# America's Children and the Environment, Third Edition

### **DRAFT Indicators**

### **Biomonitoring: Mercury**

EPA is preparing the third edition of *America's Children and the Environment* (ACE3), following the previous editions published in December 2000 and February 2003. ACE is EPA's compilation of children's environmental health indicators and related information, drawing on the best national data sources available for characterizing important aspects of the relationship between environmental contaminants and children's health. ACE includes four sections: Environments and Contaminants, Biomonitoring, Health, and Special Features.

EPA has prepared draft indicator documents for ACE3 representing 23 children's environmental health topics and presenting a total of 42 proposed children's environmental health indicators. This document presents the draft text, indicator, and documentation for the mercury topic in the Biomonitoring section.

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For more information on America's Children and the Environment, please visit <u>www.epa.gov/ace</u>. For instructions on how to submit comments on the draft ACE3 indicators, please visit <u>www.epa.gov/ace/ace3drafts/</u>.

# 1 Mercury

- 2 Mercury is a metal that is liquid at room temperature. There are three major forms of mercury: 1)
- 3 organic mercury; 2) non-elemental forms of inorganic mercury; and 3) elemental mercury.
- 4 Organic mercury, predominantly in the form of methylmercury, is found primarily in fish. Non-
- 5 elemental forms of inorganic mercury are found primarily in batteries, some disinfectants, and
- 6 some health products and creams. Lastly, elemental mercury is found in thermometers,
- 7 fluorescent bulbs, dental amalgam fillings, and other sources.<sup>1</sup>
- 8 Mercury is released from its natural form in the earth's crust as a result of both human activities
- 9 and natural processes. One major source is the burning of coal in power plants and other
- 10 facilities. Other sources of air emissions include the combustion of waste and industrial
- 11 processes that use mercury.<sup>2</sup> When released into the atmosphere, either from human activities or
- 12 from non-human sources, such as volcanoes, mercury can travel long distances on global air
- 13 currents and can be deposited on land and water far from its original source.<sup>2,3</sup> In addition to
- 14 these mercury emissions, there is concern that an increase in ice melts caused by a warming
- 15 climate may release some past mercury emissions that have been trapped in polar ice.<sup>4</sup> Moreover,
- 16 mercury deposited on the surface in the Arctic vaporizes each spring when the sunlight returns,
- 17 causing high concentrations in the atmosphere.<sup>5,6</sup>
- 18 When deposited into water systems such as rivers, lakes, and wetlands, mercury is converted by
- 19 bacteria into methylmercury. Methylmercury then bioaccumulates up the aquatic food web; fish
- 20 that live long and feed on other fish (i.e., predatory fish) can accumulate high levels of
- 21 methylmercury. The concentration of methylmercury in the larger fish at the top of the food
- 22 chain can reach levels a million times higher than in the water.<sup>7</sup> People are exposed to
- 23 methylmercury mainly through eating fish contaminated with methylmercury. This can occur
- both in commercially distributed fish that people buy in stores and restaurants and in fish that
- 25 people catch for consumption by their families and communities.
- 26 Levels of mercury in the bodies of women of child-bearing age are important because of the
- 27 potential for prenatal exposure: methylmercury crosses the placenta and blood-brain barrier
- 28 easily.<sup>8</sup> Although the prenatal period is the most sensitive period of exposure, exposure to
- 29 mercury during childhood could also pose a potential health risk.<sup>8</sup>
- 30 Prenatal exposure to methylmercury can cause adverse developmental and cognitive effects in
- 31 children. Severe adverse health effects, such as cerebral palsy, mental retardation, deafness, and
- 32 blindness, have been reported for persons prenatally exposed during high-dose mercury
- poisoning events in Japan and Iraq.<sup>8-10</sup> Prospective cohort studies of mercury's more subtle
- 34 effects have focused on island populations where frequent fish consumption leads to moderate
- 35 mercury levels in pregnant women. Results from such studies in New Zealand and the Faroe
- 36 Islands<sup>8,11-14</sup> suggested that increased prenatal mercury exposure due to maternal fish
- 37 consumption was associated with decrements in attention, language, memory, motor speed, and
- 38 visual-spatial function (like drawing). These associations were not seen in initial results reported
- 39 from a study in the Seychelles Islands.<sup>15</sup> Follow-up studies of the same area did find associations

- 1 between prenatal mercury exposure and infant neurodevelopmental problems, once researchers
- 2 adjusted for the developmental benefits of fish consumption.<sup>16 17</sup>More recent studies conducted
- 3 in Massachusetts and New York City, with maternal blood mercury levels within the range of
- 4 typical levels in the United States general population, have demonstrated associations between
- increased prenatal mercury levels and decreased vocabulary, visual-motor abilities, and
   intelligence in children.<sup>18-20</sup>Animal and epidemiological studies suggest that early life exposure
- intelligence in children. Animal and epidemiological studies suggest that early life exposur
   to methylmercury (including prenatal exposures) may also affect cardiovascular,<sup>21,22</sup>
- immune.<sup>8,23,24</sup> and reproductive health.<sup>8</sup>
- 9 Exposure to methylmercury in fish can be harmful, but other compounds naturally present in
- 10 many fish can be highly beneficial. These are called  $\operatorname{omega-3}_{25}$  fatty acids, which are nutrients that
- 11 contribute to healthy development of infants and children.<sup>25</sup> Pregnant women are advised to seek
- 12 dietary sources of these fatty acids, including many species of fish. The levels of both mercury
- 13 and omega-3 fatty acids can vary considerably by species. Thus, the type of fish, as well as
- 14 portion sizes and frequency of consumption are all important considerations for health benefits
- 15 of fish and the extent of methylmercury exposure.
- 16 Many state health departments provide advice regarding healthy sources of fish that are lower in
- 17 mercury. Links to state advice regarding fish consumption can be found at
- 18 <u>http://www.epa.gov/waterscience/fish/states.htm</u> (for an example, see Washington state's "Eat
- 19 Fish, Choose Wisely" available at <u>http://www.doh.wa.gov/ehp/oehas/fish/fishchart.htm</u>). State
- 20 advisories may address both store-bought fish and fish caught by individuals in local lakes,
- rivers, and coastal waters. Advisories from the federal government exist as well. EPA and FDA
- consumption guidance advises young children and pregnant females to consume up to 12 ounces
- a week of lower-mercury fish and shellfish, such as shrimp, canned light tuna, salmon, pollock,
- and catfish and to avoid any consumption of high mercury containing fish, such as shark,  $\frac{22}{26}$
- swordfish, tile fish or king mackerel.<sup>26</sup>
- 26 Thimerosal is an organic mercury-containing preservative that is used in some vaccines to
- 27 prevent contamination and growth of harmful bacteria in vaccine vials. The presence of
- 28 thimerosal in many vaccines administered to infants led to concerns about possible effects on
- 29 children's neurological development, including a hypothesis that mercury in vaccines could be a
- 30 contributing factor to the incidence of autism. In July 1999, the CDC, the American Academy of
- 31 Pediatrics, and vaccine manufacturers agreed to reduce or eliminate the use of thimerosal in
- vaccines as a precautionary measure. Since 2001, thimerosal has not been used in routinely
   administered childhood vaccines, with the exception of some influenza vaccines.<sup>27</sup> The Institute
- of Medicine has rejected the hypothesis of a causal relationship between thimerosal-containing
- 34 of Medicine has rejected the hypothesis of a causal relationship between thimerosal-containing 35 vaccines and autism.<sup>28</sup> Two recent studies conducted by CDC scientists have concluded that
- 36 prenatal and infant exposure to thimerosal-containing vaccines is not related to increased risk of
- 37 autism.<sup>29,30</sup>
- 38 Human exposure to the other forms of mercury-elemental and inorganic mercury- can occur at
- 39 work, through the use of products containing mercury, through ritual and folk medicine uses of
- 40 mercury as well as dental restorations with mercury-silver amalgams.<sup>2,31</sup> Sources of childhood
- 41 exposure to elemental and inorganic mercury in the home include the tracking of mercury into

