#### America's Children and the Environment, Third Edition

#### **DRAFT Indicators**

#### **Biomonitoring: Perchlorate**

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 perchlorate 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>.

#### **Perchlorate** 1

2

3 Perchlorate is a naturally occurring and man-made chemical that is used to manufacture

- fireworks, explosives, flares, and rocket fuel.<sup>1</sup> It is found naturally in the soils of the 4
- 5 southwestern United States and other arid regions of the world, and is presumed to migrate into
- 6 groundwater during the process of irrigation.<sup>2</sup> Perchlorate has also been found in groundwater
- 7 supplies near military and industrial facilities where perchlorate was used.<sup>3</sup> Perchlorate has been
- detected in surface water and in some food crops produced in the southwestern United States.<sup>2,4,5</sup> 8
- 9
- 10 Some infant formulas have been found to contain perchlorate, and the perchlorate content of the
  - formula is increased if it is prepared with perchlorate-contaminated water.<sup>6-9</sup> Children might also 11
  - be directly exposed through perchlorate-contaminated water. Perchlorate has been detected in a 12
  - variety of foods, including human breast milk, dairy products, and leafy vegetables.<sup>4,10-16</sup> 13
  - Computer modeling studies have concluded that exposure to perchlorate from food consumption 14 is much greater than exposure from drinking water in the United States.<sup>17,18</sup> A national study 15
  - representative of the U.S. population ages 6 years and older found perchlorate in the urine of 16
  - 100% of the more than 5,000 people sampled.<sup>19,20</sup> 17
  - 18
  - Exposure to perchlorate has been shown to block the uptake of iodide into the thyroid gland.<sup>21,22</sup> 19
  - 20 The transfer of iodine from blood into the thyroid gland is an essential step in the synthesis of
  - 21 thyroid hormones that regulate how the body uses energy; influence bone growth; and influence
  - 22 the development of the brain, reproductive, and cardiovascular systems.<sup>23</sup> When this transfer of
  - 23 iodide into the thyroid gland is blocked, the thyroid may not have enough iodide to make thyroid
  - 24 hormones. Increasing levels of perchlorate in the urine of females ages 12 years and older has
  - been associated with decreased thyroid hormone levels,<sup>24</sup> and tobacco smoke and perchlorate 25
  - may interact to affect thyroid function at commonly occurring perchlorate levels.<sup>25,26</sup> 26
  - 27
  - 28 Exposure to perchlorate and other thyroid-disrupting chemicals is of particular concern for
  - 29 women of childbearing age, because thyroid hormones are important for growth and
  - development of the central nervous system in fetuses and infants.<sup>27-30</sup> Reduction in a woman's 30
  - 31 thyroid hormone levels early in pregnancy puts the fetus at risk for impaired physical and mental
  - development, with the severity of the impairment depending upon the degree of hormone 32
  - deficiency.<sup>27,28</sup> Moderate deficits in maternal thyroid hormone levels during early pregnancy 33
  - 34 have been linked to reduced childhood IQ scores and other neurodevelopmental effects, as well
  - 35 as unsuccessful or complicated pregnancies. Prenatal and newborn hypothyroidism (low thyroid
  - 36 hormone levels) is a risk factor for mental retardation and other forms of impaired
  - neurodevelopment.<sup>31</sup> Low levels of thyroid hormone are widespread among U.S. adult women, potentially increasing the risk for effects on fetal development from exposure to perchlorate.<sup>28,32-</sup> 37 38
  - 39
  - 40
  - 41 EPA has decided to move forward with development of a federal drinking water standard for
  - 42 perchlorate, based on the concern for effects on thyroid hormones and the development and
  - growth of fetuses, infants, and children;<sup>5</sup> the process will include receiving input from key 43
  - 44 stakeholders as well as submitting any formal rule to a public comment process. California and

- Massachusetts have set perchlorate drinking water standards in their states.<sup>35</sup> No standards exist 1
- 2 3 for perchlorate in food.
- 4 The following indicator shows the distribution of median perchlorate concentrations in women
- ages 16 to 49 years, based on concerns for effects on children from perchlorate exposures in
- 5 6 women who are pregnant or may become pregnant.
- 7

# Indicator PER1: Perchlorate in women ages 16 to 49 years: Median concentrations in urine, by race/ethnicity and family

- 3 income, 2001–2004
- 4

#### **Overview**

Indicator PER1 presents concentrations of perchlorate in urine of U.S. women ages 16 to 49 years. The data are from a national survey that collects urine specimens from a representative sample of the population, and then measures the concentration of total perchlorate in the urine. These indicators present comparisons of perchlorate in urine of women of different race/ethnicities and income levels. The focus on women of child-bearing age is based on concern for potential effects on children from exposures to women who are or may become pregnant.

5

#### 6 NHANES

- 7 Data for this indicator are 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
- 12 measures concentrations of environmental chemicals in blood and urine samples collected from
- 13 NHANES participants.<sup>20</sup> Concentrations of perchlorate in urine have been measured in a
- 14 representative subset of NHANES participants ages 6 years and older beginning with the 2001–
- 15 2002 survey cycle.<sup>19</sup> NHANES data from 2001–2004 for women ages 16 to 49 years are used for
- 16 Indicator PER1.

#### 17 Perchlorate Urine Measurement

- 18 The amount of perchlorate in urine is commonly used as a measurement of perchlorate exposure.
- 19 Perchlorate is metabolized and excreted quickly, with an elimination half-life on the order of
- 20 hours.<sup>19</sup> Therefore, perchlorate measured in humans is indicative of recent exposures. The
- 21 widespread detection of perchlorate, combined with the fact that perchlorate has a short half-life,
- 22 indicates that perchlorate exposure is widespread and relatively continuous.
- 23

#### 24 Creatinine Adjustment

- 25 NHANES data for perchlorate are based on a single urine sample for each person surveyed, and
- 26 can be subject to substantial variability due to normal changes in an individual's urinary output.
- For example, a urine sample from an individual who is dehydrated would be smaller in volume,
- and would have a higher chemical concentration than if she or he were well hydrated. This
- 29 variability is due only to the volume of the urine sample, and may mask differences between
- 30 individuals in levels of perchlorate.
- 31

- 1 To help reduce measurement variability related to fluctuations in urine output, these indicators
- 2 report perchlorate measurements in micrograms per gram of creatinine, rather than micrograms
- 3 per liter of urine.<sup>36</sup> Creatinine is a byproduct of muscle metabolism that is excreted in urine at a
- relatively constant rate, independent of the volume of urine. The constant excretion of creatinine
   in urine allows for an adjustment that partially accounts for the measurement variability due to
- 5 in urine allows for an adjustment that partially accounts for the measurement variability due to 6 changes in urinary output.
- 7
- 8 Creatinine correction is widely used in urinary biomonitoring,<sup>20</sup> but the adjustment does have
- 9 important limitations. Urinary creatinine concentrations can vary due to age, sex, diet, health  $\frac{37.38}{7.38}$
- 10 status (specifically renal function), body-mass index, race/ethnicity, and pregnancy status.<sup>37,38</sup>
- 11 Thus the creatinine adjustment improves the comparability of chemical measurements across
- 12 individuals, but the variability in creatinine concentrations may still affect comparisons between
- 13 individuals or populations.

