school lunches and at home (Table 2) because a relatively large amount of experimental data (at least 20) was available.\(^{(23,24)}\) Since only 4 data sets were obtained for rice bowls and soup bowls\(^{(21)}\) that were used by children aged 1–6 years, BPA migration from these tableware items was assumed to follow a uniform distribution.

It was assumed that 11.7% of children aged 1–6 years consumed meals 3 times a day using PC tableware that consisted of a rice bowl, a soup bowl, and a small dish. This
percentage was obtained from a survey of nursery school children in 1998.\(^{(22)}\)

For students aged 7–14 years, the use of PC tableware in school lunches was considered. The percentage of students who used PC tableware in school lunches was derived from a series of surveys conducted by the Ministry of Education, Culture, Sports, Science and Technology\(^{(25)}\) and ranged between 9.1% in 2003 and 35.0% in 1998. In this age group, it was assumed that a rice bowl, a soup bowl, a deep dish, and a small dish made of PC were used in the school lunch and no PC tableware was used during other meals. Apart from PC tableware, EXR-coated chopsticks are a potential source of BPA exposure. It was assumed that EXR-coated chopsticks were used in all 3 meals in a day by all individuals aged 1 year and above, although quantitative data was unavailable on the use of EXR-coated chopsticks. For individuals aged >14 years, EXR-coated chopsticks were presumed to be a unique source of BPA exposure among tableware.

### 2.5 Migration from toys

Due to the mouthing behavior of infants, they may ingest BPA from toys made of plastics such as PC and EXRs in which BPA was used as a monomer and some grades of polyvinyl chloride (PVC) in which BPA was used as an additive. The intake from toys depends on a daily mouthing time and the rate of migration. The daily mouthing time for toys was obtained by surveys on the mouthing behavior of 50 infants observed by their mothers\(^{(26)}\) and of 25 infants recorded by video cameras.\(^{(27)}\) It was characterized by a normal distribution with a mean of 41.7 min and a standard deviation of 13.7 min for infants aged 0–5 months and a mean of 73.9 min and a standard deviation of 32.9 min for infants aged 6–11 months. The rate of migration was assumed to follow a uniform distribution with a minimum value of 0 \(\mu g/cm^2/min\), which reflected toys that did not contain BPA, and a maximum value of 0.0162 \(\mu g/cm^2/min\), which was the highest value obtained from the literature.\(^{(28)}\) This assumption would also result in the overestimation of the frequency of higher migration because only a few types of toys made of PC, EXRs, and some grades of PVC would contain BPA, while most of the toys that infants play with would not. The surface area of the toys mouthed by infants was presumed to be 10 cm\(^2\).
2.6 Intake from air

In order to estimate BPA intake from air, parameters such as indoor air concentration, outdoor air concentration, time spent indoors versus that spent outdoors, breathing rate, and rate of BPA absorption from the lungs were required. The BPA concentration in indoor air was assumed to follow a uniform distribution in the range of 0 to 8.1 ng/m³. The BPA concentration in outdoor air was assumed to follow a uniform distribution in the range of 0 to 28 ng/m³. Applying these uniform distributions would result in the overestimation of the frequency of higher concentrations because available data on the BPA concentration in air were biased toward lower values. However, since adequate information was unavailable on a realistic shape of the BPA concentration distribution, we used this assumption considering the possibility of overestimating the intake from air. It was assumed that 90% of the time was spent indoors and 10% outdoors. The breathing rate was calculated by the following equation:

\[
\text{breathing rate [m}^3/\text{day]} = 20 \times (\text{body weight [kg]}/70)^{3/4}. 
\] (3)

Age-specific lognormal distributions were assigned to the body weight. The rate of BPA absorption from the lungs was assumed to be 100% because no information was available for this parameter.