- 1 the home from the workplace by parents, mercury-containing devices in the home, and very
- 2 rarely from intentionally heating mercury in the home for the purpose of extracting gold, as
- 3 noted in a few case reports in the United States.<sup>32</sup> In schools, the most common sources of
- exposure are elemental and inorganic mercury stored in science laboratories, and mercury from
   broken instruments such as thermometers. Some school gymnasium floors manufactured
- broken instruments such as thermometers. Some school gymnastum noors manufactured
   between 1960 and 1980 may contain a mercury catalyst that releases mercury vapors into the
- 7 air.<sup>32,33</sup> Unlike organic mercury, the adverse health effects of elemental and inorganic mercury
- 8 exposure in childhood have not been extensively studied; however elemental mercury vapor can
- 9 be readily absorbed by the lungs and inhaling high mercury concentrations can lead to lung
- 10 problems, neurobehavioral effects, mood changes, and tremors.<sup>34</sup>
- 11 Because mercury exposure in pregnant women is a concern for children health, studies have
- 12 measured the level of mercury in women's bodies. Mercury can be measured in blood and often
- 13 called "blood mercury." Among women 16 to 49 years of age in the United States, levels of
- 14 mercury in blood tend to be highest for Native American, Pacific Islander, Asian American, and
- 15 multi-racial women.<sup>35-37</sup> A survey of adults in New York City found that blood mercury levels
- 16 were three times higher than the national levels. Asian Americans in this study had higher blood
- 17 mercury levels than other race/ethnicity groups.<sup>38</sup> Among women ages 16 to 49 years in the
- 18 United States, blood mercury levels are higher for those who eat fish more often or in higher 39.35
- 19 quantities.  $^{39,35}$  Asian American populations have been identified as high consumers of seafood
- 20 compared with White non-Hispanics or Black non-Hispanics.<sup>38</sup>
- 21 For women of all races, blood mercury levels tend to be higher in those women with higher
- family incomes.<sup>36,38,40</sup> Fish consumption rates are highest among women with relatively high
- family incomes, and this higher rate of fish consumption leads to increased blood mercury
- 24 levels.<sup>36,40</sup> Concentrations of total mercury in blood among women also seem to vary with
- 25 geographic region, and potentially by coastal region. Based on data from 1999–2004, blood
- mercury levels for women ages 16 to 49 years were higher in the Northeastern region of the
   United States compared with other regions.<sup>36</sup> Estimated mercury intake from fish consumption
- also follows this observed pattern. Women living in coastal regions had blood mercury levels
- 29 higher than those living in noncoastal regions, and among coastal populations, the highest blood
- 30 mercury levels were reported for the Atlantic and Pacific coastal regions, followed by the Gulf
- 31 Coast and Great Lakes regions, respectively.
- 32 The following indicator shows the distribution of total mercury in blood among women within
- the child-bearing age ranges of 16 to 49 years. Mercury exposure in women who can have
- 34 children is important due to concerns for neurodevelopmental effects from prenatal exposure.<sup>8</sup>
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### Indicator B4: Mercury in women ages 16 to 49 years: Median 1 and 95<sup>th</sup> percentile concentrations in blood, 1999-2008

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## **Overview**

Indicator B4 presents levels of mercury in blood of U.S. women ages 16 to 49 years. The data are from a national survey that collects blood specimens from a representative sample of the population, and then measures the concentration of mercury in blood. The indicator shows the change in blood mercury concentrations over time. The focus is on women of child-bearing age because increasing blood levels of mercury during pregnancy have been associated with increased risk of adverse children's health outcomes.

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### 6 NHANES

- 7 This indicator presents data from the National Health and Nutrition Examination Survey
- 8 (NHANES). NHANES is a nationally representative survey designed to assess the health and
- 9 nutritional status of the civilian noninstitutionalized U.S. population, conducted by the Centers
- 10 for Disease Control and Prevention (CDC). Interviews and physical examinations are conducted
- 11 with approximately 5,000 people each year. CDC's National Center for Environmental Health
- measures concentrations of environmental chemicals in blood and urine samples collected from 12
- NHANES participants.<sup>41</sup> Concentrations of total blood mercury have been measured in a 13
- representative subset of NHANES participants ages 1 to 5 years and women ages 16 to 49 years 14
- 15 beginning with the 1999–2000 survey cycle. Starting with the 2003–2004 survey cycle,
- NHANES measured blood mercury in all participants ages 1 year and older.<sup>42</sup> NHANES data 16
- 17 from 1999-2006 for women of child-bearing age are used for Indicator B4.

### 18 **Measurement of Mercury in NHANES**

- 19 Organic, inorganic, and total mercury can be measured in blood; NHANES reports total blood
- 20 mercury for all survey years starting with 1999–2000, and inorganic blood mercury starting with
- 21 the 2003–2004 NHANES survey cycle. The concentration of total mercury in blood is a marker
- 22 of exposure to methylmercury in populations where fish consumption is the predominant source
- 23 of mercury exposure. Previous analysis shows that, in general, methylmercury accounts for a
- 24 large percentage of total mercury in blood among women of child-bearing age in the United
- States.<sup>35</sup> 25

### 26 **Birthrate Adjustment**

- 27 This indicator uses measurements of mercury in blood of women ages 16 to 49 years to represent
- 28 the distribution of mercury exposures to women who are pregnant or may become pregnant.
- However, blood mercury levels increase with age,<sup>42</sup> and women of different ages have a different 29
- likelihood of giving birth. For example, in 2003–2004, women aged 27 years had a 12% annual 30
- 31 probability of giving birth, and women aged 37 years had a 4% annual probability of giving
- 32 birth.<sup>43</sup> A birthrate-adjusted distribution of women's blood mercury levels is used in calculating

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this indicator, meaning that the data are weighted using the age-specific probability of a woman 1 giving birth.44

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

Indicator B4 presents the median (50<sup>th</sup> percentile) and 95<sup>th</sup> percentile of blood mercury levels for 5 6 each two-year survey period. The median is the value in the middle of the distribution of blood 7 mercury: half of the women have blood mercury levels greater than the median, and half have 8 blood mercury levels below the median. The median can be thought of as representing a typical 9 exposure. The 95<sup>th</sup> percentile is a value representing the upper range of blood mercury levels: 5% of women have blood mercury levels greater than the 95<sup>th</sup> percentile. This value therefore can be 10 11 thought of as representing a relatively high exposure among women, but not a maximum level.

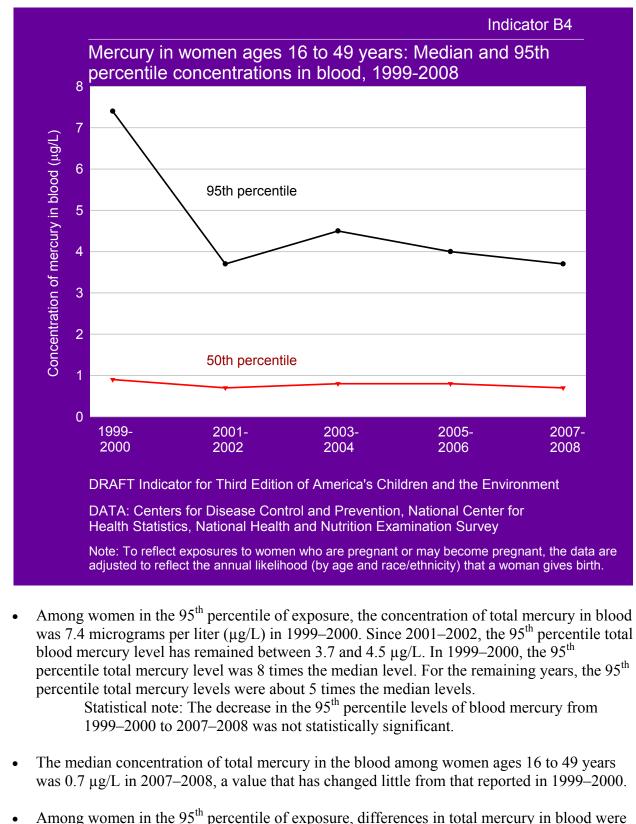
12

13 In addition to indicator B4, supplemental tables show differences in blood mercury levels in

- women of child-bearing age, for different race/ethnicity groups and levels of family income. 14
- Another table displays the median and 95<sup>th</sup> percentile blood mercury levels for children ages 1 to 15
- 16 5 years.

