America's Children and the Environment, Third Edition

DRAFT Indicators

Biomonitoring: Polychlorinated biphenyls (PCBs)

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 PCBs topic in the Biomonitoring section.

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

Polychlorinated Biphenyls (PCBs)

Polychlorinated biphenyls (PCBs) are a family of industrial chemicals that were produced in the United States from 1929 to 1979, used primarily as insulating fluids in capacitors, transformers, and other electrical equipment.[1] PCBs were also used as plasticizers in many paints, plastics, and rubber products, and had numerous applications in industry and building construction.[1] Manufacture and use of PCBs was banned in the United States in 1979,[2] but continued use in enclosed equipment manufactured prior to the ban is allowed. PCBs remain widely distributed in the environment, and they are also present at many Superfund sites.[3] Although levels of PCBs in environmental samples have declined from their peak, the rate of decline has slowed in recent years.[4,5] The persistent nature of PCBs and their distribution through the food chain has resulted in continuing human exposure.

Children born to mothers who were exposed to high concentrations of a mixture of PCBs and polychlorinated dibenzofurans in poisoning incidents in Taiwan and Japan exhibited a number of adverse health effects, including neurodevelopmental effects such as cognitive deficits, developmental delays, effects on motor skills, and behavioral effects.[6-10]

Following the poisoning incidents, several studies have been conducted to examine the neurodevelopmental effects of PCBs at more typical exposure levels. Many of these studies have linked early-life exposure to PCBs with neurodevelopmental effects, such as lowered intelligence, and behavioral deficits, including inattention and impulsive behavior.[11-17] The observed effects have been most frequently associated with exposure in the womb resulting from the mother having eaten food contaminated with PCBs,[18-22] but some studies have detected relationships between adverse effects and PCB exposure during infancy and childhood.[16,22-24] Although there is some inconsistency in the epidemiological literature, the overall evidence supports a concern for effects of PCBs on children's neurological development.[10,23,25-27]

Prenatal PCB exposures have also been associated with immunological effects, such as increased infections, in multiple studies.[28-34] Possible other effects of exposure to PCBs—with limited or inconclusive evidence—include preterm birth and low birthweight,[10] and effects on the timing of puberty in both boys and girls.[35] PCBs are also considered "reasonably anticipated to be human carcinogens," based on experimental animal studies.[36]

Some PCBs are structurally and toxicologically related to the chemical 2,3,7,8-tetrachlorodibenzo-p-dioxin, and are sometimes referred to as "dioxin-like chemicals." The developing fetus and breastfeeding infants may be at risk for neurodevelopmental and immunological effects from exposure to dioxin-like chemicals that have accumulated in the mother's body over many years.[37]

Due to the continued presence of PCBs in fish, meat, poultry, dairy products, and breast milk, dietary intake is an important pathway of exposure for PCBs.[3] Recent findings suggest that the presence of PCBs in indoor dust and indoor air may constitute an important exposure pathway for some portion of the population.[38-41] The importance of PCBs in indoor environments may be

greater for toddlers than for adults and children of other ages because of their elevated contact with house dust.[38] A study of homes with unusually high indoor air concentrations of PCBs found that a PCB-containing wood flooring finish applied in the 1950s and 1960s can be a major contributor to current elevations of PCBs in blood for people living in those homes.[40] PCBs have also been found in caulk in some schools and other buildings constructed or renovated before the late 1970s, which may contribute significantly to indoor air and dust levels of PCBs in those buildings.[42] Finally, the inadvertent presence of PCBs has been found in pigments that are currently manufactured for use in paints, inks, textiles, paper, cosmetics, leather, and other materials.[43,44]

Blood levels of PCBs generally increase with age, because these chemicals are persistent.[45,46] However, due to the decline in levels of PCBs in the environment and in foods over the past three decades, young people today are exposed to lower levels of PCBs through the diet than were previous generations.[3,47]

Although environmental levels of PCBs have been declining, there are concerns that some past PCB emissions trapped in polar ice may be released to the environment in coming years with increasing ice melts.[48,49]

The following indicator presents levels of PCBs in blood of women of childbearing age, based on concerns for effects on children from prenatal exposures to PCBs. No indicator is presented for PCBs in children due to the limited availability of data.

Indicator PCB1: PCBs in women ages 16 to 49 years: Median concentrations in blood serum, by race/ethnicity and family income, 2001–2004

Overview

Indicator PCB1 presents concentrations of PCBs 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 PCBs in the blood. The indicator presents comparisons of PCBs in blood for women of different race/ethnicities, and for women of different income levels. The focus is on women of child-bearing age because blood levels of PCBs during pregnancy have been associated with adverse children's health outcomes.

