

## Bisphenol A (BPA)

Bisphenol A (BPA) is a high-volume industrial chemical used in the production of epoxy resins and polycarbonate plastics. Polycarbonate plastics may be encountered in many products, notably food and drink containers, while epoxy resins are frequently used as inner liners of metallic food and drink containers to prevent corrosion. The use of BPA in food contact materials is regulated by the U.S. Food and Drug Administration.<sup>1,2</sup> BPA also serves as a coating on some types of thermal paper that are often used as receipts from cash registers, automatic teller machines, and other similar devices. It is used in the polyvinyl chloride (PVC) industries as well as in metal foundries where it is used to make casts and moldings. The primary route of human exposure to BPA is believed to be through diet, when BPA migrates from food and drink containers.<sup>3-5</sup> Migration is more likely to occur when the container is heated or washed.<sup>5,6</sup> Other possible sources of BPA exposure include air, dust, water, and dental sealants.<sup>3,5</sup>

Biomonitoring studies demonstrate that BPA exposure is prevalent in the United States, with detectable levels of BPA present in 93% of tested urine samples.<sup>7</sup> Because BPA is metabolized quickly in the body,<sup>8</sup> the high frequency of detection indicates that exposures are occurring regularly within the U.S. population. Exposures to BPA of infants and children up to age 6 years are estimated to be greater than BPA exposures in older children and adults.<sup>3</sup>

Much of the scientific interest in BPA is related to published research suggesting that BPA may be an endocrine disrupting chemical.<sup>9,10</sup> Endocrine disruptors act by interfering with the biosynthesis, secretion, action, or metabolism of naturally occurring hormones.<sup>9,11</sup> Given the importance of hormones in human physiology, there is concern in the scientific community over the potential for endocrine disruptors to adversely affect children's health, particularly in reproduction, early and adolescent development, and behavior.<sup>9</sup> BPA is described as a "weakly estrogenic" chemical, because its affinity for binding to estrogen receptors is approximately 10,000-fold weaker than natural estrogen.<sup>12</sup>

Recent attention to the developmental effects of BPA is based on several laboratory studies and a better understanding of the mechanisms by which BPA exerts an estrogenic effect.<sup>10,13-15</sup> In animal studies, exposure to high levels of BPA during pregnancy or lactation resulted in reduced birth weight, slowed growth, reduced survival, and delayed time to the onset of puberty in offspring.<sup>16-19</sup> Animal studies have also found that low-dose BPA exposure was associated with insulin resistance.<sup>20,21</sup> In addition, one study found that low-dose BPA exposure in pregnant animals was associated with symptoms similar to gestational diabetes, suggesting that BPA exposures may have adverse effects in pregnant women.<sup>22</sup> Other studies have found relationships between prenatal or early-life BPA exposure and neurological effects as well as the development of breast and prostate cancer in adult animals.<sup>23-25</sup> The effects of low-dose exposure to BPA in lab animals are debated within the scientific community, with some researchers finding no developmental effects, while others have identified behavioral and neural effects, abnormal urinary tract development, development of lesions in the prostate

gland, and early onset of puberty in females.<sup>3,23,26-36</sup> Differences in reported results on the timing of puberty between low and high dose studies may be a result of dose differences, study design, or species of animal.<sup>3</sup> Based on a critical review of the existing scientific literature, in 2008 the National Toxicology Program (NTP) determined that there was “some concern” (the midpoint on a five-level scale ranging from “negligible” to “serious”)<sup>i</sup> for effects of BPA on the brain, behavior, and prostate gland in fetuses, infants, and children; “minimal concern” for effects on the mammary gland and onset of puberty in females; and “negligible concern” for fetal or neonatal mortality, birth defects, or reduced birth weight and growth.<sup>3</sup>