### **Statistical Testing** 17

- 18 Statistical analysis has been applied to the biomonitoring indicators to determine whether any
- 19 changes in chemical concentrations over time, or any differences in chemical concentrations
- 20 between demographic groups, are statistically significant. These analyses use a 5% significance
- 21 level (p < 0.05), meaning that a conclusion of statistical significance is made only when there is
- no more than a 5% chance that the observed change over time or difference between 22
- 23 demographic groups occurred randomly. It should be noted that when statistical testing is
- 24 conducted for differences among multiple demographic groups (e.g., considering both
- 25 race/ethnicity and income level), the large number of comparisons involved increases the
- 26 probability that some differences identified as statistically significant may actually have occurred 27 randomly.
- 28
- 29 A finding of statistical significance for a biomonitoring indicator depends not only on the
- 30 numerical difference in the value of a reported statistic between two groups, but also on the
- 31 number of observations in the survey, the amount of variability among the observations, and
- 32 various aspects of the survey design. For example, if two groups have different median levels of
- 33 a chemical in blood or urine, the statistical test is more likely to detect a difference when samples
- 34 have been obtained from a larger number of people in those groups. Similarly, if there is low
- 35 variability in levels of the chemical within each group, then a difference between groups is more
- 36 likely to be detected. A finding that there is or is not a statistically significant difference in
- 37 exposure levels between two groups or in exposure levels over time does not necessarily suggest
- 38 any interpretation regarding the health implications of those differences.



• Among women in the 95<sup>th</sup> percentile of exposure, differences in total mercury in blood were observed across race/ethnicity groups. For the years 2005–2008, White non-Hispanic women

1 2 3 4 5 6 7	<ul> <li>had a blood mercury level of 4.0 μg/L, Black non-Hispanics had 2.7 μg/L, Mexican-American women had 2.2 μg/L, and women in the "Other" race/ethnic group had 6.5 μg/L. These values changed for each race/ethnicity group when stratified by income level. (See Table B4b.)</li> <li>Statistical note: All of these differences are statistically significant after adjustment for differences by race in income or age profiles, except for the difference between Black non-Hispanic and women in the "Other" race/ethnic group.</li> </ul>
8 • 9 10 11 12 13 14 15 16	<ul> <li>Among women in the 95<sup>th</sup> percentile of exposure, women living at or above the poverty level had higher blood levels of total mercury (4.0 µg/L) compared with women living below poverty level (2.4 µg/L). The same trend was also observed within all race/ethnicity groups. (See Table B4b.)</li> <li>Statistical note: Among all women this difference was statistically significant. The differences by income level within the single race/ethnicity groups were statistically significant only after accounting for differences in age profile, with the exception of White non-Hispanic women, for which there was no statistically significant difference between women of different income levels.</li> </ul>
17 • 18 19	The median and 95 <sup>th</sup> percentile values for women of child-bearing age are about 2 to 3 times those of children ages 1 to 5 years. (See Table B4 and Table B4c.)
20 21 22 23 24 25 26 27 28 29	<ul> <li>Among children ages 1 to 5 years in the 95<sup>th</sup> percentile of exposure, the concentration of total mercury in blood declined from 2.3 μg/L in 1999–2000 to 1.3 μg/L in 2007–2008. The median blood mercury level for children ages 1 to 5 years stayed relatively constant for the same time period. (See Table B4c.)</li> <li>Statistical note: The decline in 95<sup>th</sup> percentile blood mercury levels in children was statistically significant. There was no statistically significant change in median blood mercury levels in children.</li> </ul>

# Data Tables

Table B4: Mercury in women ages 16 to 49 years: Median and 95th percentile concentrationsin blood, 1999-2008

		Concentration of mercury in blood (µg/L)							
	1999- 2000	2005- 2006	2007- 2008						
Median	0.9	0.7	0.8	0.8	0.7				
95 <sup>th</sup> percentile	7.4	3.7	4.5	4.0	3.7				

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

NOTE: The distribution of the data for women ages 16 to 49 years is adjusted for the likelihood that a woman of a particular age and race/ethnicity gives birth in a particular year. The intent of this adjustment is to approximate the distribution of exposure to pregnant women. Results will therefore differ from a characterization of exposure to adult women without consideration of birthrates.

### 12 13 14 15 16 17 18

# Table B4a. Mercury in women ages 16 to 49 years: Median concentrations in blood, by race/ethnicity and family income, 2005-2008

	Concentration of mercury in blood (µg/dL)								
				<u>&gt;</u> Poverty					
Race / Ethnicity	All Incomes	< Poverty Level	≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income			
All Races/ Ethnicities	0.8	0.6	0.8	0.7	0.9	0.7			
White non- Hispanic	0.7	0.5	0.8	0.6	0.8	NA**			
Black non- Hispanic	0.8	0.8	0.8	0.8	0.8	1.0			
Mexican- American	0.7	0.6	0.7	0.6	0.8	0.6			
Other†	1.2	0.8	1.4	1.3	1.7	0.9			

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

NOTE: The distribution of the data for women ages 16 to 49 years is adjusted for the likelihood that a woman of a particular age and race/ethnicity gives birth in a particular year. The intent of this adjustment is to approximate the distribution of exposure to pregnant women. Results will therefore differ from a characterization of exposure to adult women without consideration of birthrates.

† "Other" includes Asian non-Hispanic; Native American non-Hispanic; Hispanic other than Mexican-American; those reporting multi-racial; and those with a missing value for race/ethnicity.

\*\* The estimate is not reported because it has large uncertainty: the relative standard error, RSE, is at least 40% (RSE = standard error divided by the estimate).

# Table B4b. Mercury in women ages 16 to 49 years: 95<sup>th</sup> percentile concentrations in blood, by race/ethnicity and family income, 2005-2008

		Concentration of mercury in blood (µg/dL)								
		_		<u>&gt;</u> Poverty	Unknown Income					
Race / Ethnicity	All < Poverty Incomes Level		≥ Poverty Level	100-200% of Poverty Level			> 200% of Poverty Level			
All Races/ Ethnicities	3.8	2.4	4.0	3.3	4.4	2.8				
White non- Hispanic	4.0	2.9*	4.0	2.4	4.3	2.5				
Black non- Hispanic	2.7	2.1	2.8	2.3	3.2	2.9*				
Mexican- American	2.2	1.9	2.4	2.6	2.3	2.1				
Other†	6.5	NA**	6.5	4.1	6.5	6.1*				

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

NOTE: The distribution of the data for women ages 16 to 49 years is adjusted for the likelihood that a woman of a particular age and race/ethnicity gives birth in a particular year. The intent of this adjustment is to approximate the distribution of exposure to pregnant women. Results will therefore differ from a characterization of exposure to adult women without consideration of birthrates.

† "Other" includes Asian non-Hispanic; Native American non-Hispanic; Hispanic other than Mexican-American; those reporting multi-racial; and those with a missing value for race/ethnicity.

\* The estimate should be interpreted with caution because the standard error of the estimate is relatively large: the relative standard error, RSE, is at least 30% but is less than 40% (RSE = standard error divided by the estimate).

\*\* The estimate is not reported because it has large uncertainty: the relative standard error, RSE, is at least 40% (RSE = standard error divided by the estimate).

### Table B4c: Mercury in children ages 1 to 5 years: Median and 95<sup>th</sup> percentile concentrations in blood, 1999-2008

	Concentration of mercury in blood (µg/L)						
	1999- 2000	2005- 2006	2007- 2008				
Median	0.3	0.3	0.3	0.2	0.2		
95 <sup>th</sup> percentile	2.3	1.9	1.8	1.4	1.3		

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

# 6 7 8 9 10 10 11 12 13

### Table B4d: Mercury in children ages 1 to 17 years: Median and 95<sup>th</sup> percentile concentrations in blood, by age group, 2005-2008

		Concentration of mercury in blood (µg/L)							
	All ages	Ages 1 to <2 years	Age 2 to Age 3 to <3 years <6 years		Age 6 to <11 years	Age 11 to <16 years	Age 16 to <18 years		
Median	0.4	0.2	0.2	0.2	0.4	0.4	0.5		
95 <sup>th</sup> percentile	1.9	1.4*	1.3	1.4	1.9	1.9	2.4		

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

\* The estimate should be interpreted with caution because the standard error of the estimate is relatively large: the relative standard error, RSE, is at least 30% but is less than 40% (RSE = standard error divided by the estimate).

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- women of childbearing age with adjustment for age-specific natality. Environmental Research 111 (1):149-155.