### 14 Birthrate Adjustment

- 15 Indicator PER1 uses measurements of perchlorate in urine of women ages 16 to 49 years to
- 16 reflect the potential distribution of perchlorate exposures to women who are pregnant or may
- 17 become pregnant. However, women of different ages have a different likelihood of giving birth.
- 18 For example, in 2003–2004, women aged 27 had a 12% annual probability of giving birth, and
- 19 women aged 37 had a 4% annual probability of giving birth.<sup>39</sup> A birthrate-adjusted distribution
- 20 of women's perchlorate levels is used in calculating this indicator, meaning that the data are
- 21 weighted using the age-specific probability of a woman giving birth.<sup>40</sup>

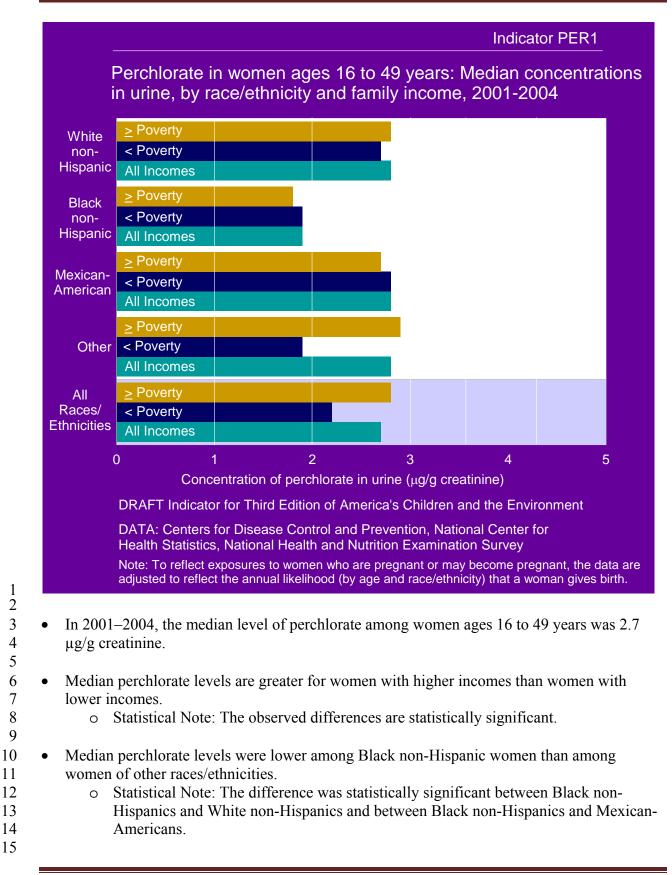
#### 22 Data Presented in the Indicator

- 23 This indicator presents median perchlorate levels for women ages 16 to 49 years for different
- 24 population groups defined by race/ethnicity and family income. The median is the value in the
- 25 middle of the distribution of perchlorate levels in urine: half of the measured population has
- 26 perchlorate levels greater than the median, and half has perchlorate levels below the median. The 27 median can be thought of as representing a typical exposure.
- 28
- 29 Four race/ethnicity groups are presented: White non-Hispanic, Black non-Hispanic, Mexican-
- 30 American, and "Other." The "Other" race/ethnicity category includes Asian non-Hispanic,
- 31 Native American non-Hispanic, Hispanic other than Mexican-American, those reporting multiple
- racial categories, and those with a missing value for race/ethnicity. The data are also tabulated
- 32 across three income categories: all incomes, below the poverty level, and greater than or equal to
- 34 the poverty level. The perchlorate levels presented in this indicator are for the combined survey
- 35 years 2001–2002 and 2003–2004. The 2001–2002 and 2003–2004 data are combined for this
- 36 indicator to increase the statistical reliability of the estimates for each race/ethnicity and income
- 37 group, and to reduce any possible influence of geographic variability in exposure. No time series
- is shown because data from only two NHANES cycles are too limited to depict possible changesover time.
- 39 40
- 41 The NHANES survey does not collect urine samples from children less than six years of age, and
- 42 thus cannot capture the exposure of infants, who may be exposed to unhealthy levels of
- 43 perchlorate due to the presence of perchlorate in breast milk and some infant formula.<sup>8,9,12,13,25</sup>

Urinary perchlorate levels in children ages 6 to 17 years are provided in Tables PER1b and
 PER1c.

#### 3 Statistical Testing

- 4 Statistical analysis has been applied to the biomonitoring indicators to determine whether any
- 5 changes in chemical concentrations over time, or any differences in chemical concentrations
- 6 between demographic groups, are statistically significant. These analyses use a 5% significance
- 7 level ( $p \le 0.05$ ), meaning that a conclusion of statistical significance is made only when there is
- 8 no more than a 5% chance that the observed change over time or difference between
- 9 demographic groups occurred randomly. It should be noted that when statistical testing is
- 10 conducted for differences among multiple demographic groups (e.g., considering both
- 11 race/ethnicity and income level), the large number of comparisons involved increases the
- 12 probability that some differences identified as statistically significant may actually have occurred 13 randomly.
- 14
- 15 A finding of statistical significance for a biomonitoring indicator depends not only on the
- 16 numerical difference in the value of a reported statistic between two groups, but also on the
- 17 number of observations in the survey, the amount of variability among the observations, and
- 18 various aspects of the survey design. For example, if two groups have different median levels of
- 19 a chemical in blood or urine, the statistical test is more likely to detect a difference when samples
- 20 have been obtained from a larger number of people in those groups. Similarly, if there is low
- 21 variability in levels of the chemical within each group, then a difference between groups is more
- 22 likely to be detected. A finding that there is or is not a statistically significant difference in
- 23 exposure levels between two groups or in exposure levels over time does not necessarily suggest
- any interpretation regarding the health implications of those differences.