NHANES

Data used in this indicator come from the National Health and Nutrition Examination Survey (NHANES). NHANES is a nationally representative survey designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population, conducted by the Centers for Disease Control and Prevention (CDC). Interviews and physical examinations are conducted for 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 NHANES participants.[50] Concentrations of PCBs in blood serum have been measured in a representative subset of NHANES participants ages 12 years and older beginning with the 1999–2000 survey cycle. NHANES data from 2001–2002 and 2003–2004 are used for Indicator PCB1.

Data from 1999–2000 are not included in the indicator because less sensitive measurement techniques were used in those years, and PCB levels could not be determined in a large proportion of the blood samples. Improvements in measurement sensitivity were achieved in 2001–2002, with further improvements in 2003–2004 resulting in successful measurement of PCBs in a majority of samples.[46]

PCB Congeners

There are 209 possible PCBs, referred to as "congeners," which are defined by the number of chlorine atoms (from 1 to 10) and their position in the chemical structure. Most of these congeners were not present in the manufactured PCB mixtures and have not been measured in environmental or human samples. NHANES sampled for 34 PCB congeners in 2001–2002, and added 4 congeners in 2003–2004 for a total of 38 congeners.

The indicator uses data on four specific congeners: PCBs 118, 138, 153, and 180. These four congeners are generally found at higher levels in the environment—and in human blood samples— than other PCB congeners. This combination of congeners has been frequently used

to represent PCB exposure in the epidemiological studies described above that identified children's health concerns for PCBs. These four congeners were measured successfully in the majority of samples for women ages 16 to 49 years in 2001–2002, and in virtually all samples for this population group in 2003–2004. Levels of the four congeners in each sample are added together for the indicator, as has been done in many epidemiological studies. For samples in which any of the four congeners were not detectable, a default value below the detection limit was assigned for purposes of calculating the summed total. This assumption has only a small impact on the indicator values, because all four congeners were detected in most samples in the combined four-year (2001–2004) data set.

Lipid Adjustment

PCB concentrations are measured in blood serum. PCBs are lipophilic, meaning that they tend to accumulate in fat. Body burdens of PCBs are measured and expressed on a lipid-adjusted basis, as these are expected to better represent body burden than unadjusted values.[50] The indicator uses lipid- adjusted concentrations, meaning that the concentration of PCBs in serum is divided by the concentration of lipid in serum. The resulting units are nanograms of PCB per gram of lipid (ng/g lipid) in serum.

Birthrate Adjustment

This indicator uses measurements of PCBs in the blood of women ages 16 to 49 years to represent the distribution of PCB exposures to women who are pregnant or may become pregnant. However, women of different ages have a different likelihood of giving birth. For example, in 2003–2004, women aged 27 years had a 12% annual probability of giving birth, and women aged 37 years had a 4% annual probability of giving birth.[51] A birthrate-adjusted distribution of women's PCB levels is used in calculating this indicator, meaning that the data are weighted using the age-specific probability of a woman giving birth.[52]

Data Presented in the Indicator

The indicator presents median PCBs in blood serum, computed as the sum of PCBs 118, 138, 153, and 180, for different population groups defined by race/ethnicity and family income. The median is the value in the middle of the distribution of blood serum PCB levels: half of the women have levels greater than the median, and half have levels below the median. The median can be thought of as representing a typical exposure. To represent the upper range of the exposure distribution, 95th percentile values are presented for each population group in the data tables.

