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March 30, 2009

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428, Attn: Section 8(e) & FYI
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Submission To TSCA 8(e)/FYI Database Re: PFOA/PFOS

To TSCA 8(e)/FYI Database:

We are hereby providing the following information for inclusion in the TSCA 8(e)/ FYI databases with respect to PFOA/PFOS:

1. C-8 Science Panel, "Status Report: Residents' PFOA serum concentrations before and after granular activated carbon filtration at public water systems in Little Hocking, Ohio and Lubeck, West Virginia" (March 23, 2009);

2. C-8 Science Panel, "Status Report: Relationship of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with pregnancy outcome among women with elevated community exposure to PFOA" (March 23, 2009);

3. C-8 Science Panel, Media Press Kit/Presentation Slides (March 26, 2009);

4. Steenland, K., et al, "Predictors of PFOA Levels in a Community Surrounding a Chemical Plant," Environ. Health Persp.(online at doi:10.1289/ehp/0800294 (March 23, 2009); and

5. Letter from ATSDR to West Virginia Department of Health and Human Services Re: PFOA drinking water recommendations (February 10, 2009).

Very truly yours,

Robert A. Bilott

RAB:mdm
Enclosure

Contains No CBI CONTAINS NO CBI

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Status report: Residents' PFOA serum concentrations before and after granular activated carbon filtration at public water systems in Little Hocking, Ohio and Lubeck, West Virginia

The C8 Science Panel (Kyle Steenland, Tony Fletcher, David Savitz)

March 23, 2009

This report summarizes the findings from the first year of the C8 Half Life Study, which follows 200 residents with repeated blood samples and interviews in order to study the rate of decline in PFOA serum concentrations over time. A detailed report will be submitted to a peer-reviewed journal for publication. Dr. Scott Bartell will be the principal author of this report; Science Panel member Dr. Kyle Steenland worked closely with Dr. Bartell on this report.

Summary

Background:. Lubeck Public Service District began filtering public water in June 2007 in order to remove PFOA, and Little Hocking Water Association began filtering public water in November 2007. We are studying PFOA serum concentrations over time, including immediately after water filtration, in 200 residents served by these two water districts. The rate of removal, which can also be expressed as a "half life" (the time required for half of the PFOA to be removed from the body), is critical for estimating past rate of exposures to PFOA based on recent PFOA serum concentrations. There is not much existing information on the rate of PFOA removal from the body. The best available study of the rate of removal of PFOA from the human body was based on only 26 retired PFOA workers with no recent PFOA exposures, including only 2 women.

Methods: In May 2007 we recruited 150 adults served by Lubeck and 50 adults served by Little Hocking, based on their responses in the C8 Health Project. Both men and women with a variety of ages were included. Participants were required to have a PFOA serum concentration measurement of 50 ng/mL or greater during the C8 Health Project; this level is about 10 times higher than the level found on the average among the general US population. Participants were also required to have residential water service provided by Lubeck Public Service District or Little Hocking Water Association, to have not reported growing vegetables at home at the time of the C8 Health Project, to have never been employed by DuPont Company, to not have had any other job working worked with PFOA since 2000, and to have signed a consent form allowing C8 Health Project data to be shared with the C8 Science Panel. Two groups of participants were recruited for each of the two water districts: 1.) those reporting primary use of public water for drinking at home, both in the C8 Health Project and in May 2007, and 2.) a smaller group consisting of those reporting primary use of bottled water for drinking at home. Participants donated up to 6 samples each during the first year of the study. The Lubeck participants were followed for one year after water filtration, and the Little Hocking participants were followed for three months prior to water filtration and six months after water filtration. Average decreases in PFOA serum concentrations are reported for 197 participants who donated blood before and after the installation of water filters in Lubeck and Little Hocking, as well as the estimated average half-life.

Results: Average serum PFOA concentrations in June 2007 for participants served by Lubeck Public Service District were 122 ng/mL among public water drinkers and 58 ng/mL among bottled water drinkers. Average serum PFOA concentrations in December 2007 for participants served by Little Hocking Water Association were 368 ng/mL among public water drinkers and 140 ng/mL among bottled water drinkers.