Epidemiological data on the effects of BPA in human populations are limited. Studies of the U.S. general population have reported that adults with higher recent BPA exposure (as represented by urinary BPA concentrations) are more likely to have coronary heart disease, diabetes, immune dysfunction, and liver enzyme abnormalities.<sup>37-39</sup> Some of these associations are postulated to be due to non-estrogenic effects of BPA,<sup>38</sup> although there is limited understanding of the mechanisms by which BPA exposure may lead to an adverse health effect. Studies of workers in China reported an association between exposure to high levels of BPA and an increased risk of self-reported sexual dysfunction,<sup>40,41</sup> and that BPA exposure to pregnant workers was associated with decreased offspring birthweight.<sup>42</sup> A study of children in Ohio reported an association between prenatal BPA exposure, at levels typical for the general population, and aggression and hyperactivity in 2-year-old children.<sup>43</sup> Similar associations between behavioral effects and BPA exposure have been seen in animal studies.<sup>3,44,45</sup> However, another study of prenatal BPA exposure conducted in New York City found no association between prenatal BPA exposure and social behavior deficits in children at ages 7 to 9 years.<sup>46</sup> In 2009, the National Institutes of Health announced that it would spend \$30 million over two years to better understand the link between low-dose BPA exposure and human health effects.

Studies have shown that detectable levels of BPA are present in human urine samples from all age groups including infants, toddlers, children and adults.<sup>3,47-52</sup> BPA has been identified in the blood of pregnant women,<sup>53</sup> and also can cross the placenta, potentially exposing the fetus.<sup>54</sup> Previous studies have identified higher levels of BPA in the urine of children ages 6 to 11 years compared with adults,<sup>47,49,50</sup> and found that consumption of soda and school lunches was also associated with higher urinary BPA concentrations.<sup>50</sup> Infants and young children also have a higher estimated daily intake of BPA compared with adults.<sup>3,48</sup> Although less information is available on BPA levels in infants than in older children, one study found that premature infants in intensive care units had greater urinary BPA concentrations than those observed in other infants or even older children, though the route of exposure for the premature infants is unclear.<sup>55</sup> Some laboratory animal studies have found that younger animals are less effective at metabolizing BPA than older animals are; while it has been proposed that such findings may apply to human infants and developing fetuses, this hypothesis is debated in the scientific literature.<sup>3,36,52,56-61</sup> One important part of ongoing research is to better understand how BPA is absorbed, distributed, metabolized, and excreted by the body, and how those processes change

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<sup>i</sup> More information on NTP concern levels is available at <http://www.niehs.nih.gov/news/media/questions/sya-bpa.cfm>.

with age and with route of exposure.<sup>56-58,60-62</sup> Interpretation of these data will allow us to understand how environmental exposure equates to the internal dose routinely measured in biomonitoring studies.

The two indicators that follow use the best nationally representative data currently available on urinary BPA levels over time for women of child-bearing age and children. Indicator B11 presents median and 95<sup>th</sup> percentile concentrations of BPA in urine for women ages 16 to 49 years. Indicator B12 presents median and 95<sup>th</sup> percentile concentrations of BPA in urine for children ages 6 to 17 years. Both indicators have been updated since the publication of *America's Children and the Environment, Third Edition* (January 2013) to include data from 2011–2012.

### Indicator B11: Bisphenol A in women ages 16 to 49 years: Median and 95th percentile concentrations in urine, 2003–2012

### Indicator B12: Bisphenol A in children ages 6 to 17 years: Median and 95th percentile concentrations in urine, 2003–2012

**About the Indicators:** Indicators B11 and B12 present concentrations of bisphenol A (BPA) in urine of U.S. women ages 16 to 49 years and children ages 6 to 17 years. The data are from a national survey that collects urine specimens from a representative sample of the population every two years, and then measures the concentration of total BPA in the urine. Indicator B11 presents concentrations of BPA in women's urine over time and Indicator B12 presents concentrations of BPA in children's urine over time. The focus on both women of child-bearing age and children is based on concern for potential adverse effects in children born to women who have been exposed to BPA and in children exposed to BPA.