2.7 Intake from drinking water

BPA intake from drinking water was calculated by multiplying the BPA concentration in drinking water by the daily consumption of water. The drinking water BPA concentration was assumed to follow a uniform distribution in the range of 0 to 0.17 µg/L. The daily consumption of water was assumed to be constant at 2 L because data that could identify the shape of a specific statistical distribution for this parameter were not obtained.

2.8 Intake estimated from urinary excretion

Völkel et al. determined the metabolism and kinetics of BPA in humans following the oral administration of 5 mg of BPA. They suggested that BPA glucuronide was a unique metabolite, and urinary elimination followed a first-order reaction with a half-life of 5.4 h. Their results indicate that body burden can be expressed as

\[
C_t = C_0 \cdot e^{-kt}, 
\] (4)

where \(C_0\) is the body burden immediately after BPA ingestion [µg/kg], \(C_t\) is the body burden \(t\) h after the ingestion [µg/kg], and \(k\) is the first-order rate constant with a value of 0.128 h⁻¹ that is derived from the half-life of 5.4 h. The urinary excretion \(X\) [µg] in \(t\) h after the ingestion can be described as

\[
X = (C_0 - C_t) \cdot M \\
= C_0 \cdot M \cdot (1 - e^{-kt}), 
\] (5)

where \(M\) [kg] is the body weight. When \(X\) is obtained from the measurement of BPA
concentration in urine and urine volume, the BPA intake \(= C_0 \cdot M\) is estimated as \(X(1 - e^{-k \cdot t})\).

A relatively large amount of data has recently been published on the BPA concentration in the urine of Japanese adults. Since the BPA concentrations determined by enzyme-linked immunosorbent assay (ELISA) may be overestimated,\(^{(39)}\) we excluded them from our assessment. Most of the remaining studies reported the concentrations in spot urine samples. However, the short biological half-life of BPA could result in a high variability in its concentration in spot urine samples within a day. Therefore, because the spot urine samples appeared to be unsuitable for estimating the daily intake of BPA, we also excluded studies using them. Finally, we were left with 2 studies that had been conducted by Tsukioka et al.\(^{(40)}\) and Arakawa et al.\(^{(8)}\) in which 24-h urine samples were analyzed. Tsukioka et al.\(^{(40)}\) collected the 24-h urine samples from 11 male and 11 female volunteers and Arakawa et al.\(^{(8)}\) collected these samples from 36 male subjects. These two studies indicated that the interindividual variability in daily urinary excretion, which was obtained by multiplying the BPA concentration in the 24-h urine sample by daily urine volume, was characterized by a lognormal distribution. A geometric mean of 1.32 \(\mu g/day\) and a geometric standard deviation of 1.97 were derived from the results of Tsukioka et al.\(^{(40)}\) On the otherhand, a geometric mean of 2.25 \(\mu g/day\) and a geometric standard deviation of 2.34 were obtained from the results of Arakawa et al.\(^{(8)}\) Arakawa et al.\(^{(8)}\) also collected 24-h urine samples from 5 healthy adults for 5 consecutive days and reported the intra- and interindividual variabilities in the daily urinary excretion to be 91% and 84%, respectively, by an analysis of variance. We presumed that the intra- and interindividual variabilities were almost the same.

The daily BPA intake was estimated using Monte Carlo simulation with the following assumptions.

1. Interindividual variability in daily urinary excretion is characterized by a lognormal distribution. The parameters of the distribution (i.e., geometric mean and geometric standard deviation) are uncertain; however, the geometric mean is located between 1.32 and 2.25 \(\mu g/day\), and the geometric standard deviation lies between 1.97 and 2.34, which are derived from Tsukioka et al.\(^{(40)}\) and Arakawa et al.\(^{(8)}\)

2. Intraindividual variability in daily urinary excretion is equivalent to the interindividual variability in daily urinary excretion. This assumption is based on the result of Arakawa et al.\(^{(8)}\)

3. The amount of BPA in a 24-h urine sample (i.e., daily urinary excretion) is equivalent to the amount of BPA ingested during the day before sampling (i.e., daily intake per person). This assumption is based on equation (5), which indicates that 95% of ingested BPA is excreted in urine within 24 h.