For Lubeck residential customers, the average decrease in PFOA serum concentrations in the year after filtration (between June 2007 and June 2008) was 32 ng/mL (26%) for those primarily consuming public water at home (n=130), and 16 ng/mL (28%) for those primarily consuming bottled water at home (n=17). For Little Hocking customers, the average decrease in PFOA serum concentrations in the six months after filtration (between December 2007 and June 2008) was 39 ng/mL (11%) for public water consumers (n=39) and 28 ng/mL (20%) for bottled water consumers (n=11). The estimated average rate of decrease in serum PFOA concentration after water filtration for all four groups is 26% per year. Our best preliminary estimate of the average PFOA serum half-life using these data is 2.3 years (95% CI: 2.1 to 2.4 years). Individual estimated half-lives varied widely in our study; most lie between 1.5 to 4.6 years.

PFOA serum concentrations were already decreasing over time before filtration began among Little Hocking residents, but the average rate of decrease was estimated to be 60% faster after filtration.

Interpretation: PFOA serum concentrations have decreased substantially among our study participants between 2007 and 2008; much of this decrease appears to be due to water filtration. "Bottled water drinkers" reported primarily drinking bottled water while at home, but may have routinely used public water for cooking, coffee, etc., or may have been exposed at work or other locations besides home. During our study some individuals also switched from public to bottled water, or from bottled to public water. These factors may explain why filtration appeared to be effective at decreasing serum PFOA concentrations among both public water drinkers and bottled water drinkers.

Long half-lives cannot always be accurately calculated from shorter studies. We will be requesting two more blood samples from our participants during the next few years, and expect to report more precise half-life estimates when this study is completed in 2012.

Status report: Relationship of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with pregnancy outcome among women with elevated community exposure to PFOA

The C8 Science Panel (David Savitz, Kyle Steenland, Tony Fletcher)

March 23, 2009

This report summarizes the findings relating PFOA (C8) and PFOS (C8S) in the serum of female participants in the C8 Health Project, which was carried out in 2005-2006 in the Mid-Ohio Valley and recent pregnancy outcome. A full report of these findings will be submitted to a peer-reviewed scientific journal.

Background: Perfluorooctanoic acid (PFOA, also known at C8) and perfluorooctane sulfonate (PFOS, also known at C8S) are chemicals which do not occur in nature but have been widely used in chemical production for some time and remain in the environment. They are found in the blood of most Americans at levels of around 4 ng/mL (nanogram/milliliter) for PFOA and 21 ng/mL for PFOS. PFOA has been found in the blood of pregnant women, in umbilical cord blood, and in breast milk. A few studies have looked at maternal PFOA and PFOS level and birth outcomes like gestational age and birthweight, but the studies have been limited in quality and the results were inconsistent.

Methods: We conducted a study of C8 Health Project participants to examine the relationship between PFOA and PFOS in serum and pregnancy outcome among community residents in Ohio and West Virginia who lived or worked in six water districts contaminated with PFOA from a chemical plant. In 2005-2006, they provided blood specimens, which were used to measure PFOA and PFOS in the serum (the clear liquid part of the blood after blood cells have been taken out) and women answered questions about their pregnancy history. We excluded twins and other multiple pregnancies, and studied miscarriages, stillbirths, and live births in the 5 years prior to C8 Health Project enrollment among women who lived within the same water district from the start of the pregnancy through the time of enrollment. We made this restriction to be sure that the PFOA level measured at C8 Health Project enrollment would be a good estimate of the level at the time of pregnancy. We compared the levels of PFOA and PFOS in pregnancies that ended in a miscarriage, preeclampsia, preterm birth, low birthweight birth, or birth defects with healthy pregnancies using multiple regression techniques that adjust for other variables which could influence pregnancy outcome. The results are presented in terms of odds ratios (ORs) that reflect the relative risk, i.e., the risk of the problem in more exposed pregnancies divided by the risk in less exposed pregnancies. An OR above 1.0 indicates an increased risk of the outcome in the more exposed group vs. the less exposed group. We also present a measure of how precise the estimates are, a 95% confidence interval, which reflects the range of plausible values taking chance into account.