- In 2001–2004, the 95<sup>th</sup> percentile level of perchlorate among women ages 16 to 49 years was  $11.0 \ \mu g/g$  creatinine. (See Table PER1a.)
- The median perchlorate level among children ages 6 to 10 years was twice as high as the level found in women of childbearing age in 2001–2004, while the median perchlorate level among children ages 11 to 17 years was 11% higher than that of women. The 95<sup>th</sup> percentile level among children ages 6 to 10 years was 68% higher than that of women, while the 95<sup>th</sup>
- 8 percentile level among children ages 11 to 17 years was 3% lower than that of women. (See
- 9 Tables PER1b and PER1c.)

10

1 2

# Data Tables

Table PER1. Perchlorate in women ages 16 to 49 years: Median concentrations in urine, byrace/ethnicity and family income, 2001-2004

	Median concentration of perchlorate in urine (µg/g creatinine)							
		<		<u>&gt;</u> Poverty	(Detail)			
Race / Ethnicity	All Incomes	Poverty Level	≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income		
All Races/ Ethnicities	2.7	2.2	2.8	2.6	2.8	NA**		
White Non- Hispanic	2.8	2.7	2.8	2.6	3.0	NA**		
Black Non- Hispanic	1.9	1.9	1.8	1.8	1.9	NA**		
Mexican- American	2.8	2.8	2.7	3.3	2.5	4.3		
Other†	2.8	1.9	2.9	2.8	4.0*	NA**		

<sup>89</sup> 10111 121314 1516177 18192021 22324 252627

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 PER1a. Perchlorate in women ages 16 to 49 years: 95<sup>th</sup> percentile concentrations in

urine, by race/ethnicity and family income, 2001-2004

1 2 3

	95 <sup>th</sup> percentile concentration of perchlorate in urine ( $\mu$ g/g creatinine)							
				<u>&gt;</u> Poverty				
Race / Ethnicity	All < Poverty Incomes Level		≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income		
All Races/ Ethnicities	11.0	9.5	11.0	11.0	NA**	16.0		
White Non- Hispanic	11.7	NA**	NA**	NA**	NA**	12.4		
Black Non- Hispanic	8.3	8.3	7.0	8.9	5.3	NA**		
Mexican- American	11.2	15.5	NA**	9.2	NA**	11.2		
Other†	14.0	4.9*	11.3	5.4*	NA**	NA**		

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

NOTES:

- 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.
- Perchlorate does not appear to accumulate in bodily tissues; thus, the distribution of NHANES urinary perchlorate levels may overestimate high-end exposures as a result of collecting one-time urine samples rather than collecting urine for a longer time period.<sup>18</sup>

† "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 PER1b. Perchlorate in children ages 6 to 17 years: Median concentrations in urine, byrace/ethnicity and family income, 2001-2004

Ages 6-10							
Median concentration of perchlorate in urine					creatinine)		
		<		<u>&gt;</u> Poverty			
Race / Ethnicity	All Incomes Level		≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income	
All Races/ Ethnicities	5.4	5.1	5.5	5.3	5.9	6.1	
White Non- Hispanic	5.5	NA**	5.5	5.1	5.9	7.5	
Black Non- Hispanic	4.5	4.7	4.3	3.8	4.5	4.8	
Mexican- American	6.1	5.6	6.7	7.7	6.3	5.7	
Other†	6.4	NA**	6.4	5.4	6.5	No data	

#### Ages 11-17

Median concentration of perchlorate in urine (µg/g creatinine)

		<		<u>&gt;</u> Poverty (Detail)			
Race / Ethnicity	All Incomes Poverty ≥ Poverty Level Level		100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income		
All Races/ Ethnicities	3.0	2.6	3.1	2.8	3.2	3.4	
White Non- Hispanic	3.0	2.5	3.2	2.5	3.3	3.8	
Black Non- Hispanic	2.5	2.4	2.5	2.4	2.6	2.9	
Mexican- American	3.3	3.3	3.3	3.5	3.3	2.8	
Other†	3.2	NA**	3.2	3.8*	2.9	NA**	

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

† "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 PER1c. Perchlorate in children ages 6 to 17 years: 95<sup>th</sup> percentile concentrations in urine, by race/ethnicity and family income, 2001-2004

Ages 6-10						
	95 <sup>th</sup> perce	entile conco	entration of per	chlorate in urin	e (µg/g creati	nine)
		<		<u>&gt;</u> Poverty (Detail)		
Race / Ethnicity	All Incomes	Poverty Level	≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income
All Races/ Ethnicities	18.5	17.2	19.3	NA**	18.5	NA**
White Non- Hispanic	20.0	NA**	20.0	NA**	19.3	44.0
Black Non- Hispanic	15.0	11.0	16.0	NA**	NA**	18.0
Mexican- American	17.0	17.2	16.0	15.5	16.0	16.8
Other†	NA**	NA**	14.0	11.1	14.0	No data
Agoc 11-17						•

Ages 11-17

	95 <sup>th</sup> perce	95 <sup>th</sup> percentile concentration of perchlorate in urine (µg/g creatinine)					
		<		<u>&gt;</u> Poverty (Detail)			
Race / Ethnicity	All Incomes	Poverty Level	≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income	
All Races/ Ethnicities	10.7	11.3	10.1	11.0	9.8	12.8	
White Non- Hispanic	9.2	9.7	9.1	NA**	8.9	12.8	
Black Non- Hispanic	9.3	9.6	8.2	9.0	8.2	5.1	
Mexican- American	12.0	NA**	12.0	11.0	NA**	7.3*	
Other†	13.0	16.8	12.3	10.3	12.3	NA**	

<sup>9</sup> 10

11

12 13 14

15

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

NOTE: Perchlorate does not appear to accumulate in bodily tissues; thus, the distribution of NHANES urinary perchlorate levels may overestimate high-end exposures as a result of collecting one-time urine samples rather than collecting urine for a longer time period.<sup>18</sup>

† "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).

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# 1 Metadata

2

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) reported by an adult informant.