4. A measure of long-term exposure to BPA can be represented by the annual average of daily BPA intake.

The scheme of the Monte Carlo simulation is shown in Fig. 2. First, one value of the geometric mean and one of the geometric standard deviation were sampled from each uniform distribution to specify one of the alternative lognormal distributions that represented the intraindividual variability in the daily intake per person. Next, 365 values were sampled from this distribution, and the sampled values were averaged to derive an annual average of daily BPA intake per person. This was divided by a body weight value sampled from a lognormal distribution characterized by a geometric mean of 63.4 kg and a geometric standard deviation of 1.17 for males or by a geometric mean of 52.1 kg and a geometric
standard deviation of 1.18 for females to be transformed into an annual average of daily BPA intake per kg of body weight. Two hundred and fifty types of alternative distributions that represented the intraindividual variability in the daily BPA intake per person were produced, and 500 predicted values of the annual average daily BPA intake per kg of body weight were produced for each alternative distribution of the daily BPA intake per person. Latin hypercube sampling was applied to all samplings.

3. Results and Discussion

3.1 Daily BPA intake estimated by aggregating the amount of inhalation and ingestion through all possible exposure pathways

Figure 3 shows yearly changes in the averages and in the 95th percentiles of daily BPA intake for 6 age groups of Japanese individuals estimated by aggregating the amounts of inhalation and ingestion described in Fig. 1. For infants aged 0–5 months, 6–11 months, and children aged 1–6 years, the daily intake could be estimated only in 1998 because the percentage of infants who used PC feeding bottles and the percentage of children aged 1–6 years who used PC tableware were available only for that year. The distributions of the BPA concentrations in all exposure media (i.e., air, water, food, and consumer products) were assumed to be stable during the period from 1995 to 2002, except for the BPA concentration distribution in canned drinks. The BPA concentration in canned drinks has been assumed to be 0 µg/L since 2001. This is because almost all of the drink cans manufactured in and after 2001 appear to have been substituted by alternative cans the insides of which were not coated with EXRs but laminated by a PET film.

Since 1995, the daily BPA intake, particularly of high-exposure populations (i.e., 95th percentiles) showed a slight tendency to decline among individuals aged 7 years and above. This appears to be due to a decrease in the consumption of canned food and drinks and a change in food preference. As shown in Table 1, canned food items containing relatively large amounts of BPA were those that were included in food groups 8 (vegetables, mushrooms, and seaweeds), 10 (fish and shellfish), and 11 (meat and eggs). The concen-
tration in canned drinks included in food group 9 (seasoning and beverages) was also comparatively high. In the case of non-canned food, food items that belonged to food groups 6 (fruits), 10, and 11 contained a larger amount of BPA than others. Comparing the data from 1995 and 2000, the consumption of canned food, canned drinks, and non-canned food included in food groups 6, 8, 9, 10, and 11 slightly decreased or remained at the same level. A relatively large decrease in the daily intake occurred between 2000 and 2001 (i.e., 0.1–0.2 μg/kg/day for the averages and 0.2–0.6 μg/kg/day for the 95th percentiles). This would result from the alteration of the method used to inactivate the inside surface of drink cans, as described above.

Table 3 shows the average amounts of BPA exposure for males from each pathway in 1998. The daily BPA intake for children aged 1–6 years was 1.2 μg/kg/day on average and 3.9 μg/kg/day for the 95th percentile, which was the highest among all the age groups. This was due to a relatively high dietary consumption per body weight and the use of PC tableware. However, since social concern for endocrine disrupting chemicals began to increase in 1998 in Japan and certain proportions of PC tableware as well as PC feeding bottles have been substituted for non-PC articles since 1998, the exposure from PC tableware would be reduced in recent years. We could not evaluate this quantitatively because of the lack of data on the most recent use frequency of PC tableware.