# 1 Metadata

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Metadata for	National Health and Nutrition Examination Survey (NHANES)
Brief description of the data set	The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States, using a combination of interviews, physical examinations, and laboratory analysis of biological specimens.
Who provides the data set?	Centers for Disease Control and Prevention, National Center for Health Statistics.
How are the data gathered?	Laboratory data are obtained by analysis of blood and urine samples collected from survey participants at NHANES Mobile Examination Centers. Health status is assessed by physical examination. Demographic and other survey data regarding health status, nutrition and health-related behaviors are collected by personal interview, either by self-reporting or, for children under 16 and some others, as reported by an informant.
What documentation is available describing data collection procedures?	See <u>http://www.cdc.gov/nchs/nhanes.htm</u> for detailed survey and laboratory documentation by survey period.
What types of data relevant for children's environmental health indicators are available from this database?	Concentrations of environmental chemicals in urine, blood, and serum. Body measurements. Health status, as assessed by physical examination, laboratory measurements and interview responses. Demographic information.
What is the spatial representation of the database (national or other)?	NHANES sampling procedures provide nationally- representative data. Analysis of data for any other geographic area (region, state, etc.) is possible only by special arrangement with the NCHS Research Data Center, and such analyses may not be representative of the specified area.
Are raw data (individual measurements or survey responses) available?	Individual laboratory measurements and survey responses are generally available. Individual survey responses for some questions are not publicly released.
How are database files obtained?	http://www.cdc.gov/nchs/nhanes.htm
Are there any known data quality or data analysis concerns?	Some environmental chemicals have large percentages of values below the detection limit. Data gathered by interview, including demographic information, and responses regarding health status, nutrition and health-related behaviors are self- reported, or (for individuals age 16 years and younger)

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Metadata for	National Health and Nutrition Examination Survey (NHANES)
	reported by an adult informant.
What documentation is available describing QA procedures?	http://www.cdc.gov/nchs/nhanes.htm includes detailed documentation on laboratory and other QA procedures. Data quality information is available at http://www.cdc.gov/nchs/about/policy/quality.htm.
For what years are data available?	Some data elements were collected in predecessor surveys to NHANES beginning in 1959; collection of data on environmental chemicals began with measurement of blood lead in NHANES II, 1976-1980. The range of years for measurement of environmental chemicals varies; apart from lead and cotinine (initiated in NHANES III), measurement of environmental chemicals began with 1999-2000 or later NHANES.
What is the frequency of data collection?	Data are collected on continuous basis, but are grouped into NHANES cycles: NHANES II (1976-1980); NHANES III phase 1 (1988-1991); NHANES III phase 2 (1991-1994); and continuous two-year cycles beginning with 1999-2000 and continuing to the present.
What is the frequency of data release?	Data are released in two-year cycles (e.g. 1999-2000); particular data sets from a two-year NHANES cycle are released as available.
Are the data comparable across time and space?	Detection limits can vary across time, affecting some comparisons. Some contaminants are not measured in every NHANES cycle. Within any NHANES two-year cycle, data are generally collected and analyzed in the same manner for all sampling locations.
Can the data be stratified by race/ethnicity, income, and location (region, state, county or other geographic unit)?	Data are collected to be representative of the U.S. population based on age, sex, and race/ethnicity. The public release files allow stratification by these and other demographic variables, including family income range and poverty income ratio. Data cannot be stratified geographically except by special arrangement with the NCHS Research Data Center.

# 1 Methods

### 2 3 **Indicator**

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B4. Mercury in women ages 16 to 49 years: Median and 95<sup>th</sup> percentile concentrations in blood, 1999-2008

# 8 Summary

- 9 10 Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease
- 11 Control and Prevention, has conducted the National Health and Nutrition Examination Surveys
- 12 (NHANES), a series of U.S. national surveys of the health and nutrition status of the
- 13 noninstitutionalized civilian population. The National Center for Environmental Health at CDC
- 14 measures environmental chemicals in blood and urine samples collected from NHANES
- 15 participants.<sup>i</sup> This indicator uses total blood mercury measurements in women ages 16 to 49
- 16 years. The NHANES 1999-2000 and 2001-2002 surveys included total blood mercury data for
- 17 children ages 1 to 5 years and women ages 16 to 49 years. The NHANES 2003-2004, 2005-
- 18 2006, and 2007-2008 surveys included total blood mercury data for all participants ages 1 year
- and older. Indicator B4 gives the median and  $95^{\text{th}}$  percentile concentrations of total blood
- 20 mercury for women ages 16 to 49 years for each survey cycle. The median is the estimated 21 concentration such that 50% of all noninstitutionalized civilian women ages 16 to 49 years
- 22 during the survey period have a total blood mercury concentration below this level; the
- 23 population distribution was adjusted by age-specific birthrates to reflect exposures to women
- 24 who are pregnant or may become pregnant. The 95<sup>th</sup> percentile is the estimated concentration
- such that 95% of all noninstitutionalized civilian women ages 16 to 49 years during the survey
- 26 period have a total blood mercury concentration below this level. Table B4a gives the median
- concentration of total blood mercury for women ages 16 to 49 years for 2005-2008, stratified
- both by race/ethnicity and family income. Table B4b gives the 95<sup>th</sup> percentile concentration of
- total blood mercury for women ages 16 to 49 years for 2005-2008, stratified both by
- 30 race/ethnicity and family income. Table B4c gives the median and  $95^{\text{th}}$  percentile concentrations
- of total blood mercury for children ages 1 to 5 years for each survey cycle. The survey data were
- 32 weighted to account for the complex multi-stage, stratified, clustered sampling design.
- 33

# 34 Data Summary35

IndicatorB4. Mercury in women ages 16 to 49 years:<br/>Median and 95th percentile concentrations in<br/>blood, 1999-2008.Time Period1999-2008.DataTotal blood mercury in women ages 16 to 49<br/>YearsYears1999-2001-2003-2005-2007-

<sup>&</sup>lt;sup>i</sup> Centers for Disease Control and Prevention. 2009. Fourth National Report on Human Exposure to Environmental Chemicals. Atlanta, GA. Available at: <u>www.cdc.gov/exposurereport</u>.

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Indicator	B4. Mercury in women ages 16 to 49 years: Median and 95 <sup>th</sup> percentile concentrations in						
	Median a	and 95 <sup>th</sup> pe	ercentile c	oncentrati	ons in		
	blood, 19	blood, 1999-2008.					
2000 2002 2004 2006							
Limits of Detection $(\mu g/L)^*$	0.14	0.14	0.14 or	0.2 or	0.28		
			0.2	0.32			
Number of Non-missing Values**	1,709	1,928	1,728	1,880	1,585		
Number of Missing Values	235	212	172	205	164		
Percentage Below Limit of Detection***	7	4	8	18	19		

\* The Limit of Detection (LOD) is defined as the level at which the measurement has a 95% probability of being greater than zero.

\*\*Non-missing values include those below the analytical LOD, which are reported as LOD/ $\sqrt{2}$ . As an exception, for 2001-2002, CDC reported values below the limit of detection as LOD/2.

\*\*\*This percentage is survey-weighted using the NHANES survey weights for the given period and is weighted by age-specific birthrates.

# **Overview of Data Files**

The following files are needed to calculate this indicator. The files together with the survey
 documentation and SAS programs for reading in the data are available at the NHANES website:
 <u>http://www.cdc.gov/nchs/nhanes.htm</u>.

- NHANES 1999-2000: Demographic file demo.xpt. Laboratory file lab06.xpt. The demographic file demo.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), laboratory survey weight (WTMEC2YR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The laboratory file lab06.xpt contains SEQN and the total blood mercury (LBXTHG). The two files are merged using the common variable SEQN.
- NHANES 2001-2002: Demographic file demo\_b.xpt. Laboratory file l06\_b.xpt. The demographic file demo\_b.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), laboratory survey weight (WTMEC2YR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The laboratory file l06\_b.xpt contains SEQN and the total blood mercury (LBXTHG). The two files are merged using the common variable SEQN.
- NHANES 2003-2004: Demographic file demo\_c.xpt. Laboratory file l06bmt\_c.xpt. The demographic file demo\_c.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), laboratory survey weight (WTMEC2YR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The laboratory file l06bmt\_c.xpt contains SEQN and the total blood mercury (LBXTHG).
   The two files are merged using the common variable SEQN.
- NHANES 2005-2006: Demographic file demo\_d.xpt. Mercury Laboratory file
   thgihg\_d.xpt. The demographic file demo\_d.xpt is a SAS transport file that contains the
   subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), race/ethnicity