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Metadata for	National Health and Nutrition Examination Survey (NHANES)
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 predecessors 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**

4 5

PER1. Perchlorate in women ages 16 to 49 years: Median concentrations in urine, by

6 race/ethnicity and family income, 2001-2004.7

#### 8 Summary 9

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>1</sup> This indicator uses creatinine-adjusted urine measurements of perchlorate in
- 16 women ages 16 to 49 years. The NHANES 2001-2002 and 2003-2004 surveys included urine
- perchlorate data for children and adults ages 6 years and over. Indicator PER1 gives the median
   creatinine-adjusted concentrations of perchlorate for women ages 16 to 49 years for 2001-2004,
- 19 stratified both by race/ethnicity and family income. The median is the estimated concentration
- 20 such that 50% of all noninstitutionalized civilian women ages 16 to 49 years during the survey
- 21 period have a perchlorate concentration below this level; the population distribution was adjusted
- by age-specific birth rates to estimate the median pre-natal exposure to perchlorate. Table PER1a
- gives the 95<sup>th</sup> percentile concentrations of perchlorate for women ages 16 to 49 years for 2001 2004, stratified both by race/ethnicity and family income. The 95<sup>th</sup> percentile for women is the
- 25 estimated concentration such that 95% of all noninstitutionalized civilian women ages 16 to 49
- 26 years during the survey period have a perchlorate concentration below this level. Table PER1b
- 27 gives the median concentrations of perchlorate for children ages 6 to 10 years and children ages
- 28 11 to 17 years for 2001-2004, stratified both by race/ethnicity and family income. The median
- for children is the estimated concentration such that 50% of all noninstitutionalized civilian children ages 6 to 10 years or 11 to 17 years have a perchlorate concentration below this level.
- children ages 6 to 10 years or 11 to 17 years have a perchlorate concentration below this level.
   Table PER1c gives the 95<sup>th</sup> percentile concentrations of perchlorate for children ages 6 to 10
- years and 11 to 17 years for 2001-2004, stratified both by race/ethnicity and family income. The
- years and 11 to 17 years for 2001-2004, stratified both by race/ethnicity and family income.
   95<sup>th</sup> percentile for children is the estimated concentration such that 95% of all

35 95 percentile for children is the estimated concentration such that 95% of all
 34 noninstitutionalized civilian children ages 6 to 10 years or 11 to 17 years have a perchlorate

- noninstitutionalized civilian children ages 6 to 10 years or 11 to 1 / years have a perchlorate
- 35 concentration below this level. The survey data were weighted to account for the complex multi-
- 36 stage, stratified, clustered sampling design.
- 37

#### 38 Data Summary

39

IndicatorPER1. Perchlorate in women ages 16 to 49 years: Median<br/>concentrations in urine, by race/ethnicity and family income,

<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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	2001-2004.						
Time Period	2001-2004	2001-2004					
Data	Urine perchlo	rate (creatinine	adjusted)				
Years/Subgroup	2001-2002/	2003-2004/	2001-2002/	2003-2004/			
	Women 16-	Women 16-	Children 6-	Children 6-			
	49	49	17	17			
Limits of Detection ( $\mu$ g/L)	0.05	0.05	0.05	0.05			
Number of Non-missing	657	616	1,021	858			
Values*							
Number of Missing Values	43	7	37	1			
Percentage Below Limit of	0	0	0	0			
Detection**							

\*\*This percentage is survey-weighted using the NHANES survey weights for the given period and, for women ages 16 to 49 years, 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>www.cdc.gov/nchs/nhanes.htm</u>.

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 NHANES 2001-2002: Demographic file demo\_b.xpt. Surplus Specimen Laboratory Component: Nitrate, thiocyamate, perchlorate (Surplus Urine) ssno3p\_b.xpt. The demographic file demo\_b.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), race/ethnicity (RIDRETH1), poverty income ratio (INDFMPIR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The Laboratory file ssno3p\_b.xpt contains SEQN, urine perchlorate (SSXUPH), urine creatinine (URXUCR) and the sub-sample survey weight (WTUIO2YR). The two files are merged using the common variable SEQN.

- 20 NHANES 2003-2004: Demographic file demo c.xpt. Urinary Perchlorate Laboratory file • 21 104per c.xpt. The demographic file demo c.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), race/ethnicity 22 23 (RIDRETH1), poverty income ratio (INDFMPIR), pseudo-stratum (SDMVSTRA) and 24 the pseudo-PSU (SDMVPSU). The Urinary Perchlorate laboratory file 104per c.xpt 25 contains SEQN, urine perchlorate (URXUP8), creatinine-adjusted urine perchlorate 26 (URXUP8CA), and the sub-sample C survey weight (WTSC2YR). The two files are 27 merged using the common variable SEQN.
- 28

#### 29 National Health and Nutrition Examination Surveys (NHANES)

- 30
- 31 Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease
- 32 Control and Prevention, has conducted the National Health and Nutrition Examination Surveys
- 33 (NHANES), a series of U.S. national surveys of the health and nutrition status of the
- 34 noninstitutionalized civilian population. The National Center for Environmental Health at CDC

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- 1 measures environmental chemicals in blood and urine samples collected from NHANES
- 2 participants. This indicator and tables uses urine perchlorate measurements from NHANES
- 3 2001-2002 and 2003-2004 in women ages 16 to 49 years and children ages 6 to 17 years. The
- 4 NHANES data were obtained from the NHANES website: <u>http://www.cdc.gov/nchs/nhanes.htm</u>.
- 5 This analysis uses the creatinine-adjusted urine perchlorate concentration ( $\mu g/g$  creatinine). The
- 6 unadjusted perchlorate concentration is reported as  $\mu$ g/L. The creatinine concentration is
- 7 reported as mg/dL. For 2001-2002, the creatinine-adjusted perchlorate concentration was
- 8 calculated from the raw data as the ratio Unadjusted perchlorate/( $0.01 \times$  Creatinine)  $\mu$ g/g
- 9 creatinine. For 2003-2004, the creatinine-adjusted perchlorate concentration was reported as the
- 10 variable URXUP8CA.
- 11
- 12 The NHANES use a complex multi-stage, stratified, clustered sampling design. Certain
- 13 demographic groups were deliberately over-sampled, including Mexican-Americans and Blacks.
- 14 Oversampling is performed to increase the reliability and precision of estimates of health status
- 15 indicators for these population subgroups. The publicly released data includes survey weights to
- adjust for the over-sampling, non-response, and non-coverage. The statistical analyses used the
- 17 sub-sample laboratory survey weights (WTUIO2YR for 2001-2002 and WTC2YR for 2003-
- 18 2004) to re-adjust the urine perchlorate data to represent the national population.
- 19

#### 20 Age-Specific Birth Rates

21

In addition to the NHANES survey weights, the data for women of child-bearing age (ages 16 to 49 years) were also weighted by the birth rate for women of the given age and race/ethnicity to estimate pre-natal exposures. Thus the overall weight in each two year period is the product of the 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 of the two year period.<sup>ii</sup>

27 28

#### 29 Race/Ethnicity and Family Income

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31 For this indicator, the percentiles were calculated for demographic strata defined by the

- 32 combination of race/ethnicity and family income.
- The family income was characterized based on the INDFMPIR variable, which is the ratio of the
- 35 family income to the poverty level. The National Center for Health Statistics used the U.S.
- 36 Census Bureau Current Population Survey to define the family units, and the family income for
- 37 the respondent was obtained during the interview. The U.S. Census Bureau defines annual
- 38 poverty level money thresholds varying by family size and composition. The poverty income
- 39 ratio (PIR) is the family income divided by the poverty level for that family. Family income was 40 stratified into the following groups:
- 40 41 42
- Below Poverty Level: PIR < 1

<sup>&</sup>lt;sup>ii</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.