## NHANES

The National Health and Nutrition Examination Survey (NHANES) provides nationally representative biomonitoring data for BPA. NHANES is designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population and is conducted by the National Center for Health Statistics, part of the Centers for Disease Control and Prevention (CDC). Interviews and physical examinations are conducted with approximately 10,000 people in each two-year survey cycle. CDC's National Center for Environmental Health measures concentrations of environmental chemicals in blood and urine samples collected from NHANES participants. Summaries of the measured values for more than 200 chemicals are provided in the *Fourth National Report on Human Exposure to Environmental Chemicals*.<sup>63</sup>

## Bisphenol A and its Metabolites

Indicators B11 and B12 present urinary levels of BPA in women of child-bearing age and children. The reported measurements of BPA in urine represent "total BPA," which includes both free BPA and non-estrogenic metabolites of BPA (only free BPA is considered active based on measures of estrogenicity). Measured levels in the U.S. population may be composed predominantly of these metabolites,<sup>64</sup> but total BPA levels reflect previous exposure to the biologically active form of BPA and there is debate in the scientific community over the potential for conversion of non-estrogenic metabolites back to free BPA in various tissues.<sup>65</sup> Recent work has also highlighted the potential for conversion of non-estrogenic metabolites of BPA to the active form when crossing the placenta, increasing the relevance of total BPA measurements to children's health.<sup>54,66</sup> All values are reported as micrograms of BPA per liter of urine ( $\mu\text{g/L}$ ).

Concentrations of BPA in urine have been measured in a representative subset of NHANES participants ages 6 years and older beginning with the 2003–2004 survey cycle. In 2011–2012,

NHANES collected BPA biomonitoring data for 2,489 individuals ages 6 years and older, including 536 women ages 16 to 49 years and 852 children ages 6 to 17 years. BPA was detected in about 89% of all individuals sampled. The frequency of BPA detection was 89% in women ages 16 to 49 years,<sup>ii</sup> and 90% in children ages 6 to 17 years. The median and 95<sup>th</sup> percentile BPA levels in urine for all NHANES participants in 2011–2012 were 1 µg/L and 9 µg/L, respectively. The widespread detection of BPA, combined with the fact that BPA has a short half-life, indicates that BPA exposure is widespread and relatively continuous.

### Individual Variability in Urinary Measurements

NHANES data for BPA are based on measurements made using a single urine sample for each person surveyed. Due to normal changes in an individual's urinary output throughout the day, this variability in urinary volume, among other factors related to the measurement of chemicals that do not accumulate in the body,<sup>67</sup> may mask differences between individuals in levels of BPA. Since BPA does not appear to accumulate in bodily tissues, the distribution of NHANES urinary BPA levels may overestimate high-end exposures (e.g., at the 95<sup>th</sup> percentile) as a result of collecting one-time urine samples.<sup>8,68,69</sup> Many studies account for differences in hydration levels by reporting the chemical concentration per gram of creatinine. Creatinine is a byproduct of muscle metabolism that is excreted in urine at a relatively constant rate, independent of the volume of urine, and can in some circumstances partially account for the measurement variability due to changes in urinary output.<sup>70</sup> However, urinary creatinine concentrations differ significantly among different demographic groups, and are strongly associated with an individual's muscle mass, age, sex, diet, health status (specifically renal function), body mass index, and pregnancy status.<sup>71,72</sup> Thus, these indicators present the unadjusted BPA concentrations so that any observed differences in concentrations between demographic groups are not due to differences in creatinine excretion rates. These unadjusted urinary levels from a single sample may either over- or underestimate urinary levels for a sampled individual. However, for a representative group, it can be expected that a median value based on single samples taken throughout the day will provide a good approximation of the median for that group. Furthermore, due to the large number of subjects surveyed, we expect that differences in the concentrations of BPA that might be attributed to the volume of the urine sample would average out within and across the various comparison groups.