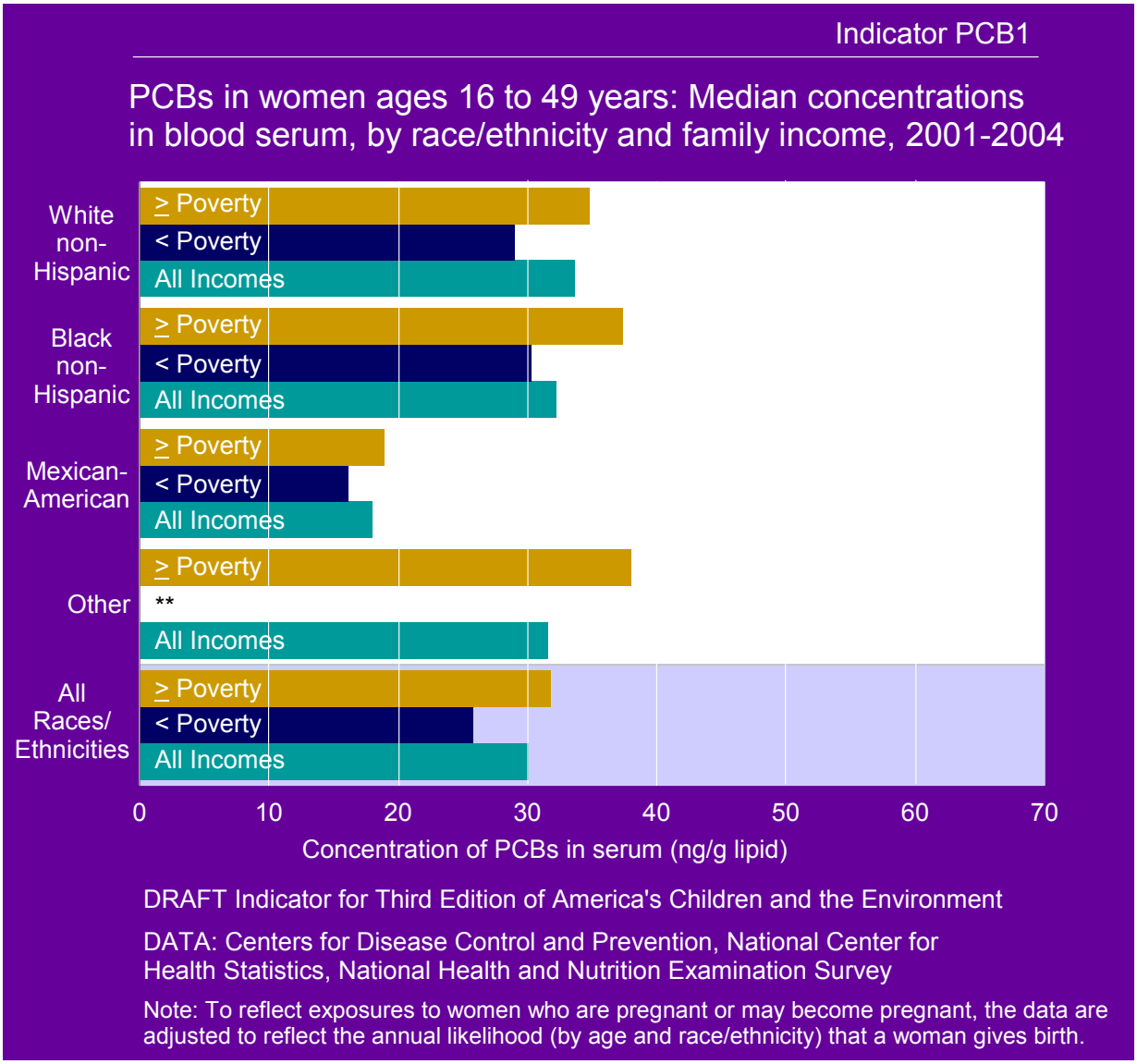
Four race/ethnicity groups are presented: White non-Hispanic, Black non-Hispanic, Mexican-American, and "Other." The "Other" race/ethnicity category includes Asian non-Hispanic, Native American non-Hispanic, Hispanic other than Mexican American, those reporting multiple racial categories, and those with a missing value for race/ethnicity. The data are also tabulated across three income categories: all incomes, below the poverty level, and greater than or equal to the poverty level. The data from two NHANES cycles (2001–2002 and 2003–2004) are combined to increase the statistical reliability of the estimates for each race/ethnicity and income 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 changes over time.

Statistical Testing

Statistical analysis has been applied to the biomonitoring indicators to determine whether any changes in chemical concentrations over time, or any differences in chemical concentrations between demographic groups, are statistically significant. These analyses use a 5% significance level ($p \leq 0.05$), 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 demographic groups occurred randomly. It should be noted that when statistical testing is conducted for differences among multiple demographic groups (e.g., considering both race/ethnicity and income level), the large number of comparisons involved increases the probability that some differences identified as statistically significant may actually have occurred randomly.

A finding of statistical significance for a biomonitoring indicator depends not only on the numerical difference in the value of a reported statistic between two groups, but also on the number of observations in the survey, the amount of variability among the observations, and various aspects of the survey design. For example, if two groups have different median levels of a chemical in blood or urine, the statistical test is more likely to detect a difference when samples have been obtained from a larger number of people in those groups. Similarly, if there is low variability in levels of the chemical within each group, then a difference between groups is more likely to be detected. A finding that there is or is not a statistically significant difference in exposure levels between two groups or in exposure levels over time does not necessarily suggest any interpretation regarding the health implications of those differences.



** 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).

- In 2001–2004, the median level of PCBs among women ages 16 to 49 years was 30 ng/g lipid.

- PCB levels were higher overall for women with higher incomes than for women with lower incomes, but these differences are not statistically significant for any race/ethnicity group.

- PCB levels were lower among Mexican-American women than among women any other race/ethnicity group.
    - Statistical Note: These differences were statistically significant. After accounting for other demographic differences (i.e., differences in income or age profile), the differences remained statistically significant except for that between Mexican-American women and women of "Other" race/ethnicity.

- The 95th percentile concentration of PCBs among women ages 16 to 49 years was 106 ng/g lipid. Among women of "Other" race/ethnicity, the 95th percentile PCB concentration was significantly elevated, at 245 ng/g lipid. (See Table PCB1a.)