1 2	<ul> <li>Between 100 % and 200 % of Poverty Level: 1 ≤ PIR ≤ 2</li> <li>Above 200 % of Poverty level: PIR &gt; 2</li> </ul>
3	• Above Poverty Level: PIR $\geq 1$ (combines the previous two groups)
4	<ul> <li>Unknown Income: PIR is missing</li> </ul>
5	• Onknown meonie. I ik is missing
6 7	Race/ethnicity was characterized using the RIDRETH1 variable. The possible values of this variable are:
8	
9	• 1. Mexican American
10	• 2. Other Hispanic
11	• 3. Non-Hispanic White
12	• 4. Non-Hispanic Black
13	• 5. Other Race – Including Multi-racial
14	• "." Missing
15	Cotto and 5 in challen all New History is simple more memory of the theory White an Discharged
16	Category 5 includes: all Non-Hispanic single race responses other than White or Black; and
17	multi-racial responses.
18 19	For this indicator, the RIDRETH1 categories 2, 5, and missing were combined into a single
20	"Other" category. This produced the following categories:
20	other category. This produced the following categories.
22	• White non-Hispanic: RIDRETH1 = 3
23	<ul> <li>Black non-Hispanic: RIDRETH1 = 4</li> </ul>
24	• Mexican-American: RIDRETH1 = 1
25	• Other: RIDRETH1 = 2 or 5 or missing
26	• Other. RIDRETTT 2 of 5 of missing
27	The "Other" category includes Asian non-Hispanic; Native American non-Hispanic; Hispanic
28	other than Mexican-American; those reporting multi-racial; and those with a missing value for
29	race/ethnicity.
30	
31	Calculation of Indicator
32	
33	Indicator PER1 is the median for urine perchlorate in women of ages 16 to 49 years, stratified by
34	race/ethnicity and family income. Table PER1a is the 95 <sup>th</sup> percentile for urine perchlorate in
35	women ages 16 to 49 years, stratified by race/ethnicity and family income. Table PER1b is the
36	median for urine perchlorate in children of ages 6 to 10 and 11 to 17 years, stratified by
37	race/ethnicity and family income. Table PER1c is the 95 <sup>th</sup> percentile for urine perchlorate in
38	children of ages 6 to 10 and 11 to 17 years, stratified by race/ethnicity and family income. The
39	median for women ages 16 to 49 is the estimated concentration such that 50% of all
40	noninstitutionalized civilian women ages 16 to 49 years during the survey period have urine
41	perchlorate concentrations below this level. The 95 <sup>th</sup> percentile for women ages 16 to 49 is the
42	estimated concentration such that 95% of all noninstitutionalized civilian women ages 16 to 49
43	years during the survey period have urine perchlorate concentrations below this level. To adjust
44	the NHANES data to represent pre-natal exposures, the data for each woman surveyed were

multiplied by the estimated number of births per woman of the given age and race/ethnicity. The
 birth rate adjustment was not applied to children ages 6 to 17 years.

3

4 To simply demonstrate the calculations, we will use the NHANES 2001-2004 urine perchlorate 5 values for women ages 16 to 49 years of all race/ethnicities and all incomes as an example. We 6 have rounded all the numbers to make the calculations easier:

7

8 We begin with all the non-missing NHANES 2001-2004 urine perchlorate values for women 9 ages 16 to 49 years. Assume for the sake of simplicity that valid perchlorate data were available 10 for every sampled woman. Each sampled woman has an associated annual survey weight that estimates the annual number of U.S. women represented by that sampled woman. Since two 2-11 12 year periods are combined for these analyses, the associated annual survey weight for each 13 woman is defined as WTUIO2YR/2 for 2001-2002 and WTSC2YR/2 for 2003-2004, so that the 14 combined 2001-2004 sample represents the annual population. Each sampled woman also has an 15 associated birth rate to adjust for the numbers of annual births per woman of the given age, race, 16 and ethnicity. The product of the annual survey weight and the birth rate estimates the annual 17 number of U.S. births represented by that sampled woman, which we will refer to as the adjusted 18 survey weight. For example, the lowest urine perchlorate measurement for a woman between 16 19 and 49 years of age is 0.2  $\mu$ g/g creatinine with an annual survey weight of 41,000, a birth rate of 20 0.0022, and thus an adjusted survey weight of 90, and so represents 90 births. The total of the 21 adjusted survey weights for the sampled women equals 4 million, the total number of annual 22 U.S. births to women ages 16 to 49 years. The second lowest measurement is 0.3 µg/g creatinine 23 with an adjusted survey weight of 4,700, and so represents another 4,700 U.S. births. The highest 24 measurement is 250 µg/g creatinine with an adjusted survey weight of 200, and so represents another 200 U.S. births.

25 26

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

28 U.S. population of births to women ages 16 to 49 years. We have 90 values of  $0.2 \mu g/g$ 

29 creatinine from the lowest measurement, 4,700 values of 0.3  $\mu$ g/g creatinine from the second

30 lowest measurement, and so on, up to 200 values of 250  $\mu$ g/g creatinine from the highest 31 measurement. Arranging these 4 million values in increasing order, the 2 millionth value is 2.7

 $\mu g/g$  creatinine. Since half of the values are below 2.7 and half of the values are above 2.7, the

 $\mu g/g$  creatinine. Since half of the values are below 2.7 and half of the values are above 2.7, the median equals 2.7  $\mu g/g$  creatinine. To calculate the 95<sup>th</sup> percentile, note that 95% of 4 million

equals 3.8 million. The 3.8 millionth value is  $11 \,\mu$ g/g creatinine. Since 95% of the values are

35 below 11, the 95<sup>th</sup> percentile equals 11  $\mu$ g/g creatinine.

36

37 In reality, the calculations need to take into account that urine perchlorate measurements were

38 not available for every respondent, and to use exact rather than rounded numbers. There were

<sup>39</sup> urine perchlorate measurements for only 1,269 of the 1,323 sampled women ages 16 to 49 years.