Fig. 3. Yearly change in the average and in the 95th percentile of daily BPA intake estimated as the sum of the amounts of inhalation and ingestion for 6 age classes of Japanese individuals.
For all individuals aged 6 months and above, food was the most significant source of BPA intake. For individuals aged 1–14 years, BPA intake from canned food and drinks was almost the same as that from non-canned food and drinks. On the other hand, for individuals aged 15 years and above, BPA intake from canned food and drinks was approximately twice as large as that from non-canned food and drinks. This would reflect a difference in the consumption of canned beverages that contained a relatively large amount of BPA.

The daily BPA intakes from food, which ranged between 0.004 and 0.11 µg/kg/day for adults, can be derived from the results of the duplicate diet studies conducted by Imanaka\(^5\) and the Ministry of the Environment of Japan\(^6\) on the assumption that the amount of food consumed was 2.1 kg/day and the body weight was 50 kg. In the total diet study performed in Tokyo,\(^7\) it was found that the daily BPA intakes for children aged 2–6 years and adults were 0.00475 µg/kg/day and 0.00195 µg/kg/day, respectively. In this study, the estimated average BPA intake from food for male adults aged >19 years was between 0.16 µg/kg/day in 2002 and 0.43 µg/kg/day in 1995. The 5th percentile and 95th percentile of the BPA intake from food for adults aged >19 years for the simulated years were 0.04–0.08 µg/kg/day and 0.4–1.23 µg/kg/day, respectively. On the whole, our estimates were higher than those of the duplicate or total diet studies, although part of the range of our estimates overlapped with that of other estimates. This was due to the assumption that the BPA concentrations in foods followed uniform distributions, which would result in the overestimation of the frequency of higher BPA concentrations in food. In addition, there is a possibility that the previous diet studies failed to adequately account for foods with high BPA concentrations but with a low consumption frequency such as canned food and drinks because these diet studies were conducted for a short period of 1 to 3 days.

<table>
<thead>
<tr>
<th>exposure pathway</th>
<th>aged 0–5 months</th>
<th>aged 6–11 months</th>
<th>aged 1–6 years</th>
<th>aged 7–14 years</th>
<th>aged 15–19 years</th>
<th>aged &gt;19 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>breast milk</td>
<td>0</td>
<td>0</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>formula (water)</td>
<td>0.012</td>
<td>0.0096</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>feeding bottle</td>
<td>0.015</td>
<td>0.014</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>baby food</td>
<td>–</td>
<td>0.085</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>toys</td>
<td>0.026</td>
<td>0.069</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>air</td>
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<td>0.0021</td>
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<td>0.0015</td>
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<tr>
<td>water</td>
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<td>–</td>
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<td>0.0053</td>
<td>0.0029</td>
<td>0.0027</td>
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<td>–</td>
<td>0.38</td>
<td>0.21</td>
<td>0.20</td>
<td>0.29</td>
</tr>
<tr>
<td>non-canned food and drink</td>
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<td>–</td>
<td>0.38</td>
<td>0.21</td>
<td>0.13</td>
<td>0.12</td>
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<tr>
<td>tableware</td>
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<td>–</td>
<td>0.40</td>
<td>0.12</td>
<td>0.024</td>
<td>0.022</td>
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<tr>
<td>daily intake</td>
<td>0.028 (breast milk)</td>
<td>0.16 (breast milk)</td>
<td>1.2</td>
<td>0.55</td>
<td>0.36</td>
<td>0.43</td>
</tr>
</tbody>
</table>
                      | 0.055 (formula) | 0.18 (formula)
3.2 Daily BPA intake estimated from urinary excretion

The Monte Carlo simulation that propagated uncertainty and variability in parameters for urinary excretions produced 95% confidence intervals about the daily intake for high-, average-, and low-exposure populations (Table 4). The 95% confidence intervals about the daily intake for high-exposure populations (i.e., 95th percentiles) were 0.037–0.064 µg/kg/day for males and 0.043–0.075 µg/kg/day for females, and the values for average-exposure populations were 0.028–0.049 µg/kg/day for males and 0.034–0.059 µg/kg/day for females. Since Tsukioka et al.⁴⁰ and Arakawa et al.⁸ appear to have determined BPA concentrations in urine samples collected after 2000, the daily intakes estimated above would reflect recent values.