Data Tables

Table PCB1. PCBs in women ages 16 to 49 years: Median concentrations in blood serum, by race/ethnicity and family income, 2001-2004

Race / Ethnicity	Median concentration of PCBs in serum (ng/g lipid)					
	All Incomes	< Poverty Level	≥ Poverty Level	≥Poverty (Detail)		Unknown Income
				100-200% of Poverty Level	> 200% of Poverty Level	
All Races/ Ethnicities	30.1	25.8	31.8	29.0	33.3	29.2
White non-Hispanic	33.6	29.0	34.8	32.9	35.9	39.5
Black non-Hispanic	32.2	30.3	37.4	40.0*	37.4	83.5
Mexican-American	18.0	16.1	18.9	15.4	24.6	13.2
Other†	31.6	NA**	38.0	31.6	49.9	NA**

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

NOTES:

- Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.
- 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 PCB1a. PCBs in women ages 16 to 49 years: 95th percentile concentrations in blood serum, by race/ethnicity and family income, 2001-2004

Race / Ethnicity	95th percentile concentration of PCBs in serum (ng/g lipid)					
	All Incomes	< Poverty Level	≥ Poverty Level	≥Poverty (Detail)		Unknown Income
				100-200% of Poverty Level	> 200% of Poverty Level	
All Races/ Ethnicities	106.2	87.6	111.3	105.9	114.6	83.5*
White non-Hispanic	108.7	87.6	114.6	121.8	114.6	73.1
Black non-Hispanic	101.8	74.3	118.0	118.0*	122.5	150.3
Mexican-American	49.1	NA**	58.1	42.9	NA**	30.4
Other†	245.2	267.2	191.3	245.2	122.9	NA**

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

NOTES:

- Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.
- 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.

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Metadata

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 http://www.cdc.gov/nchs/nhanes.htm 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.

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

Indicator

PCB1. PCBs in women ages 16 to 49 years: Median concentrations in blood serum, by race/ethnicity and family income, 2001-2004.

Summary

Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention, has conducted the National Health and Nutrition Examination Surveys (NHANES), a series of U.S. national surveys of the health and nutrition status of the noninstitutionalized civilian population. The National Center for Environmental Health at CDC measures environmental chemicals in blood and urine samples collected from NHANES participants.[i] This indicator uses lipid-adjusted serum PCB measurements of PCBs 118, 138, 153 and 180 in women ages 16 to 49 years, summed together. The NHANES 2001-2002 and 2003-2004 surveys included serum PCB data for children and adults ages 12 years and over. Indicator PCB1 gives the median concentrations of the sum of the four PCBs for women ages 16 to 49 years for 2001-2004, stratified both by race/ethnicity and family income. The median is the estimated concentration such that 50% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have a sum of the four PCB concentrations below this level; a birthrate-adjusted distribution of women's PCB levels is used in calculating this indicator, meaning that the data are weighted using the age-specific probability of a woman giving birth. Table PCB1a gives the 95th percentile concentrations of the sum of the four PCBs for women ages 16 to 49 years for 2001-2004, stratified both by race/ethnicity and family income. The 95th percentile is the estimated concentration such that 95% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have a sum of the four PCB concentrations below this level; the population distribution was weighted to account for the complex multi-stage, stratified, clustered sampling design.

Data Summary

Indicator	PCB1. PCBs in women ages 16 to 49 years: Median concentrations in blood serum, by race/ethnicity and family income, 2001-2004.							
Time Period	2001-2004							
Data	Serum PCB (lipid adjusted) for four PCBs							
Years/PCB	2001-2002/118	2001-2002/138	2001-2002/153	2001-2002/180	2003-2004/118	2003-2004/138	2003-2004/153	2003-2004/180
Limits of Detection (ng/g	10.5	10.5	10.5	10.5	0.6	0.4	1.1	0.4

[i] Centers for Disease Control and Prevention. 2009. Fourth National Report on Human Exposure to Environmental Chemicals. Atlanta, GA. Available at: www.cdc.gov/exposurereport.

Indicator	PCB1. PCBs in women ages 16 to 49 years: Median concentrations in blood serum, by race/ethnicity and family income, 2001-2004.							
lipid)*								
Number of Non-missing Values**	644	641	644	643	519	520	519	520
Number of Missing Values	56	59	56	57	108	107	108	107
Percentage Below Limit of Detection***	50	18	11	32	0	0	0	0

* The Limit of Detection (LOD) is defined as the level at which the measurement has a 95% probability of being greater than zero. LODs vary among samples. The highest LOD among all the samples is shown.
**Non-missing values include those below the analytical limit of detection (LOD), which are reported as LOD/√2. 1,158 sampled women 16 to 49 years had non-missing values for all four PCB congeners. 6 sampled women 16 to 49 years had missing values for some but not all of the four PCB congeners.
***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: http://www.cdc.gov/nchs/nhanes.htm.