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(RIDRETH1), poverty income ratio (INDFMPIR), laboratory survey weight 1 2 (WTMEC2YR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The 3 Mercury laboratory file thging d.xpt contains SEQN and the total blood mercury 4 (LBXTHG). The two files are merged using the common variable SEQN. 5 6 NHANES 2007-2008: Demographic file demo e.xpt. Mercury Laboratory file 7 thging e.xpt. The demographic file demo e.xpt is a SAS transport file that contains the 8 subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), race/ethnicity 9 (RIDRETH1), poverty income ratio (INDFMPIR), laboratory survey weight 10 (WTMEC2YR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The 11 Mercury laboratory file thging e.xpt contains SEQN and the total blood mercury 12 (LBXTHG). The two files are merged using the common variable SEQN. 13 14 15 National Health and Nutrition Examination Surveys (NHANES) 16 17 Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease 18 Control and Prevention, has conducted the National Health and Nutrition Examination Surveys 19 (NHANES), a series of U.S. national surveys of the health and nutrition status of the 20 noninstitutionalized civilian population. The National Center for Environmental Health at CDC 21 performs all measurements of environmental chemicals in blood and urine (211 chemicals in 22 2003-2004) by advanced analytical techniques. The indicator used is total blood mercury 23 measurements from NHANES 1999-2000, 2001-2002, 2003-2004, 2005-2006, and 2007-2008 in 24 women ages 16 to 49 years and children ages 1 to 5 years. The NHANES data were obtained 25 from the NHANES website: http://www.cdc.gov/nchs/nhanes.htm. Following the CDC 26 recommended approach, values below the analytical limit of detection (LOD) were replaced by 27  $LOD/\sqrt{2}$ .<sup>ii</sup> However, as an exception, for 2002-2002, values below the limit of detection of 0.14 28  $\mu$ g/L were replaced by 0.07  $\mu$ g/L in the publicly released data. This exception does not impact the tabulated median and 95<sup>th</sup> percentile values for 1999-2000 since those percentiles exceeded 29 30 the limit of detection. 31 32 The NHANES use a complex multi-stage, stratified, clustered sampling design. Certain 33 demographic groups were deliberately over-sampled, including Mexican-Americans and Blacks. 34 Oversampling is performed to increase the reliability and precision of estimates of health status 35 indicators for these population subgroups. The publicly released data includes survey weights to 36 adjust for the over-sampling, non-response, and non-coverage. The statistical analyses used the 37 laboratory survey weights (WTMEC2YR) to re-adjust the total blood mercury data to represent 38 the national population. 39 40 **Age-Specific Birthrates** 41 42 In addition to the NHANES survey weights, the data for women of child-bearing age (ages 16 to 43 49) were also weighted by the birthrate for women of the given age and race/ethnicity to estimate <sup>ii</sup> See Hornung RW, Reed LD. 1990. Estimation of average concentration in the presence of nondetectable values.

pre-natal exposures. Thus the overall weight in each two year period is the product of the 1 2 NHANES survey weight and the total number of births in the two calendar years for the given age and race/ethnicity, divided by twice the corresponding population of women at the midpoint 3 4 of the two year period.<sup>iii</sup> For the years 2007-2008, the natality and total population data used to 5 compute the birthrate adjustments are not currently publicly available. For those two years the 6 birthrate adjustments were estimated from the 2005-2006 data. 7 8 **Race/Ethnicity and Family Income** 9 10 For Tables B4a and B4b, the percentiles were calculated for demographic strata defined by the combination of race/ethnicity and family income. 11 12 13 The family income was characterized based on the INDFMPIR variable, which is the ratio of the 14 family income to the poverty level. The National Center for Health Statistics used the U.S. 15 Census Bureau Current Population Survey to define the family units, and the family income for the respondent was obtained during the interview. The U.S. Census Bureau defines annual 16 17 poverty level money thresholds varying by family size and composition. The poverty income 18 ratio (PIR) is the family income divided by the poverty level for that family. Family income was 19 stratified into the following groups: 20 21 • Below Poverty Level: PIR < 1 • Between 100% and 200% of Poverty Level:  $1 \le PIR \le 2$ 22 23 • Above 200% of Poverty level: PIR > 224 • Above Poverty Level:  $PIR \ge 1$  (combines the previous two groups) 25 • Unknown Income: PIR is missing 26 27 Race/ethnicity was characterized using the RIDRETH1 variable. The possible values of this 28 variable are: 29 30 1. Mexican American • 31 • 2. Other Hispanic 32 • 3. Non-Hispanic White 33 • 4. Non-Hispanic Black 34 • 5. Other Race – Including Multi-racial 35 • "." Missing 36 37 Category 5 includes: all Non-Hispanic single race responses other than White or Black; and 38 multi-racial responses. 39 40 For this indicator, the RIDRETH1 categories 2, 5, and missing were combined into a single 41 "Other" category. This produced the following categories: 42

<sup>&</sup>lt;sup>iii</sup> Axelrad, D.A., Cohen, J. 2011. Calculating summary statistics for population chemical biomonitoring in women of childbearing age with adjustment for age-specific natality. *Environmental Research* 111 (1): 149-155.

- White non-Hispanic: RIDRETH1 = 3
- Black non-Hispanic: RIDRETH1 = 4
- Mexican-American: RIDRETH1 = 1
- Other: RIDRETH1 = 2 or 5 or missing

The "Other" category includes Asian non-Hispanic; Native American non-Hispanic; Hispanic other than Mexican-American; those reporting multi-racial; and those with a missing value for race/ethnicity.

# 10 Calculation of Indicator

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Indicator B4 is the median and 95<sup>th</sup> percentile for total blood mercury in women of ages 16 to 49 12 13 years, stratified by NHANES survey cycle. Tables B4a and B4b present the median and 95<sup>th</sup> 14 percentile for total blood mercury in women of ages 16 to 49 years, stratified by race/ethnicity and family income. Table B4c presents the median and 95<sup>th</sup> percentile for total blood mercury in 15 16 children of ages 1 to 5, stratified by NHANES survey cycle. The median is the estimated 17 concentration such that 50% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have total blood mercury concentrations below this level. The 95<sup>th</sup> 18 19 percentile is the estimated concentration such that 95% of all noninstitutionalized civilian women 20 ages 16 to 49 years during the survey period have total blood mercury concentrations below this 21 level. To adjust the NHANES data to represent prenatal exposures, the data for each woman 22 surveyed was multiplied by the estimated number of births per woman of the given age and race/ethnicity.

23 24

To simply demonstrate the calculations, we will use the NHANES 2007-2008 total blood mercury values for women ages 16 to 49 years of all race/ethnicities and all incomes as an example. We have rounded all the numbers to make the calculations easier:

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29 We begin with all the non-missing NHANES 2007-2008 total blood mercury values for women

- 30 ages 16 to 49 years. Assume for the sake of simplicity that valid data on total blood mercury
- 31 were available for every sampled woman. Each sampled woman has an associated annual survey
- weight WTMEC2YR that estimates the annual number of U.S. women represented by that
   sampled woman. Each sampled woman also has an associated birthrate giving the numbers of
- annual births per woman of the given age, race, and ethnicity. The product of the annual survey
- 35 weight and the birthrate estimates the annual number of U.S. births represented by that sampled
- 36 woman, which we will refer to as the adjusted survey weight. For example, the lowest total blood
- 37 mercury measurement for a woman between 16 and 49 years of age is  $0.2 \,\mu$ g/L with an annual
- survey weight of 15,000, a birthrate of 0.03, and thus an adjusted survey weight of 450, and so
- represents 450 births. The total of the adjusted survey weights for the sampled women equals 4
- 40 million, the total number of annual U.S. births to women ages 16 to 49 years. The second-lowest
- 41 measurement is also  $0.2 \mu g/L$  with an adjusted survey weight of 4,000, and so represents another
- 42 4,000 U.S. births. The highest measurement was 15.1  $\mu$ g/L, with an adjusted survey weight of
- 43 1,200, and so represents another 1,200 U.S. births.
- 44