Results: The average serum PFOA was 48.8 ng/mL and the middle value (median) was 21.2 ng/mL. The average PFOS concentration was 15.0 ng/mL and the median was 13.6 ng/mL. Among all pregnancies, 249 (13.5%) were reported to have ended in miscarriage. Among live

births, 329 (20.9%) were reported as preterm, 80 (5.0%) as low birthweight, 156 (9.8%) were complicated by preeclampsia, and 74 (7.4%) noted a birth defect.

Neither PFOA nor PFOS was related to miscarriage. Preeclampsia was modestly increased when PFOA levels were above the median compared to below the median (OR = 1.3, 95% CI = 0.9, 1.9) and when PFOS levels were above the median (OR =1.4, 95% CI = 1.0, 2.0). Neither PFOA nor PFOS was related to preterm birth. Low birthweight did not follow any clear relationship with PFOA, except for some tendency for lower risk with higher exposure. PFOS exposures above the median were weakly related to low birthweight (OR = 1.6, 95% CI = 1.0, 2.6). Both PFOA and PFOS were weakly related to birth defects. For PFOA, there was no increase in risk for exposure above the median, but a modest, imprecise indication of an elevation in risk was above the 90th percentile (OR = 1.7, 95% CI = 0.8, 3.6) based on 12 cases in the uppermost category. For PFOS, there was an increased risk above the 75th percentile, with adjusted odds ratios of 1.8 for both 75th to 90th and >90th percentiles. Congenital heart defects were the single most common type of birth defect; however, with only 13 heart defect cases numbers were too sparse for adjusted analyses.

Conclusion: We found little or no support for a possible relationship between PFOA or PFOS exposure and miscarriage or preterm birth, nor between PFOA and low birthweight. PFOS above the median was associated with low birthweight, but there was no increasing risk with higher level of PFOA in the blood. The results for preeclampsia and birth defects were more suggestive of a possible relationship for both PFOA and PFOS – slightly stronger for PFOS. Even for these outcomes, the relative risks were only modestly elevated and none showed clear increasing risk with higher exposure. Overall, the data provide little support for PFOA or PFOS being related to pregnancy outcome, with some uncertainty regarding preeclampsia and aggregated birth defects.

C8 Science Panel

For Release March 26, 2009 For More Info: Lisa Collins, 304/483-1355

C8 Science Panel Reports on Half-Life, Pregnancy Outcomes and Immune Markers

The C8 Science Panel, chosen to determine whether a probable link exists between C8 and any human disease as part of a class action settlement of a lawsuit involving releases of a chemical known as C8 from DuPont's Washington Works in Wood County, West Virginia presented findings from three studies in Parkersburg, WV, on March 26. Reports of all results were first filed with the court in Wood County, WV, and are now available through the C8 Science Panel website, www.c8sciencepanel.org.

The following reports were presented and discussed:

- Reproductive outcomes in relation to C8 among participants in the 2005-2006 C8 Health Project
- Rate of C8 clearance from the body after installation of water filters
- Immune Function in relation to C8 among participants in the 2005-2006 C8 Health Project

The Science Panel also invited those present, and any interested member of the public, to visit their website to subscribe to an e-newsletter the group will issue periodically as new information comes available. "It is our goal to be as open and available as possible, and to share information with the interested public as we have it. We look forward to using this direct method of communication to let people know what is happening with our ongoing studies," said Dr. Kyle Steenland on behalf of the group.

The Science Panel is made up of three scientists from universities in London, Atlanta and New York. The three panelists were agreed upon by both DuPont and the plaintiffs. They are Dr. Tony Fletcher, Dr. Kyle Steenland, and Dr. David Savitz. More information on the panel and its work can be found at www.c8sciencepanel.org.

Complete releases on each report follow.