- NHANES 2001-2002: Demographic file demo_b.xpt. Laboratory 28POC file l28poc_b. 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 l28poc_b.xpt contains SEQN, the lipid-adjusted PCB 118, 138, 153, and 180 (LBX118LA, LBX138LA, LBX153LA, LBX180LA), the PCB 118, 138, 153, and 180 non-detect comment codes (LBD118LC, LBD138LC, LBD153LC, LBD180LC), and the PCB sub-sample laboratory survey weight (WTSPO2YR). The two files are merged using the common variable SEQN.

- NHANES 2003-2004: Demographic file demo_c.xpt. Dioxins, Furans, and Coplanar PCBs Laboratory file l28dfp_c.xpt. The Non-dioxin-like PCB Laboratory file l28npb_c. The demographic file demo_c.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 Dioxins, Furans and Co-planar PCB laboratory file l28dfp_c.xpt contains SEQN, the lipid-adjusted PCB 118 (LBX118LA), the PCB 118 non-detect comment code (LBD118LC), and the PCB sub-sample laboratory survey weight (WTSC2YR). The Non-dioxin-like PCB laboratory file l28npb_c.xpt contains SEQN, the lipid-adjusted PCB 138, 153, and 180 (LBX138LA, LBX153LA, LBX180LA), the PCB 138, 153, and 180 non-detect comment codes (LBD138LC, LBD153LC, LBD180LC), and the PCB sub-sample laboratory survey weight (WTSC2YR). The three files are merged using the common variable SEQN.

National Health and Nutrition Examination Surveys (NHANES)

Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention, has conducted the National Health and Nutrition Examination Surveys (NHANES), a series of U.S. national surveys of the health and nutrition status of the noninstitutionalized civilian population. The National Center for Environmental Health at CDC measures environmental chemicals in blood and urine samples collected from NHANES participants. This indicator uses serum PCB measurements of four PCBs from NHANES 2001-2002 and 2003-2004 in women ages 16 to 49. The NHANES data were obtained from the NHANES website: http://www.cdc.gov/nchs/nhanes.htm. Following the CDC recommended approach, values below the analytical limit of detection (LOD) were replaced by LOD/√2.[ii] This analysis uses the sum of the four PCB congeners 118, 138, 153 and 180 listed in the following table. If some but not all of the four PCB congeners are missing, then the sum is over the non-missing PCB congeners. In the rest of this section, we will refer to this sum as the total serum PCB.

PCB Congener	Full name	SAS name (lipid-adjusted)	SAS name for non-detect comment code*
118	2,3',4,4',5-pentachlorophenyl	LBX118LA	LBD118LC
138	2,2',3,4,4',5- and 2,3,3',4,4',6-hexachlorophenyl	LBX138LA	LBD138LC
153	2,2',4,4',5,5'-hexachlorophenyl	LBX153LA	LBD153LC
180	2,2',3,4,4',5,5'-heptachlorophenyl	LBX180LA	LBD180LC

*The non-detect comment code equals 1 if the measurement is below the analytical limit of detection, and equals 0 if the measurement is at or above the analytical limit of detection.

The NHANES use a complex multi-stage, stratified, clustered sampling design. Certain demographic groups were deliberately over-sampled, including Mexican-Americans and Blacks. Oversampling is performed to increase the reliability and precision of estimates of health status 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 PCB sub-sample laboratory survey weights (WTSPO2YR for 2001-2002 and WTSC2YR for 2003-2004) to re-adjust the serum PCB data to represent the national population.

Age-Specific Birthrates

[ii] See Hornung RW, Reed LD. 1990. Estimation of average concentration in the presence of nondetectable values. *Applied Occupational and Environmental Hygiene* 5:46–51.

In addition to the NHANES survey weights, the data for women of child-bearing age (ages 16 to 49) were also weighted by the birthrate 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.[iii]

Race/Ethnicity and Family Income

For this indicator, the percentiles were calculated for demographic strata defined by the combination of race/ethnicity and family income.

The family income was characterized based on the INDFMPIR variable, which is the ratio of the family income to the poverty level. The National Center for Health Statistics used the U.S. 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 poverty level money thresholds varying by family size and composition. The poverty income ratio (PIR) is the family income divided by the poverty level for that family. Family income was stratified into the following groups:

- Below Poverty Level: PIR < 1
- Between 100 % and 200 % of Poverty Level: 1 ≤ PIR ≤ 2
- Above 200 % of Poverty level: PIR > 2
- Above Poverty Level: PIR ≥ 1 (combines the previous two groups)
- Unknown Income: PIR is missing

Race/ethnicity was characterized using the RIDRETH1 variable. The possible values of this variable are:

- 1. Mexican American
- 2. Other Hispanic
- 3. Non-Hispanic White
- 4. Non-Hispanic Black
- 5. Other Race – Including Multi-racial
- "." Missing

Category 5 includes: all Non-Hispanic single race responses other than White or Black; and multi-racial responses.