3.3 Comparison between estimates of the daily intake derived from 2 approaches

Both approaches that were used in this study in estimating the daily BPA intake have advantages and disadvantages. The “aggregate” approach, which estimated the daily BPA intake by aggregating the amount of BPA inhalation and ingestion through all possible exposure pathways, can evaluate the contribution of each source and the yearly changes in exposure. In addition, it can adequately incorporate age-specific sources such as PC feeding bottles, toys, and PC tableware. However, this approach has to rely on certain assumptions for exposure pathways for which sufficient data are not available; this in turn results in an increased degree of uncertainty in the estimates. In this study, when insufficient data were available for the required parameters, relatively conservative assumptions that would result in the overestimation of daily BPA intake were applied.

The backward calculation approach that estimated the daily intake from urinary excretion appeared to be more reliable than the aggregate approach because the backward calculation approach used a simple and experimentally verified functional relationship between BPA ingestion and urinary excretion with fewer assumptions. However, the backward calculation approach can estimate daily intake only in adults in whom urinary BPA concentrations have been determined at present and cannot produce any information on exposure sources.

The daily BPA intake for individuals aged >19 years estimated between 2001 and 2002 by the aggregate approach was between 0.19 and 0.23 µg/kg/day on average and between 0.44 and 0.56 µg/kg/day for the 95th percentile. The average and 95th percentile intakes estimated by the aggregate approach were 4 to 7 times and 7 to 13 times higher, respectively, than those estimated by the backward calculation approach. These differences would result from the assumption applied to the aggregate approach that BPA concentrations in food items were characterized by uniform distributions. Therefore, we considered that estimates

Table 4
95% confidence intervals about the annual average of daily BPA intakes estimated from urinary excretion [µg/kg/day].

<table>
<thead>
<tr>
<th></th>
<th>low-exposure population (5th percentile)</th>
<th>average-exposure population (average)</th>
<th>high-exposure population (95th percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>adult male</td>
<td>0.021–0.037</td>
<td>0.028–0.049</td>
<td>0.037–0.064</td>
</tr>
<tr>
<td>adult female</td>
<td>0.025–0.044</td>
<td>0.034–0.059</td>
<td>0.043–0.075</td>
</tr>
</tbody>
</table>
derived by the backward calculation approach would provide more realistic values than those derived by the aggregate approach.

3.4 Risk characterization

The age group with the highest BPA exposure was 1–6 years as shown in Fig. 3. The aggregate approach estimated that the daily intakes for the high-exposure populations (95th percentile) in this age group were 3.9 µg/kg/day and 4.1 µg/kg/day for males and females, respectively, in 1998. These estimates are strictly conservative and the latest actual intakes for these populations will be much lower. This is because the frequency of use of PC tableware has significantly decreased since 1998 in addition to the fact that the aggregate approach tends to overestimate daily BPA intake. Despite the conservativeness of this estimation, the estimated daily intakes were lower than that of the EU’s temporary TDI of 10 µg/kg/day(3) as well as the US EPA’s RfD of 50 µg/kg/day.(4) Thus, it is unlikely that humans, including infants and young children, are at unacceptable risks from possible exposure to BPA in air, water, food, and consumer products.

Acknowledgment

This research was conducted under the Comprehensive Chemical Substances Assessment and Management Program, with the funding of New Energy and Industrial technology Development Organization of Japan (NEDO).

References