### Birth Rate Adjustment

Indicator B11 uses measurements of BPA in urine of women ages 16 to 49 years to represent the distribution of BPA exposures to women who are pregnant or may become pregnant. However, women of different ages have a different likelihood of giving birth. For example, in 2003–2004, women aged 27 had a 12% probability of giving birth, and women aged 37 had a 4% probability of giving birth.<sup>73</sup> A birth rate-adjusted distribution of women's BPA levels is used

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<sup>ii</sup> The percentage for women ages 16 to 49 years is calculated with the birth rate adjustment described below.

in calculating this indicator,<sup>iii</sup> meaning that the data are weighted using the age-specific probability of a woman giving birth.<sup>74</sup>

### **Data Presented in the Indicators**

Indicators B11 presents median and 95<sup>th</sup> percentile concentrations of BPA in urine over time for women ages 16 to 49 years, using NHANES data from 2003–2012.

Indicator B12 presents median and 95<sup>th</sup> percentile concentrations of BPA in urine over time for children ages 6 to 17 years, using NHANES data from 2003–2012.

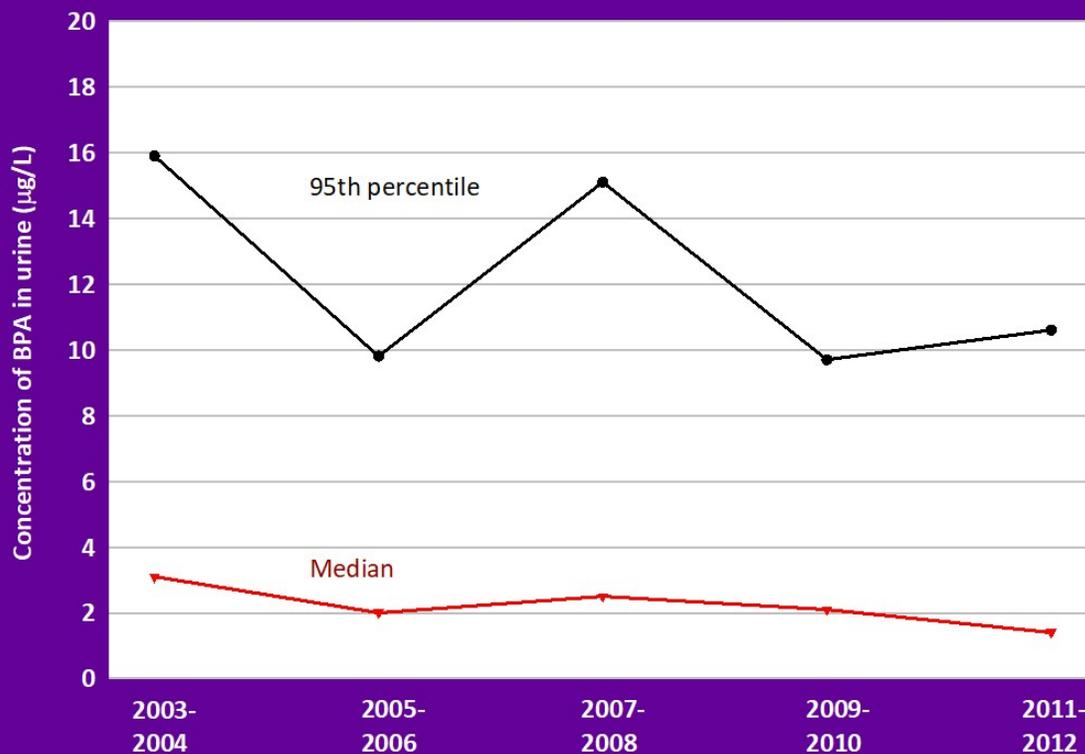
Additional information showing how the median and 95<sup>th</sup> percentile levels of BPA in urine vary by race/ethnicity and family income for women ages 16 to 49 years is presented in supplemental data tables for these indicators. Data tables also display information showing how the median and 95<sup>th</sup> percentile levels of BPA in urine vary by race/ethnicity, family income, and age for children ages 6 to 17 years.