For this indicator, the RIDRETH1 categories 2, 5, and missing were combined into a single "Other" category. This produced the following categories:

[iii] 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.

Calculation of Indicator

Indicator PCB1 is the median for total serum PCB in women of ages 16 to 49 years, stratified by race/ethnicity and family income. Table PCB1a is the 95th percentile for total serum PCB in women of ages 16 to 49 years, stratified by race/ethnicity and family income. The median is the estimated concentration such that 50% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have total serum PCB concentrations below this level. The 95th percentile is the estimated concentration such that 95% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have total serum PCB concentrations below this level. To adjust the NHANES data to represent prenatal exposures, the data for each woman surveyed was multiplied by the estimated number of births per woman of the given age and race/ethnicity.

To simply demonstrate the calculations, we will use the NHANES 2001-2004 total serum PCB 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:

We begin with all the non-missing NHANES 2001-2004 total serum PCB values for women ages 16 to 49 years. Assume for the sake of simplicity that valid data on total serum PCB were available 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-year periods are combined for these analyses, the associated annual survey weight for each woman is defined as WTSPO2YR/2 for 2001-2002 and WTSC2YR/2 for 2003-2004, so that the combined 2001-2004 sample represents the annual population. 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 weight and the birthrate estimates the annual number of U.S. births represented by that sampled woman, which we will refer to as the adjusted survey weight. For example, the lowest total serum PCB measurement for a woman between 16 and 49 years of age is 4.6 ng/g lipid with an annual survey weight of 10,000, a birthrate of 0.03, and thus an adjusted survey weight of 300, and so represents 300 births. The total of the adjusted survey weights for the sampled women equals 4 million, the total number of annual U.S. births to women ages 16 to 49 years. The second lowest measurement is also 4.6 ng/g lipid with an adjusted survey weight of 800, and so represents another 800 U.S. births. The highest measurement was 715.5 ng/g lipid, with an adjusted survey weight of only 4, because it was for a 48 year old woman, and so represents another 4 U.S. births.

To calculate the median, we can use the adjusted survey weights to expand the data to the entire U.S. population of births to women ages 16 to 49. We have 300 values of 4.6 ng/g lipid from the lowest measurement, 800 values of 4.6 ng/g lipid from the second lowest measurement, and so on, up to 4 values of 715.5 ng/g lipid from the highest measurement. Arranging these 4 million values in increasing order, the 2 millionth value is 30.1 ng/g lipid. Since half of the values are below 30.1 and half of the values are above 30.1, the median equals 30.1 ng/g lipid. To calculate the 95th percentile, note that 95% of 4 million equals 3.8 million. The 3.8 millionth value is 106.2 ng/g lipid. Since 95% of the values are below 106.2, the 95th percentile equals 106.2 ng/g lipid.

In reality, the calculations need to take into account that total serum PCB measurements were not available for every respondent, and to use exact rather than rounded numbers. There were total serum PCB measurements for only 1,164 of the 1,327 sampled women ages 16 to 49 years. These 1,164 sampled women included 1,158 women with measured concentrations for all four congeners and 6 women with measured concentrations for only one, two, or three of the four congeners; for those six women the total serum PCB is defined as the sum of the non-missing congeners. The adjusted survey weights for all 1,327 sampled women add up to 4.2 million, the U.S. population of births to women ages 16 to 49. The adjusted survey weights for the 1,164 sampled women with total serum PCB data add up to 3.7 million. Thus the available data represent 3.7 million values and so represent only 90 % of the U.S. population of births. The median and 95th percentiles are given by the 1.85 millionth (50 % of 3.7 million) and 3.52 millionth (95 % of 3.7 million) U.S. birth's value. These calculations assume that the sampled women with valid total serum PCB data are representative of women giving birth without valid total serum PCB data. The calculations also assume that the sampled women are representative of women that actually gave birth in 2001-2004, since NHANES information on pregnancy and births was not incorporated into the analysis.

Equations

These percentile calculations can also be given as the following mathematical equations, which are based on the default percentile calculation formulas from Statistical Analysis System (SAS) software. Exclude all missing total serum PCB values. Suppose there are n women of ages 16 to 49 years with valid total serum PCB values. Arrange the total serum PCB concentrations in increasing order (including tied values) so that the lowest concentration is x(1) with an adjusted survey weight of w(1), the second lowest concentration is x(2) with an adjusted survey weight of w(2), …, and the highest concentration is x(n) with an adjusted survey weight of w(n).

1. Sum all the adjusted survey weights to get the total weight W:

$$W = \Sigma[1 \le i \le n]\ w(i)$$

2. Find the largest number i so that the total of the weights for the i lowest values is less than or equal to W/2.

$$\Sigma[j \le i]\ w(j) \le W/2 < \Sigma[j \le i + 1]\ w(j)$$

3. Calculate the median using the results of the second step. We either have

$$\Sigma[j \le i]\, w(j) = W/2 < \Sigma[j \le i + 1]\, w(j)$$

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:

$$\text{Median} = [x(i) + x(i + 1)]/2 \text{ if } \Sigma[j \le i]\, w(j) = W/2$$

In the second case we define the median as the i + 1'th value:

$$\text{Median} = x(i + 1) \text{ if } \Sigma[j \le i]\, w(j) < W/2$$

(The estimated median does not depend upon how the tied values of x(j) are ordered).