C8 Science Panel

REPORT 1:
C8 Science Panel Completes Pregnancy Outcome Study

The C8 Science Panel has completed a new evaluation of the relationship between C8 (also known as PFOA) and C8S (also known as PFOS) in the blood and reproductive health. This analysis is based on recent pregnancies among the Mid-Ohio Valley residents who participated in the C8 Health Project in 2005-2006. A summary of the results of this effort has now been filed with the court in Wood County, West Virginia, as required under a court settlement of a class action suit in 2004, and will be available at the C8 Science Panel website, www.c8sciencepanel.org.

Women who participated in the C8 Health Project were asked about each of their pregnancies, indicating in the questionnaire whether they had a miscarriage (loss of the pregnancy before 20 weeks), preeclampsia (a complication of pregnancy with high blood pressure and protein in the urine), low birth weight (infant weighing less than 5½ pounds), preterm birth (infant born 3 weeks or more before the due date), or birth defects (abnormal development of the infant during pregnancy). C8 is present at relatively high levels among many Mid-Ohio Valley residents due to drinking water contaminated with C8 coming from the local DuPont chemical plant. DuPont did not release C8S from the plant, and C8S levels in Mid-Ohio Valley residents are similar to levels in the general US population.

The statistical analysis focused only on those women who reported pregnancies within the 5 years before the C8 Health Project was conducted and lived in the same water district during those five years. This was done so that the serum levels measured by the C8 Health Project would be as close as possible to the levels that the mothers would have had while they were pregnant.

Higher levels of C8 and C8S were not found to be related to miscarriage or preterm birth. There were some weak relationships between both C8 and C8S with preeclampsia and birth defects in the infants, but the evidence to suggest that risk increases with greater exposure is not consistent. The Science Panel found no indication that C8 was related to low birthweight using more complete exposure data than a study recently conducted by researchers at the University of Pennsylvania, but C8S did show a weak relationship. Because there is some inaccuracy in the reports on pregnancy, and the number of pregnancies that could be included in this stage of the analysis was limited, the Science Panel could not draw conclusions regarding whether either of these chemicals were associated with problems in pregnancy.

The panel will be conducting a more comprehensive analysis of pregnancies reported to the C8 Health Project, including more years prior to the C8 Health Project and using more complete data on past exposures which will be available from another Science Panel project. An additional Science Panel study will be conducted on all the births in the area using birth certificates. Combining these studies, as well as data from other investigators, the C8 Science Panel will determine whether a probable link exists between C8 and reproductive outcomes.

The Science Panel was chosen to determine whether a probable link exists between C8 and any human disease as part of a class action settlement of a lawsuit involving releases of a chemical known as C8 from DuPont's Washington Works in Wood County, West Virginia. The Science Panel is made up of three scientists from universities in London, Atlanta and New York. The three panelists were agreed upon by both DuPont and the plaintiffs. They are Dr. Tony Fletcher, Dr. Kyle Steenland, and Dr. David Savitz. More information on the panel and its work can be found at www.c8sciencepanel.org.

REPORT 2: C8 Science Panel releases initial half-life study findings

The C8 Science Panel has announced a first preliminary estimate of the time it takes the body to clear C8 from its system once the source of the chemical has been filtered.

Lubeck Public Service District in West Virginia began filtering public water in June 2007 in order to remove PFOA, and Little Hocking Water Association in Ohio began filtering public water in November 2007. The C8 Science Panel has been conducting a C8 Half Life Study to determine how fast C8 is removed from the body after water filters have been installed and exposure to C8 is reduced. "Half life" refers to the time is takes the body to clear one half of its C8.

The Science Panel has been measuring PFOA serum concentrations over time for 200 residents served by these two water districts, starting in June 2007. Two groups of participants were recruited for each of the two water districts: 1.) those reporting primary use of public water for drinking at home, both in the C8 Health Project and in May 2007, and 2.) a smaller group consisting of those reporting primary use of bottled water for drinking at home.