Please see the Introduction to the Biomonitoring section for an explanation of the terms “median” and “95<sup>th</sup> percentile,” a description of the race/ethnicity and income groups used in the ACE3 biomonitoring indicators, and information on the statistical significance testing applied to these indicators.

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<sup>iii</sup> There may be multiple ways to implement an adjustment to the data that accounts for birth rates by age. The National Center for Health Statistics has not fully evaluated the method used in ACE, or any other method intended to accomplish the same purpose, and has not used any such method in its publications. NCHS and EPA are working together to further evaluate the birth rate adjustment method used in ACE and alternative methods.

**Bisphenol A in women ages 16 to 49 years: Median and 95th percentile concentrations in urine, 2003-2012**



Data: Centers for Disease Control and Prevention, National Center for Health Statistics and National Center for Environmental Health, National Health and Nutrition Examination Survey

Note: To reflect exposures to women who are pregnant or may become pregnant, the estimates are adjusted for the probability (by age and race/ethnicity) that a woman gives birth.

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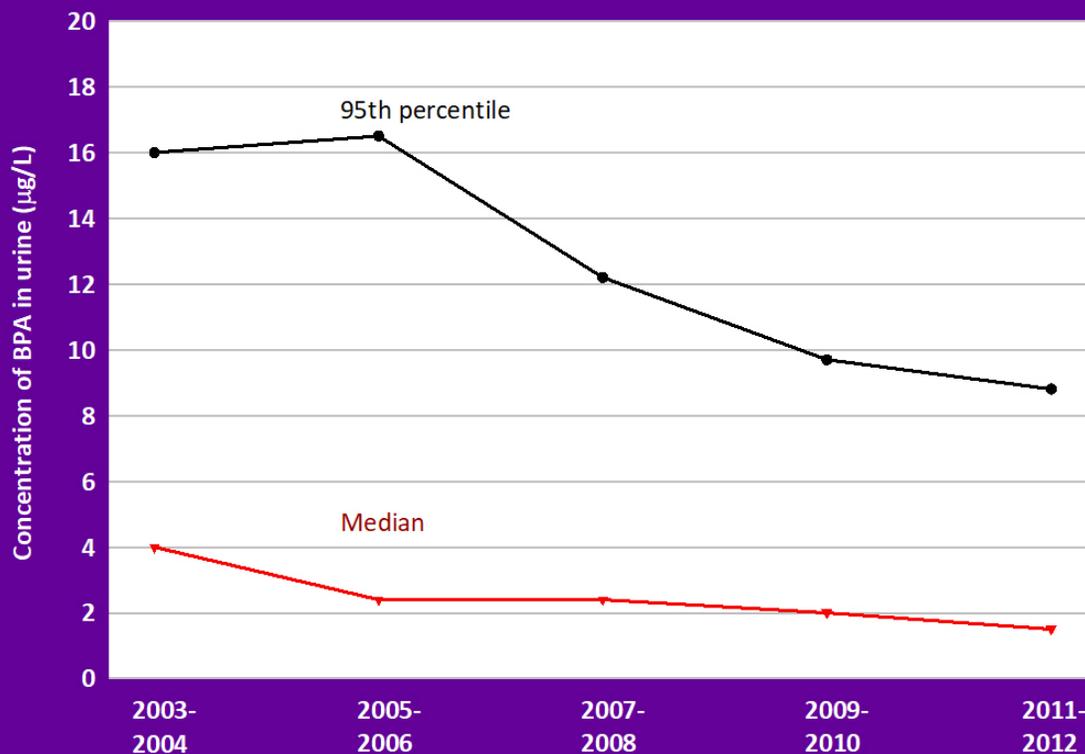
**Data characterization**

- Data for this indicator are obtained from an ongoing continuous survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- BPA is measured in urine samples obtained from individual survey participants.