1 To calculate the median, we can use the adjusted survey weights to expand the data to the entire

- 2 U.S. population of births to women ages 16 to 49. We have 450 values of  $0.2 \mu g/L$  from the
- 3 lowest measurement, 4,000 values of 0.2  $\mu$ g/L from the second lowest measurement, and so on,
- 4 up to 1,200 values of 15.1  $\mu$ g/L from the highest measurement. Arranging these 4 million values 5 in increasing order, the 2 millionth value is 0.7  $\mu$ g/L. Since half of the values are below 0.7 and
- half of the values are above 0.7, the median equals 0.7  $\mu$ g/L. Since half of the values are below 0.7 and half of the values are above 0.7, the median equals 0.7  $\mu$ g/L. To calculate the 95<sup>th</sup> percentile,
- note that 95% of 4 million equals 3.8 million. The 3.8 millionth value is  $3.7 \,\mu$ g/L. Since 95% of
- 8 the values are below 3.7, the 95<sup>th</sup> percentile equals  $3.7 \mu g/L$ .
- 9
- 10 In reality, the calculations need to take into account that total blood mercury measurements were
- 11 not available for every respondent, and to use exact rather than rounded numbers. There were 12 total blood mercury measurements for only 1,585 of the 1,749 sampled women ages 16 to 49
- 13 years. The adjusted survey weights for all 1,749 sampled women add up to 4.1 million, the U.S.
- 14 population of births to women ages 16 to 49. The adjusted survey weights for the 1,585 sampled
- 15 women with total blood mercury data add up to 3.8 million. Thus the available data represent 3.8
- 16 million values and so represent only 92 % of the U.S. population of births. The median and 95<sup>th</sup>
- 17 percentiles are given by the 1.9 millionth (50 % of 3.8 million) and 3.61 millionth (95 % of 3.8
- 18 million) U.S. birth's value. These calculations assume that the sampled women with valid total
- 19 blood mercury data are representative of women giving birth without valid total blood mercury
- data. The calculations also assume that the sampled women are representative of women that
- 21 actually gave birth in 2007-2008, since NHANES information on pregnancy and births was not 22 incorporated into the analysis
- incorporated into the analysis.
- 23 24
- 24 <u>Equations</u> 25
- 26 These percentile calculations can also be given as the following mathematical equations, which 27 are based on the default percentile calculation formulas from Statistical Analysis System (SAS)
- are based on the default percentile calculation formulas from Statistical Analysis System (SAS)
   software. Exclude all missing total blood mercury values. Suppose there are n women of ages 16
- 29 to 49 years with valid total blood mercury values. Arrange the total blood mercury
- 30 concentrations in increasing order (including tied values) so that the lowest concentration is x(1)31 with an adjusted survey weight of w(1), the second lowest concentration is x(2) with an adjusted 32 survey weight of w(2), ..., and the highest concentration is x(n) with an adjusted survey weight 33 of w(n).
- 35 1. Sum all the adjusted survey weights to get the total weight W:
- 36 37

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- $W = \Sigma[1 \le i \le n] w(i)$
- 2. Find the largest number i so that the total of the weights for the i lowest values is less than orequal to W/2.
- 41 42
- $\Sigma[j \le i] w(j) \le W/2 < \Sigma[j \le i+1] w(j)$
- 4344 3. Calculate the median using the results of the second step. We either have
- 45 46
- $\Sigma[j \le i] w(j) = W/2 < \Sigma[j \le i+1] w(j)$
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or  $\Sigma[j \le i] w(j) < W/2 < \Sigma[j \le i + 1] w(j)$ In the first case we define the median as the average of the i'th and i + 1'th values: Median = [x(i) + x(i + 1)]/2 if  $\Sigma[i \le i] w(i) = W/2$ In the second case we define the median as the i + 1'th value: Median = x(i + 1) if  $\Sigma[i \le i] w(i) < W/2$ (The estimated median does not depend upon how the tied values of x(i) are ordered). A similar calculation applies to the 95<sup>th</sup> percentile. The first step to calculate the sum of the weights, W, is the same. In the second step, find the largest number i so that the total of the weights for the i lowest values is less than or equal to 0.95W.  $\Sigma[j \le i] w(j) \le 0.95W \le \Sigma[j \le i+1] w(j)$ In the third step we calculate the 95<sup>th</sup> percentile using the results of the second step. We either have  $\Sigma[j \le i] w(j) = 0.95W < \Sigma[j \le i + 1] w(j)$ or  $\Sigma[j \le i] w(j) < 0.95W < \Sigma[j \le i + 1] w(j)$ In the first case we define the 95<sup>th</sup> percentile as the average of the i'th and i + 1'th values: 95<sup>th</sup> Percentile = [x(i) + x(i + 1)]/2 if  $\Sigma[i \le i] w(i) = 0.95W$ In the second case we define the 95th percentile as the i + 1'th value: 95<sup>th</sup> Percentile = x(i + 1) if  $\Sigma[i \le i] w(i) < 0.95W$ **Relative Standard Error** The uncertainties of the median and 95<sup>th</sup> percentile values were calculated using a revised version of the CDC method given in CDC 2005,<sup>iv</sup> Appendix C, and the SAS® program provided by CDC. The method uses the Clopper-Pearson binomial confidence intervals adapted for 

<sup>&</sup>lt;sup>iv</sup> CDC Third National Report on Human Exposure to Environmental Chemicals. 2005

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complex surveys by Korn and Graubard (see Korn and Graubard, 1999, <sup>v</sup> p. 65). The following text is a revised version of the Appendix C. For the birthrate adjusted calculations for women ages 16 to 49, the sample weight is adjusted by multiplying by the age-specific birthrate.

> Step 1: Use SAS® Proc Univariate to obtain a point estimate P<sub>SAS</sub> of the percentile value. Use the Weight option to assign the exact correct sample weight for each chemical result.

> **Step 2:** Use SUDAAN® Proc Descript with Taylor Linearization DESIGN = WR (i.e., sampling with replacement) and the proper sampling weight to estimate the proportion (p) of subjects with results less than and not equal to the percentile estimate P<sub>SAS</sub> obtained in Step 1 and to obtain the standard error (se<sub>n</sub>) associated with this proportion estimate. Compute the degrees-of-freedom adjusted effective sample size

$$n_{df} = (t_{num}/t_{denom})^2 p(1 - p)/(se_p^2)$$

where  $t_{num}$  and  $t_{denom}$  are 0.975 critical values of the Student's t distribution with degrees of freedom equal to the sample size minus 1 and the number of PSUs minus the number of strata, respectively. Note: the degrees of freedom for t<sub>denom</sub> can vary with the demographic sub-group of interest.

Step 3: After obtaining an estimate of p (i.e., the proportion obtained in Step 2), compute the Clopper-Pearson 95% confidence interval ( $P_L(x,n_{df}), P_U(x,n_{df})$ ) as follows:

 $P_{L}(x,n_{df}) = v_{1}F_{v1,v2} (0.025)/(v_{2} + v_{1}F_{v1,v2}(0.025))$  $P_{U}(x,n_{df}) = v_{3}F_{v_{3},v_{4}}(0.975)/(v_{4} + v_{3}F_{v_{3},v_{4}}(0.975))$ 

where x is equal to p times  $n_{df}$ ,  $v_1 = 2x$ ,  $v_2 = 2(n_{df} - x + 1)$ ,  $v_3 = 2(x + 1)$ ,  $v_4 = 2(n_{df} - x)$ , and  $F_{d1,d2}(\beta)$  is the  $\beta$  quantile of an F distribution with d1 and d2 degrees of freedom. (Note: If  $n_{df}$  is greater than the actual sample size or if p is equal to zero, then the actual sample size should be used.) This step will produce a lower and an upper limit for the estimated proportion obtained in Step 2.

Step 4: Use SAS Proc Univariate (again using the Weight option to assign weights) to determine the chemical percentile values  $P_{CDC}$ ,  $L_{CDC}$  and  $U_{CDC}$  that correspond to the proportion p obtained in Step 2 and its lower and upper limits obtained in Step 3. Do not round the values of p and the lower and upper limits. For example, if p = 0.4832, then  $P_{CDC}$  is the 48.32'th percentile value of the chemical. The alternative percentile estimates P<sub>CDC</sub> and P<sub>SAS</sub> are not necessarily equal.

**Step 5:** Use the confidence interval from Step 4 to estimate the standard error of the estimated percentile P<sub>CDC</sub>:

Standard Error  $(P_{CDC}) = (U_{CDC} - L_{CDC}) / (2t_{denom})$ 

Step 6: Use the estimated percentile P<sub>CDC</sub> and the standard error from Step 4 to estimate the relative standard error of the estimated percentile P<sub>CDC</sub>:

Relative Standard Error (%) = [Standard Error ( $P_{CDC}$ ) /  $P_{CDC}$ ] × 100 %

The tabulated estimated percentile is the value of P<sub>SAS</sub> given in Step 1. The relative standard error is given in Step 6, using P<sub>CDC</sub> and its standard error.

<sup>&</sup>lt;sup>v</sup> Korn E. L., Graubard B. I. 1999. Analysis of Health Surveys. Wiley.