A similar calculation applies to the 95th 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.

$$\Sigma[j \le i]\, w(j) \le 0.95W < \Sigma[j \le i + 1]\, w(j)$$

In the third step we calculate the 95th 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 95th percentile as the average of the i'th and i + 1'th values:

$$\text{95th Percentile} = [x(i) + x(i + 1)]/2 \text{ if } \Sigma[j \le i]\, w(j) = 0.95W$$

In the second case we define the 95th percentile as the i + 1'th value:

$$\text{95th Percentile} = x(i + 1) \text{ if } \Sigma[j \le i]\, w(j) < 0.95W$$

Relative Standard Error

The uncertainties of the median and 95th percentile values were calculated using a revised version of the CDC method given in CDC 2005,[iv] Appendix C, and the SAS® program provided by CDC. The method uses the Clopper-Pearson binomial confidence intervals adapted for complex surveys by Korn and Graubard (see Korn and Graubard, 1999,[v] 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_{SAS} 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_{SAS} obtained in Step 1 and to obtain the standard error (se_p) 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_{denom} 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:

$$P_L(x,n_{df}) = v_1F_{v1,v2}\,(0.025)/(v_2 + v_1F_{v1,v2}(0.025))$$
$$P_U(x,n_{df}) = v_3F_{v3,v4}\,(0.975)/(v_4 + v_3F_{v3,v4}(0.975))$$

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 β 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_{CDC} and P_{SAS} are not necessarily equal.

Step 5: Use the confidence interval from Step 4 to estimate the standard error of the estimated percentile P_{CDC}:

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

Step 6: 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}:

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

[iv] CDC Third National Report on Human Exposure to Environmental Chemicals. 2005
[v] Korn E. L., Graubard B. I. 1999. *Analysis of Health Surveys.* Wiley.

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.

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 and PSU variables are not provided in the public release version to protect confidentiality.

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.

Questions and Comments

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.

Statistical Comparisons

Statistical analyses of the percentiles were used to determine whether the differences between percentiles for different demographic groups were statistically significant. For these analyses, the percentiles and their standard errors were calculated for each combination of age group, 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 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, for women, for the age-specific birthrate.

Using a weighted linear regression model, the percentile was assumed to be the sum of explanatory terms for age, income and/or race/ethnicity and a random error term; the error terms were assumed to be approximately independent and normally distributed with a mean of zero and a variance equal to the square of the standard error. Using this model, the difference in the value of a percentile between different demographic groups is statistically significant if the difference between the corresponding sums of explanatory terms is statistically significantly different from zero. A p-value at or below 0.05 implies that the difference is statistically significant at the 5% significance level. No adjustment is made for multiple comparisons.

For each type of comparison, we present unadjusted and adjusted analyses. The unadjusted analyses directly compare a percentile between different demographic groups. The adjusted analyses add other demographic explanatory variables to the statistical model and use the statistical model to account for the possible confounding effects of these other demographic variables. For example, the unadjusted race/ethnicity comparisons use and compare the percentiles between different race/ethnicity pairs. The adjusted race/ethnicity comparisons use the percentiles for each age/ income/race/ethnicity combination. The adjusted analyses add age, and income terms to the statistical model and compare the percentiles between different 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.

Comparisons between pairs of race/ethnicity groups are shown in Tables 1 and 2 for women ages 16 to 49 years. In Table 1, for the unadjusted "All incomes" comparisons, the only explanatory variables are terms for each race/ethnicity group. For these unadjusted comparisons, the statistical tests compare the percentiles for each pair of race/ethnicity groups. For the adjusted "All incomes (adjusted for age, income)" comparisons, the explanatory variables are terms for each race/ethnicity group together with terms for each age, and income group. For these adjusted comparisons, the statistical test compares the pair of race/ethnicity groups after accounting for any differences in the age and income distributions between the race/ethnicity groups.

In Table 1, for the unadjusted "Below Poverty Level" and "At or Above Poverty Level" comparisons, the only explanatory variables are terms for each of the twelve race/ethnicity/income combinations (combinations of four race/ethnicity groups and three

income groups). For example, in row 1, the p-value for "Below Poverty Level" compares White non-Hispanics below the poverty level with Black non-Hispanics below the poverty level. The same set of explanatory variables are used in Table 2 for the unadjusted comparisons between one race/ethnicity group below the poverty level and the same or another race/ethnicity group at or above the poverty level. The corresponding adjusted analyses include extra explanatory variables for age, so that race/ethnicity/income groups are compared after accounting for any differences due to age.