- From 2003–2004 to 2011–2012, the median concentration of BPA in urine among women ages 16 to 49 years generally decreased from 3 µg/L to 1 µg/L. The decreasing trend was statistically significant.
- From 2003–2004 to 2011–2012, the concentrations of BPA in urine at the 95<sup>th</sup> percentile varied between 10 µg/L and 16 µg/L, and was 11 µg/L in 2011–2012. There was no statistically significant trend in 95<sup>th</sup> percentile concentrations of BPA over the years shown.

- Between 2003–2004 and 2011–2012, the concentrations of BPA in the 95<sup>th</sup> percentile ranged from 5 to 8 times the median levels for women ages 16 to 49 years.
- In 2009–2012, the median concentration of BPA in urine of Black non-Hispanic women was about 4 µg/L, which was higher than the median concentrations in White non-Hispanic women, Mexican-American women, and women of “All Other Races/Ethnicities.” The differences between Black non-Hispanic women and women in other race/ethnicity groups were statistically significant. (See Table B11a.)
- Women living below the poverty level had higher median concentrations of BPA in urine than those living at or above poverty level, a difference that was not statistically significant. (See Table B11a.)
- Among White non-Hispanic women, those with family incomes below poverty level had higher median concentrations of BPA in urine than those at or above poverty level. The differences between the income groups were not statistically significant. (See Table B11a.)
- Higher concentrations of BPA were observed in the urine of women below the poverty level at the 95<sup>th</sup> percentile (13 µg/L) compared with women at or above the poverty level (9 µg/L). This difference was not statistically significant. (See Table B11b.)
- In 2009–2012, the 95<sup>th</sup> percentile concentration of BPA in urine of Black non-Hispanic women was about 15 µg/L, which was higher than the median concentrations in White non-Hispanic women and Mexican-American women. The differences between Black non-Hispanic women and White non-Hispanic women or Mexican-American women were statistically significant after adjustment for differences in age and income. (See Table B11b.)

**Bisphenol A in children ages 6 to 17 years: Median and 95th percentile concentrations in urine, 2003-2012**



Data: Centers for Disease Control and Prevention, National Center for Health Statistics and National Center for Environmental Health, National Health and Nutrition Examination Survey *America's Children and the Environment, Third Edition, Updated August 2017*

**Data characterization**

- Data for this indicator are obtained from an ongoing continuous survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- BPA is measured in urine samples obtained from individual survey participants.

- Among children ages 6 to 17 years, the median concentration of BPA in urine of children ages 6 to 17 years decreased from 4 µg/L in 2003–2004 to 2 µg/L in 2011–2012. The concentration of BPA in urine at the 95<sup>th</sup> percentile decreased from 16 µg/L in 2003–2004 to 9 µg/L in 2011–2012. These decreasing trends were statistically significant.
- Between 2003–2004 and 2011–2012, the concentrations of BPA in the 95<sup>th</sup> percentile ranged from 4 to 7 times the median levels for children ages 6 to 17 years.

- In 2009–2012, median concentrations of BPA in urine of Black non-Hispanic children ages 6 to 17 years were higher than in White non-Hispanic children, Mexican-American children, and children of “All Other Races/Ethnicities.” These differences were statistically significant. (See Table B12a.)
- BPA concentrations at the 95<sup>th</sup> percentile were similar for Black non-Hispanic, White-non Hispanic, and Mexican-American children ages 6 to 17 years in 2009–2012. (See Table B12b.)
- In 2009–2012, BPA concentrations were similar for age groups 6 to 10 years, 11 to 15 years, and 16 to 17 years, both at the median and at the 95<sup>th</sup> percentile. (See Table B12c.)

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