40 The adjusted survey weights for all 1,323 sampled women add up to 4.2 million, the U.S.

- 41 population of births to women ages 16 to 49 years. The adjusted survey weights for the 1,269
- 42 sampled women with urine perchlorate data add up to 4.0 million. Thus the available data
  43 represent 4.0 million values and so represent only 97 % of the U.S. population of births. The
- 43 represent 4.0 million values and so represent only 97% of the 0.5. population of births. The 44 median and  $95^{th}$  percentiles are given by the 2.0 millionth (50 % of 4.0 million) and 3.8 millionth
- 44 inedian and 95 percentiles are given by the 2.0 inition (50 % of 4.0 inition) and 5.8 inition (45 % of 4.0 million) U.S. birth's value. These calculations assume that the sampled women with
- 46 valid urine perchlorate data are representative of women giving birth without valid urine

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perchlorate data. The calculations also assume that the sampled women are representative of 1 2 women that actually gave birth in 2001-2004, since NHANES information on pregnancy and 3 births was not incorporated into the analysis. 4 5 Equations 6 7 These percentile calculations can also be given as the following mathematical equations, which 8 are based on the default percentile calculation formulas from Statistical Analysis System (SAS) 9 software. Exclude all missing urine perchlorate values. Suppose there are n women of ages 16 to 10 49 years with valid urine perchlorate values. Arrange the urine perchlorate concentrations in increasing order (including tied values) so that the lowest concentration is x(1) with an adjusted 11 12 survey weight of w(1), the second lowest concentration is x(2) with an adjusted survey weight of 13 w(2), ..., and the highest concentration is x(n) with an adjusted survey weight of w(n).14 15 1. Sum all the adjusted survey weights to get the total weight W: 16 17  $W = \Sigma[1 \le i \le n] w(i)$ 18 19 2. Find the largest number i so that the total of the weights for the i lowest values is less than or 20 equal to W/2. 21 22  $\Sigma[j \le i] w(j) \le W/2 \le \Sigma[j \le i+1] w(j)$ 23 24 3. Calculate the median using the results of the second step. We either have 25  $\Sigma[j \le i] w(j) = W/2 < \Sigma[j \le i + 1] w(j)$ 26 27 28 or 29 30  $\Sigma[j \le i] w(j) < W/2 < \Sigma[j \le i + 1] w(j)$ 31 32 In the first case we define the median as the average of the i'th and i + 1'th values: 33 34 Median = [x(i) + x(i + 1)]/2 if  $\Sigma[i \le i] w(i) = W/2$ 35 36 In the second case we define the median as the i + 1'th value: 37 38 Median = x(i + 1) if  $\Sigma[i \le i] w(i) < W/2$ 39 40 (The estimated median does not depend upon how the tied values of x(i) are ordered). 41 A similar calculation applies to the 95<sup>th</sup> percentile. The first step to calculate the sum of the 42 weights, W, is the same. In the second step, find the largest number i so that the total of the 43 44 weights for the i lowest values is less than or equal to 0.95W. 45 46  $\Sigma[j \le i] w(j) \le 0.95W < \Sigma[j \le i+1] w(j)$ 

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1 2 In the third step we calculate the 95<sup>th</sup> percentile using the results of the second step. We either 3 have 4 5  $\Sigma[i \le i] w(i) = 0.95W < \Sigma[i \le i + 1] w(i)$ 6 7 or 8 9  $\Sigma[j \le i] w(j) < 0.95W < \Sigma[j \le i + 1] w(j)$ 10 In the first case we define the 95<sup>th</sup> percentile as the average of the i'th and i + 1'th values: 11 12 95<sup>th</sup> Percentile = [x(i) + x(i + 1)]/2 if  $\Sigma[j \le i] w(j) = 0.95W$ 13 14 In the second case we define the  $95^{th}$  percentile as the i + 1'th value: 15 16 95<sup>th</sup> Percentile = x(i + 1) if  $\Sigma[j \le i] w(j) < 0.95W$ 17 18 19 **Relative Standard Error** 20 The uncertainties of the median and 95<sup>th</sup> percentile values were calculated using a revised 21 version of the CDC method given in CDC 2005,<sup>iii</sup> Appendix C, and the SAS® program provided 22 by CDC. The method uses the Clopper-Pearson binomial confidence intervals adapted for 23 24 complex surveys by Korn and Graubard (see Korn and Graubard, 1999<sup>iv</sup>, p. 65). The following 25 text is a revised version of the Appendix C. For the birth rate adjusted calculations for women 26 ages 16 to 49, the sample weight is adjusted by multiplying by the age-specific birth rate. 27 28 Step 1: Use SAS® Proc Univariate to obtain a point estimate P<sub>SAS</sub> of the percentile value. Use the Weight 29 option to assign the exact correct sample weight for each chemical result. 30 31 **Step 2:** Use SUDAAN® Proc Descript with Taylor Linearization DESIGN = WR (i.e., 32 33 34 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 35 sample size 36 37  $n_{df} = (t_{num}/t_{denom})^2 p(1 - p)/(se_p^2)$ 38 39 where  $t_{num}$  and  $t_{denom}$  are 0.975 critical values of the Student's t distribution with degrees of freedom 40 equal to the sample size minus 1 and the number of PSUs minus the number of strata, respectively. Note: 41 the degrees of freedom for t<sub>denom</sub> can vary with the demographic sub-group of interest. 42 43 Step 3: After obtaining an estimate of p (i.e., the proportion obtained in Step 2), compute the Clopper-44 Pearson 95% confidence interval ( $P_L(x,n_{df}), P_U(x,n_{df})$ ) as follows: 45 46  $P_L(x,n_{df}) = v_1 F_{v1,v2} (0.025)/(v_2 + v_1 F_{v1,v2}(0.025))$ 

<sup>&</sup>lt;sup>iii</sup> CDC Third National Report on Human Exposure to Environmental Chemicals. 2005 <sup>iv</sup> Korn E. L., Graubard B. I. 1999. *Analysis of Health Surveys*. Wiley.