Additional comparisons are shown in Table 3 for women ages 16 to 49 years. The AGAINST = "income" unadjusted p-value compares the body burdens for those below poverty level with those at or above poverty level, using the explanatory variables for the three income groups (below poverty, at or above poverty, unknown income). The adjusted p-value includes adjustment terms for age and race/ethnicity in the model.

For women, the age groups used were 16-19, 20-24, 25-29, 30-39, and 40-49.

For more details on these statistical analyses, see the memorandum by Cohen (2010).[vi]

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

				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)**
PCB	50	White non-Hispanic	Black non-Hispanic	0.622	0.211	0.893	0.033	0.759	0.363
PCB	50	White non-Hispanic	Mexican-American	< 0.0005	< 0.0005	0.002	0.009	0.001	< 0.0005
PCB	50	White non-Hispanic	Other	0.691	< 0.0005	0.588	0.477	0.702	< 0.0005
PCB	50	Black non-Hispanic	Mexican-American	0.001	< 0.0005	< 0.0005	< 0.0005	0.010	< 0.0005
PCB	50	Black non-Hispanic	Other	0.957	< 0.0005	0.572	0.307	0.991	< 0.0005
PCB	50	Mexican-American	Other	0.002	0.134	0.326	0.020	0.001	0.299
PCB	95	White non-Hispanic	Black non-Hispanic	0.601	< 0.0005	0.402	< 0.0005	0.947	0.121
PCB	95	White non-Hispanic	Mexican-American	< 0.0005	0.002	0.041	< 0.0005	0.007	< 0.0005
PCB	95	White non-Hispanic	Other	0.003	0.034	< 0.0005	< 0.0005	0.096	< 0.0005
PCB	95	Black non-Hispanic	Mexican-American	< 0.0005	< 0.0005	0.085	< 0.0005	0.020	< 0.0005
PCB	95	Black non-Hispanic	Other	0.001	< 0.0005	< 0.0005	0.550	0.125	< 0.0005
PCB	95	Mexican-American	Other	< 0.0005	< 0.0005	< 0.0005	< 0.0005	0.002	0.009

[vi] 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.

Table 2. Statistical significance tests comparing the percentiles of PCBs in women ages 16 to 49 years, between pairs of race/ethnicity/income groups at different income levels, for 2001-2004.

				P-VALUES	
Variable	**Percentile**	**RACEINC1**	**RACEINC2**	**Unadjusted**	**Adjusted (for age)**
PCB	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.307	0.004
PCB	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.291	0.032
PCB	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.021	0.031
PCB	50	White non-Hispanic, < PL	Other, ≥ PL	0.196	0.126
PCB	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.173	0.709
PCB	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.214	0.684
PCB	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.001	< 0.0005
PCB	50	Black non-Hispanic, < PL	Other, ≥ PL	0.110	0.001
PCB	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	< 0.0005	< 0.0005
PCB	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.002	< 0.0005
PCB	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.272	0.488
PCB	50	Mexican-American, < PL	Other, ≥ PL	< 0.0005	0.138
PCB	50	Other, < PL	White non-Hispanic, ≥ PL	0.731	0.154
PCB	50	Other, < PL	Black non-Hispanic, ≥ PL	0.798	0.432
PCB	50	Other, < PL	Mexican-American, ≥ PL	0.374	0.045
PCB	50	Other, < PL	Other, ≥ PL	0.798	0.103
PCB	95	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.216	< 0.0005
PCB	95	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.268	< 0.0005
PCB	95	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.177	0.105
PCB	95	White non-Hispanic, < PL	Other, ≥ PL	0.021	< 0.0005
PCB	95	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.012	0.010
PCB	95	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.044	0.035
PCB	95	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.398	< 0.0005
PCB	95	Black non-Hispanic, < PL	Other, ≥ PL	0.004	< 0.0005
PCB	95	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.001	< 0.0005
PCB	95	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.004	< 0.0005
PCB	95	Mexican-American, < PL	Mexican-American, ≥ PL	0.432	0.002
PCB	95	Mexican-American, < PL	Other, ≥ PL	0.001	0.077
PCB	95	Other, < PL	White non-Hispanic, ≥ PL	< 0.0005	0.020
PCB	95	Other, < PL	Black non-Hispanic, ≥ PL	< 0.0005	0.139
PCB	95	Other, < PL	Mexican-American, ≥ PL	< 0.0005	< 0.0005
PCB	95	Other, < PL	Other, ≥ PL	0.089	< 0.0005

Table 3. Other statistical significance tests comparing the percentiles of PCBs in women ages 16 to 49 years, for 2001-2004.

					P-VALUES	
Variable	**Percentile**	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
PCB	50	2001	2004	income	0.047	0.274
PCB	95	2001	2004	income	0.193	< 0.0005

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