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- 1 The relative standard error depends upon the survey design. For this purpose, the public release
- 2 version of NHANES includes the variables SDMVSTRA and SDMVPSU, which are the Masked
- 3 Variance Unit pseudo-stratum and pseudo-primary sampling unit (pseudo-PSU). For
- 4 approximate variance estimation, the survey design can be approximated as being a stratified
- 5 random sample with replacement of the pseudo-PSUs from each pseudo-stratum; the true stratum
- and PSU variables are not provided in the public release version to protect confidentiality.
- 7
- 8 Percentiles with a relative standard error less than 30% were treated as being reliable and were
  - 9 tabulated. Percentiles with a relative standard error greater than or equal to 30% but less than
  - 10 40% were treated as being unstable; these values were tabulated but were flagged to be
  - 11 interpreted with caution. Percentiles with a relative standard error greater than or equal to 40%,
  - 12 or without an estimated relative standard error, were treated as being unreliable; these values
  - 13 were not tabulated and were flagged as having a large uncertainty.
  - 14

# 15 Questions and Comments

- 16
- 17 Questions regarding these methods, and suggestions to improve the description of the methods,
- 18 are welcome. Please use the "Contact Us" link at the bottom of any page in the America's
- 19 Children and the Environment website.

### 1 Statistical Comparisons

2

3 Statistical analyses of the percentiles were used to determine whether the differences between 4 percentiles for different demographic groups were statistically significant. For these analyses, the 5 percentiles and their standard errors were calculated for each combination of age group, sex (in 6 the cases of children), income group (below poverty, at or above poverty, unknown income), and race/ethnicity group using the method described in the "Relative Standard Error" section. In the 7 8 notation of that section, the percentile and standard error are the values of P<sub>CDC</sub> and Standard 9 Error (P<sub>CDC</sub>), respectively. These calculated standard errors account for the survey weighting and 10 design and, for women, for the age-specific birthrate.

11

12 Using a weighted linear regression model, the percentile was assumed to be the sum of

- 13 explanatory terms for age, sex, income and/or race/ethnicity and a random error term; the error
- 14 terms were assumed to be approximately independent and normally distributed with a mean of
- 15 zero and a variance equal to the square of the standard error. Using this model, the difference in
- 16 the value of a percentile between different demographic groups is statistically significant if the
- 17 difference between the corresponding sums of explanatory terms is statistically significantly
- 18 different from zero. A p-value at or below 0.05 implies that the difference is statistically
- 19 significant at the 5% significance level. No adjustment is made for multiple comparisons.
- 20
- 21 For each type of comparison, we present unadjusted and adjusted analyses. The unadjusted
- 22 analyses directly compare a percentile between different demographic groups. The adjusted
- analyses add other demographic explanatory variables to the statistical model and use the
- 24 statistical model to account for the possible confounding effects of these other demographic
- 25 variables. For example, the unadjusted race/ethnicity comparisons use and compare the
- 26 percentiles between different race/ethnicity pairs. The adjusted race/ethnicity comparisons use
- 27 the percentiles for each age/sex/income/race/ethnicity combination. The adjusted analyses add
- age, sex, and income terms to the statistical model and compare the percentiles between different
- 29 race/ethnicity pairs after accounting for the effects of the other demographic variables. For
- example, if White non-Hispanics tend to have higher family incomes than Black non-Hispanics,
   and if the body burden strongly depends on family income only, then the unadjusted differences
- between these two race/ethnicity groups would be significant but the adjusted difference (taking
- into account income) would not be significant.
- 34

Comparisons between pairs of race/ethnicity groups are shown in Tables 1 and 2 for women ages 16 to 49 years and in Tables 3 and 4 for children ages 1 to 5 years. In Tables 1 and 3, for the unadjusted "All incomes" comparisons, the only explanatory variables are terms for each

- 38 race/ethnicity group. For these unadjusted comparisons, the statistical tests compare the
- 39 percentiles for each pair of race/ethnicity groups. For the adjusted "All incomes (adjusted for 40 age, sex, income)" comparisons, the explanatory variables are terms for each race/ethnicity
- 41 group together with terms for each age, sex, and income group. For these adjusted comparisons,
- 42 the statistical test compares the pair of race/ethnicity groups after accounting for any differences
- 43 in the age, sex and income distributions between the race/ethnicity groups. The adjustment for
- 44 sex is applicable only for children, and thus appears only in Tables 3 and 4.
- 45

In Tables 1 and 3, for the unadjusted "Below Poverty Level" and "At or Above Poverty Level" 1 2 comparisons, the only explanatory variables are terms for each of the twelve 3 race/ethnicity/income combinations (combinations of four race/ethnicity groups and three 4 income groups). For example, in row 1, the p-value for "Below Poverty Level" compares White 5 non-Hispanics below the poverty level with Black non-Hispanics below the poverty level. The 6 same set of explanatory variables are used in Tables 2 and 4 for the unadjusted comparisons 7 between one race/ethnicity group below the poverty level and the same or another race/ethnicity 8 group at or above the poverty level. The corresponding adjusted analyses include extra 9 explanatory variables for age and sex, so that race/ethnicity/income groups are compared after 10 accounting for any differences due to age or sex. 11 12 Additional comparisons are shown in Table 5 for women ages 16 to 49 years and in Table 6 for 13 children ages 1 to 5 years. The AGAINST = "income" unadjusted p-value compares the body 14 burdens for those below poverty level with those at or above poverty level, using the explanatory 15 variables for the three income groups (below poverty, at or above poverty, unknown income). 16 The adjusted p-value includes adjustment terms for age, sex (for children), and race/ethnicity in 17 the model. The AGAINST = "yearnum" p-value examines whether the linear trend in the body 18 burden is statistically significant (using the percentiles for each NHANES period regressed 19 against the midpoint of that period); the adjusted model for trend adjusts for demographic 20 changes in the populations from year to year by including terms for age, sex, income, and 21 race/ethnicity. 22 23 For women, the age groups used were 16-19, 20-24, 25-29, 30-39, and 40-49. For children, the 24 age groups used were 1, 2, 3, 4, and 5.

26 For more details on these statistical analyses, see the memorandum by Cohen (2010).<sup>vi</sup>

Table 1. Statistical significance tests comparing the percentiles of mercury in women ages 16 to

- 29 49 years, between pairs of race/ethnicity groups, for 2005-2008.
- 30

25

27

				P-VALUES						
Variable	Percentile	RACE1	RACE2	All incomes	All incomes (adjusted for age, income)	Below Poverty Level	Below Poverty Level (adjusted for age)	At or Above Poverty Level	At or Above Poverty Level (adjusted for age)	
mercury	50	White non- Hispanic	Black non- Hispanic	0.242	< 0.0005	0.018	< 0.0005	0.687	0.075	
mercury	50	White non- Hispanic	Mexican- American	0.482	0.001	0.566	0.002	0.500	0.362	
mercury	50	White non- Hispanic	Other	< 0.0005	< 0.0005	0.096	0.001	< 0.0005	< 0.0005	
mercury	50	Black non- Hispanic	Mexican- American	0.085	< 0.0005	0.133	0.144	0.329	0.008	
mercury	50	Black non- Hispanic	Other	0.004	< 0.0005	0.832	0.553	< 0.0005	< 0.0005	
mercury	50	Mexican- American	Other	< 0.0005	< 0.0005	0.235	0.150	< 0.0005	< 0.0005	

<sup>vi</sup> Cohen, J. 2010. Selected statistical methods for testing for trends and comparing years or demographic groups in ACE NHIS and NHANES indicators. Memorandum submitted to Dan Axelrad, EPA, 21 March, 2010.

# **Biomonitoring: Mercury**

				P-VALUES					
Variable	Percentile	RACE1	RACE2	All incomes	All incomes (adjusted for age, income)	Below Poverty Level	Below Poverty Level (adjusted for age)	At or Above Poverty Level	At or Above Poverty Level (adjusted for age)
mercury	95	White non- Hispanic	Black non- Hispanic	0.003	0.018	0.527	0.148	0.003	0.459
mercury	95	White non- Hispanic	Mexican- American	< 0.0005	< 0.0005	0.374	< 0.0005	0.001	0.001
mercury	95	White non- Hispanic	Other	0.016	0.024	0.826	0.006	0.004	< 0.0005
mercury	95	Black non- Hispanic	Mexican- American	0.071	< 0.0005	0.368	0.001	0.362	0.024
mercury	95	Black non- Hispanic	Other	< 0.0005	0.950	0.562	< 0.0005	< 0.0005	< 0.0005
mercury	95	Mexican- American	Other	< 0.0005	< 0.0005	0.477	< 0.0005	< 0.0005	< 0.0005

Table 2. Statistical significance tests comparing the percentiles of mercury in women ages 16 to 49 years, between pairs of race/ethnicity/income groups at different income levels, for 2005-

49 years, between pairs of race/ethnicity/income groups at different income levels, for 2005-2008.