# **Biomonitoring: Perchlorate**

1	$P_{U}(x,n_{df}) = v_{3}F_{v_{3},v_{4}}(0.975)/(v_{4} + v_{3}F_{v_{3},v_{4}}(0.975))$
1 2 3 4 5 6 7 8 9	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.
8 9 10 11 12 13	<b>Step 4:</b> 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 $P_{CDC}$ and $P_{SAS}$ are not necessarily equal.
13 14 15 16	<b>Step 5:</b> Use the confidence interval from Step 4 to estimate the standard error of the estimated percentile $P_{CDC}$ :
17 18	Standard Error $(P_{CDC}) = (U_{CDC} - L_{CDC}) / (2t_{denom})$
19 20 21	<b>Step 6:</b> Use the estimated percentile $P_{CDC}$ and the standard error from Step 4 to estimate the relative standard error of the estimated percentile $P_{CDC}$ :
21 22 23	Relative Standard Error (%) = [Standard Error ( $P_{CDC}$ ) / $P_{CDC}$ ] × 100 %
23 24 25 26	The tabulated estimated percentile is the value of $P_{SAS}$ given in Step 1. The relative standard error is given in Step 6, using $P_{CDC}$ and its standard error.
27 28 29 30 31	The relative standard error depends upon the survey design. For this purpose, the public release version of NHANES includes the variables SDMVSTRA and SDMVPSU, which are the Masked Variance Unit pseudo-stratum and pseudo-primary sampling unit (pseudo-PSU). For approximate variance estimation, the survey design can be approximated as being a stratified random sample with replacement of the pseudo-PSUs from each pseudo-stratum; the true stratum
32 33	and PSU variables are not provided in the public release version to protect confidentiality.
33 34 35 36 37 38 39 40	Percentiles with a relative standard error less than 30% were treated as being reliable and were tabulated. Percentiles with a relative standard error greater than or equal to 30% but less than 40% were treated as being unstable; these values were tabulated but were flagged to be interpreted with caution. Percentiles with a relative standard error greater than or equal to 40%, or without an estimated relative standard error, were treated as being unreliable; these values were not tabulated and were flagged as having a large uncertainty.
41	Questions and Comments
42 43 44 45	Questions regarding these methods, and suggestions to improve the description of the methods, are welcome. Please use the "Contact Us" link at the bottom of any page in the America's 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,

6 income group (below poverty, at or above poverty, unknown income), and race/ethnicity group
7 using the method described in the "Relative Standard Error" section. In the notation of that

vising the method described in the "Relative Standard Error" section. In the notation of that section, the percentile and standard error are the values of  $P_{CDC}$  and Standard Error ( $P_{CDC}$ ),

respectively. These calculated standard errors account for the survey weighting and design and,

- 10 for women, for the age-specific birth rate.
- 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

30 example, if White non-Hispanics tend to have higher family incomes than Black non-Hispanics,

31 and if the level of a chemical strongly depends on family income only, then the unadjusted

32 differences between these two race/ethnicity groups would be significant but the adjusted

33 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 6 to 17 years. In Tables 1 and 3, for the

37 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

sex is applicable only to the analyses for children, and thus appears only in Tables 3 and 4.

45

# Biomonitoring: Perchlorate

1	In Tables 1 and 3, for the unadjusted "Below Poverty Level" and "At or Above Poverty Level"
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.
6	
7	The same set of explanatory variables are used in Tables 2 and 4 for the unadjusted comparisons
8	between one race/ethnicity group below the poverty level and the same or another race/ethnicity
9	group at or above the poverty level. The corresponding adjusted analyses include extra
10	explanatory variables for age and (in the case of children) sex, so that race/ethnicity/income
11	groups are compared after accounting for any differences due to age or sex.
12	
13	Additional comparisons are shown in Table 5 for women ages 16 to 49 years and in Table 6 for
14	children ages 6 to 17 years. The AGAINST = "income" unadjusted p-value compares the
15	chemical levels for those below poverty level with those at or above poverty level, using the
16	explanatory variables for the three income groups (below poverty, at or above poverty, unknown
17	income). The adjusted p-value includes adjustment terms for age, sex, and race/ethnicity in the
18	model.
19	
20	For women, the age groups used were 16-19, 20-24, 25-29, 30-39, and 40-49. For children, the
21	age groups used were 6-10, 11-15, and 16-17.
22	
23	For more details on these statistical analyses, see the memorandum by Cohen (2010). <sup>v</sup>
24	

Table 1. Statistical significance tests comparing the percentiles of perchlorate in women ages 16
 to 49 years, between pairs of race/ethnicity groups, for 2001-2004.

	-
2	7

				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)		
perchlorate	50	White non- Hispanic	Black non- Hispanic	0.001	0.001	0.028	0.049	0.007	< 0.0005		
perchlorate	50	White non- Hispanic	Mexican- American	0.882	0.433	0.816	0.113	0.680	0.126		
perchlorate	50	White non- Hispanic	Other	0.846	0.710	0.157	0.315	0.978	0.815		
perchlorate	50	Black non- Hispanic	Mexican- American	0.001	< 0.0005	0.084	0.666	0.019	< 0.0005		
perchlorate	50	Black non- Hispanic	Other	0.126	0.001	1.000	0.051	0.138	0.008		
perchlorate	50	Mexican- American	Other	0.787	0.259	0.177	0.255	0.819	0.183		
perchlorate	95	White non- Hispanic	Black non- Hispanic	0.289	< 0.0005	0.817	< 0.0005	0.467	0.571		
perchlorate	95	White non- Hispanic	Mexican- American	0.863	< 0.0005	0.789	< 0.0005	0.933	0.274		

<sup>&</sup>lt;sup>v</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: Perchlorate**

				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)		
perchlorate	95	White non- Hispanic	Other	0.576	< 0.0005	0.345	< 0.0005	0.949	0.135		
perchlorate	95	Black non- Hispanic	Mexican- American	0.413	0.325	0.444	0.363	0.878	0.255		
perchlorate	95	Black non- Hispanic	Other	0.064	< 0.0005	0.120	< 0.0005	0.132	< 0.0005		
perchlorate	95	Mexican- American	Other	0.466	< 0.0005	0.068	< 0.0005	0.948	0.715		

1 2 3

Table 2. Statistical significance tests comparing the percentiles of perchlorate in women ages 16

to 49 years, between pairs of race/ethnicity/income groups at different income levels, for 2001-2004.

4 5

				P-VALUES		
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age	
perchlorate	50	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.799	0.915	
perchlorate	50	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.037	0.171	
perchlorate	50	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.932	0.496	
perchlorate	50	White non-Hispanic, < PL	Other, $\geq$ PL	0.866	0.989	
perchlorate	50	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.002	< 0.0005	
perchlorate	50	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.770	0.194	
perchlorate	50	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.008	< 0.0005	
perchlorate	50	Black non-Hispanic, < PL	Other, $\geq$ PL	0.156	< 0.0005	
perchlorate	50	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.942	0.001	
perchlorate	50	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.079	0.535	
perchlorate	50	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.757	< 0.0005	
perchlorate	50	Mexican-American, < PL	Other, $\geq$ PL	0.978	0.010	
perchlorate	50	Other, < PL	White non-Hispanic, $\geq$ PL	0.084	0.005	
perchlorate	50	Other, < PL	Black non-Hispanic, $\geq$ PL	0.856	0.466	
perchlorate	50	Other, < PL	Mexican-American, $\geq$ PL	0.141	< 0.0005	
perchlorate	50	Other, < PL	Other, $\geq$ PL	0.238	0.076	
perchlorate	95	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.780	0.100	
perchlorate	95	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.605	< 0.0005	
perchlorate	95	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.980	0.515	
perchlorate	95	White non-Hispanic, < PL	Other, $\geq$ PL	0.739	0.452	
perchlorate	95	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.610	0.006	
perchlorate	95	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.521	< 0.0005	
perchlorate	95	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.933	0.015	
perchlorate	95	Black non-Hispanic, < PL	Other, $\geq$ PL	0.336	< 0.0005	
perchlorate	95	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.919	0.004	
perchlorate	95	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.222	< 0.0005	
perchlorate	95	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.960	0.008	
perchlorate	95	Mexican-American, < PL	Other, $\geq$ PL	0.943	< 0.0005	
perchlorate	95	Other, < PL	White non-Hispanic, $\geq$ PL	0.295	< 0.0005	

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				P-VALUES	
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age
perchlorate	95	Other, < PL	Black non-Hispanic, $\geq$ PL	0.282	< 0.0005
perchlorate	95	Other, < PL	Mexican-American, $\geq$ PL	0.793	< 0.0005
perchlorate	95	Other, < PL	Other, $\geq$ PL	0.029	< 0.0005

1 2 3

4

Table 3. Statistical significance tests comparing the percentiles of perchlorate in children ages 6

to 17 years, between pairs of race/ethnicity groups, for 2001-2004.

				P-VALUES					
Variable	Percentile	RACE1	RACE2	All incomes	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)
perchlorate	50	White non- Hispanic	Black non- Hispanic	0.025	0.052	0.475	0.026	0.024	0.072
perchlorate	50	White non- Hispanic	Mexican- American	0.031	< 0.0005	0.012	< 0.0005	0.326	0.023
perchlorate	50	White non- Hispanic	Other	0.467	0.684	0.063	0.396	0.878	0.172
perchlorate	50	Black non- Hispanic	Mexican- American	< 0.0005	< 0.0005	0.005	< 0.0005	0.011	< 0.0005
perchlorate	50	Black non- Hispanic	Other	0.063	0.786	0.094	0.071	0.159	0.058
perchlorate	50	Mexican- American	Other	0.544	0.048	0.676	< 0.0005	0.598	0.521
perchlorate	95	White non- Hispanic	Black non- Hispanic	0.158	< 0.0005	0.690	< 0.0005	0.506	0.601
perchlorate	95	White non- Hispanic	Mexican- American	0.816	< 0.0005	0.302	< 0.0005	0.782	< 0.0005
perchlorate	95	White non- Hispanic	Other	0.738	< 0.0005	0.346	0.467	0.746	0.004
perchlorate	95	Black non- Hispanic	Mexican- American	0.014	< 0.0005	0.239	0.514	0.264	< 0.0005
perchlorate	95	Black non- Hispanic	Other	0.210	0.094	0.398	< 0.0005	0.637	< 0.0005
perchlorate	95	Mexican- American	Other	0.487	< 0.0005	0.596	< 0.0005	0.464	0.018

5 6 7

Table 4. Statistical significance tests comparing the percentiles of perchlorate in children ages 6

to 17 years, between pairs of race/ethnicity/income groups at different income levels, for 2001-2004.

8 9

				P-VAI	LUES
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age, sex)
perchlorate	50	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.061	< 0.0005
perchlorate	50	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.465	0.001
perchlorate	50	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.023	< 0.0005
perchlorate	50	White non-Hispanic, < PL	Other, $\geq$ PL	0.108	0.003
perchlorate	50	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.013	0.005
perchlorate	50	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.956	0.314

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				P-VAL	UES
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age sex)
perchlorate	50	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.008	< 0.0005
perchlorate	50	Black non-Hispanic, < PL	Other, $\geq$ PL	0.142	0.026
perchlorate	50	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.149	0.001
perchlorate	50	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.007	< 0.0005
perchlorate	50	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.573	0.398
perchlorate	50	Mexican-American, < PL	Other, $\geq$ PL	0.336	0.709
perchlorate	50	Other, < PL	White non-Hispanic, $\geq$ PL	0.282	0.002
perchlorate	50	Other, < PL	Black non-Hispanic, $\geq$ PL	0.098	0.023
perchlorate	50	Other, < PL	Mexican-American, $\geq$ PL	0.479	< 0.000
perchlorate	50	Other, < PL	Other, $\geq$ PL	0.348	0.003
perchlorate	95	White non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.244	< 0.000
perchlorate	95	White non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.458	< 0.0005
perchlorate	95	White non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.125	< 0.0005
perchlorate	95	White non-Hispanic, < PL	Other, $\geq$ PL	0.279	< 0.0005
perchlorate	95	Black non-Hispanic, < PL	White non-Hispanic, $\geq$ PL	0.221	0.546
perchlorate	95	Black non-Hispanic, < PL	Black non-Hispanic, $\geq$ PL	0.489	0.966
perchlorate	95	Black non-Hispanic, < PL	Mexican-American, $\geq$ PL	0.057	< 0.0005
perchlorate	95	Black non-Hispanic, < PL	Other, $\geq$ PL	0.179	< 0.0005
perchlorate	95	Mexican-American, < PL	White non-Hispanic, $\geq$ PL	0.744	0.786
perchlorate	95	Mexican-American, < PL	Black non-Hispanic, $\geq$ PL	0.674	0.660
perchlorate	95	Mexican-American, < PL	Mexican-American, $\geq$ PL	0.476	< 0.000
perchlorate	95	Mexican-American, < PL	Other, $\geq$ PL	0.984	< 0.0005
perchlorate	95	Other, < PL	White non-Hispanic, $\geq$ PL	0.699	< 0.0005
perchlorate	95	Other, < PL	Black non-Hispanic, $\geq$ PL	0.506	< 0.0005
perchlorate	95	Other, < PL	Mexican-American, $\geq$ PL	0.782	< 0.0005
perchlorate	95	Other, < PL	Other, $\geq$ PL	0.598	< 0.0005

1 2 3

Table 5. Other statistical significance tests comparing the percentiles of perchlorate in women ages 16 to 49 years, for 2001-2004.

4

		P-VAI	LUES			
Variable	Percentile	From	То	Against	Unadjusted	Adjusted*
perchlorate	50	2001	2004	income	0.006	< 0.0005
perchlorate	95	2001	2004	income	0.540	< 0.0005

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

5 6 7

Table 6. Other statistical significance tests comparing the percentiles of perchlorate in children ages 6 to 17 years, for 2001-2004.

8 9

		P-VAI	LUES			
Variable	Percentile	From	То	Against	Unadjusted	Adjusted*
perchlorate	50	2001	2004	income	0.027	< 0.0005
perchlorate	95	2001	2004	income	0.621	< 0.0005

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