5

				P-VALUES		
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age)	
mercury	50	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.014	< 0.0005	
mercury	50	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.009	< 0.0005	
mercury	50	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.088	< 0.0005	
mercury	50	White non-Hispanic, < PL	Other, $\geq$ PL	< 0.0005	< 0.0005	
mercury	50	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.894	0.319	
mercury	50	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.809	0.682	
mercury	50	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.466	0.083	
mercury	50	Black non-Hispanic, < PL	Other, $\geq$ PL	< 0.0005	< 0.0005	
mercury	50	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.133	0.439	
mercury	50	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.088	0.041	
mercury	50	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.365	0.933	
mercury	50	Mexican-American, < PL	Other, $\geq$ PL	< 0.0005	< 0.0005	
mercury	50	Other, < PL	White non-Hispanic, $\geq$ PL	0.769	0.266	
mercury	50	Other, < PL	Black non-Hispanic, $\geq$ PL	0.943	0.669	
mercury	50	Other, < PL	Mexican-American, $\geq$ PL	0.522	0.140	
mercury	50	Other, < PL	Other, $\geq$ PL	0.003	0.008	
mercury	95	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.309	0.075	
mercury	95	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.937	0.246	
mercury	95	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.669	0.350	
mercury	95	White non-Hispanic, < PL	Other, $\geq$ PL	0.007	< 0.0005	
mercury	95	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	< 0.0005	< 0.0005	
mercury	95	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.078	0.004	
mercury	95	Black non-Hispanic, < PL	n-Hispanic, $\leq$ PL Mexican-American, $\geq$ PL		0.673	
mercury	95	Black non-Hispanic, < PL	Other, $\geq$ PL	< 0.0005	< 0.0005	
mercury	95	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	< 0.0005	< 0.0005	
mercury	95	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.003	< 0.0005	

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# **Biomonitoring: Mercury**

				P-VAI	LUES
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age)
mercury	95	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.227	< 0.0005
mercury	95	Mexican-American, < PL	Other, $\geq$ PL	< 0.0005	< 0.0005
mercury	95	Other, < PL	White non-Hispanic, $\geq$ PL	0.764	0.116
mercury	95	Other, < PL	Black non-Hispanic, $\geq$ PL	0.774	0.042
mercury	95	Other, < PL	Mexican-American, $\geq$ PL	0.636	< 0.0005
mercury	95	Other, < PL	Other, $\geq$ PL	0.170	0.001

1 2 3

Table 3. Statistical significance tests comparing the percentiles of mercury in children ages 1 to

5, between pairs of race/ethnicity groups, for 2005-2008.

4

				P-VALUES					
Variable	Percentile	RACE1	RACE2	All	All incomes (adjusted for age, sex, income)	Below Poverty Level	Below Poverty Level (adjusted for age, sex)	At or Above Poverty Level	At or Above Poverty Level (adjusted for age, sex)
mercury	50	White non- Hispanic	Black non- Hispanic	0.004	0.909	0.002	0.004	0.001	0.096
mercury	50	White non- Hispanic	Mexican- American	0.144	0.240	0.002	0.200	1.000	0.360
mercury	50	White non- Hispanic	Other	0.011	0.003	0.008	0.546	0.015	0.003
mercury	50	Black non- Hispanic	Mexican- American	0.001	0.242	0.014	< 0.0005	0.001	0.016
mercury	50	Black non- Hispanic	Other	0.878	0.005	1.000	0.013	0.613	0.001
mercury	50	Mexican- American	Other	0.005	0.001	0.036	0.017	0.015	0.005
mercury	95	White non- Hispanic	Black non- Hispanic	0.204	< 0.0005	0.291	0.877	0.594	0.049
mercury	95	White non- Hispanic	Mexican- American	0.560	< 0.0005	0.323	0.289	0.292	0.001
mercury	95	White non- Hispanic	Other	0.074	< 0.0005	0.066	0.590	0.414	< 0.0005
mercury	95	Black non- Hispanic	Mexican- American	0.460	< 0.0005	0.914	0.277	0.220	< 0.0005
mercury	95	Black non- Hispanic	Other	0.134	< 0.0005	0.138	0.572	0.478	< 0.0005
mercury	95	Mexican- American	Other	0.099	0.449	0.166	0.468	0.343	< 0.0005

5 6

Table 4. Statistical significance tests comparing the percentiles of mercury in children ages 1 to 5

years, between pairs of race/ethnicity/income groups at different income levels, for 2005-2008.

	P-VALUES				
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age, sex)
mercury	50	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	1.000	0.656
mercury	50	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.001	0.344
mercury	50	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	1.000	0.849
mercury	50	White non-Hispanic, < PL	Other, $\geq$ PL	0.015	0.023

				P-VAL	UES	
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age, sex)	
mercury	50	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.002	< 0.0005	
mercury	50	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.763	< 0.0005	
mercury	50	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.002	< 0.0005	
mercury	50	Black non-Hispanic, < PL	Other, $\geq$ PL	0.467	0.876	
mercury	50	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.003	0.007	
mercury	50	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.009	0.349	
mercury	50	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.003	0.001	
mercury	50	Mexican-American, < PL	Other, $\geq$ PL	0.036	< 0.0005	
mercury	50	Other, < PL	White non-Hispanic, $\geq$ PL	0.008	0.156	
mercury	50	Other, < PL	Black non-Hispanic, $\geq$ PL	0.781	0.048	
mercury	50	Other, < PL	Mexican-American, $\geq$ PL	0.008	0.267	
mercury	50	Other, < PL	Other, $\geq$ PL	0.485	0.057	
mercury	95	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.360	< 0.0005	
mercury	95	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.248	< 0.0005	
mercury	95	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.830	0.528	
mercury	95	White non-Hispanic, < PL	Other, $\geq$ PL	0.328	< 0.0005	
mercury	95	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.894	< 0.0005	
mercury	95	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.622	< 0.0005	
mercury	95	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.168	0.639	
mercury	95	Black non-Hispanic, < PL	Other, $\geq$ PL	0.421	< 0.0005	
mercury	95	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.848	< 0.0005	
mercury	95	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.718	< 0.0005	
mercury	95	Mexican-American, < PL	$Mexican-American, \geq PL$	0.271	0.114	
mercury	95	Mexican-American, < PL	Other, $\geq$ PL	0.431	< 0.0005	
mercury	95	Other, < PL	White non-Hispanic, $\geq$ PL	0.135	< 0.0005	
mercury	95	Other, < PL	Black non-Hispanic, $\geq$ PL	0.263	< 0.0005	
mercury	95	Other, < PL	$Mexican-American, \geq PL$	0.062	0.344	
mercury	95	Other, < PL	Other, $\geq$ PL	0.779	< 0.0005	

Table 5. Other statistical significance tests comparing the percentiles of mercury in women ages

16 to 49 years, for 2005-2008 (trends for 1999-2008).

			P-VA	ALUES	
Percentile	From	То	Against	Unadjusted	Adjusted*
50	2005	2008	income	0.003	< 0.0005
50	1999	2008	yearnum	0.532	0.042
95	2005	2008	income	< 0.0005	< 0.0005
95	1999	2008	yearnum	0.234	0.127
	50 50 95	50         2005           50         1999           95         2005	50         2005         2008           50         1999         2008           95         2005         2008	50         2005         2008         income           50         1999         2008         yearnum           95         2005         2008         income	Percentile         From         To         Against         Unadjusted           50         2005         2008         income         0.003           50         1999         2008         yearnum         0.532           95         2005         2008         income         < 0.0005

\*For AGAINST = "income," the p-values are adjusted for age and race/ethnicity. For AGAINST = "yearnum," the p-values are adjusted for age, race/ethnicity, and income.

Table 6. Other statistical significance tests comparing the percentiles of mercury in children ages 1

1 to 5 years, for 2005-2008 (trends for 1999-2008).

2 3

			P-VA	ALUES		
Variable	Percentile	From	То	Against	Unadjusted	Adjusted*
mercury	50	2005	2008	income	0.004	0.069
mercury	50	1999	2008	yearnum	0.086	0.233
mercury	95	2005	2008	income	0.717	< 0.0005
mercury	95	1999	2008	yearnum	0.028	0.080

\*For AGAINST = "income," the p-values are adjusted for age, sex, and race/ethnicity. For AGAINST = "yearnum," the p-values are adjusted for age, sex, race/ethnicity, and income.