For Lubeck residential customers the average decrease in PFOA serum concentrations in the year after filtration began was 32 ng/ml (26%) for 130 participants primarily consuming public water at home, and 16 ng/mL (28%) for 17 participants primarily consuming bottled water at home. For Little Hocking customers, the average decrease in PFOA serum concentrations in six months after filtration began was 39 ng/mL (11%) for 39 public water consumers and 28 ng/mL (20%) for 11 bottled water consumers.

The estimated average rate of decrease in serum PFOA concentration after filtration for all four groups is 26% per year. Based on these first data of the average PFOA serum half-life, the estimated time to clear 50% of PFOA from the body is 2.3 years. For people with levels above 50 ng/ml as in our study, at this rate of removal about 95% of C8 would be removed from the body 10 years after exposure ended. The Science Panel will be requesting two more blood samples from participants during the next few years, and expects to report more precise half-life estimates when this study is completed in 2012. These new results indicate a clearance rate that is much faster than earlier estimates from a study of small groups of workers.

The Science Panel was chosen to determine whether a probable link exists between C8 and any human disease as part of a class action settlement of a lawsuit involving releases of a chemical known as C8 from DuPont's Washington Works in Wood County, West Virginia. The Science Panel is made up of three scientists from universities in London, Atlanta and New York. The three panelists were agreed upon by both DuPont and the plaintiffs. They are Dr. Tony Fletcher, Dr. Kyle Steenland, and Dr. David Savitz. More information on the panel and its work can be found at www.c8sciencepanel.org.

C8 Science Panel

REPORT 3: C8 Science Panel completes first analysis of immune marker date

The C8 Science Panel has completed first analyses of data on immune markers in relation to C8 (also known as PFOA) in the blood among the Mid-Ohio Valley residents who participated in the C8 Health Project in 2005-2006.
Participants in the C8 Health Project provided blood samples which have been analyzed for a number of immune markers as well as C8 and other fluorocarbons. Immune markers are naturally-occurring chemicals in the blood which indicate how well the immune system can fight off disease. C8 is present at relatively high levels among many Mid-Ohio Valley residents due to drinking water contaminated with C8 coming from the local DuPont chemical plant. This report was restricted to adults, 56,315 individuals at least 18 years of age. These results focus on the immune markers called immunoglobulins, anti-nuclear antibodies and C reactive protein. A decrease in immunoglobulins, such as IgA, can provide an indication of immune-suppression, which in turn can lead to an increased risk for various infections. ANA are antibodies which when increased may indicate an increase in the risk of autoimmune diseases. CRP is a marker of general inflammation and is increased in some chronic inflammatory conditions. A reduction of CRP may indicate a weakness in the ability to mount a normal inflammatory response.

These immune markers are related to a number of other factors and these, including age, sex, body mass index, smoking, and alcohol use have been included in the analyses. The results showed clear trends for three of the immune markers in this study, though the magnitude of the change was quite small. For the immunoglobulin IgA, the pattern of association indicated a significant decreasing trend with increasing C8. For the antinuclear antibodies there was an increasing trend with C8. C reactive protein fell with increasing PFOA. In each case the pattern was repeated in the same way for males and females. For the three other immunoglobulins - IgE, IgG & IgM - there were no consistent patterns.

The immune markers mainly lie in normal ranges, the amount of change was quite small, and as the level of C8 and the immune markers were measured at the same point in time, one cannot be sure of which came first. Commenting on these findings, Science Panelist Tony Fletcher said, "We continue to recommend caution in interpreting these trends. Nonetheless the fact that several of these immune markers show a pattern of change raises the concern that there may be an association between immune function and PFOA exposure in exposed persons."

The Science Panel was chosen to determine whether a probable link exists between C8 and any human disease as part of a class action settlement of a lawsuit involving releases of a chemical known as C8 from DuPont's Washington Works in Wood County, West Virginia. The Science Panel is made up of three scientists from universities in London, Atlanta and New York. The three panelists were agreed upon by both DuPont and the plaintiffs. They are Dr. Tony Fletcher, Dr. Kyle Steenland, and Dr. David Savitz. More information on the panel and its work can be found at www.c8sciencepanel.org.

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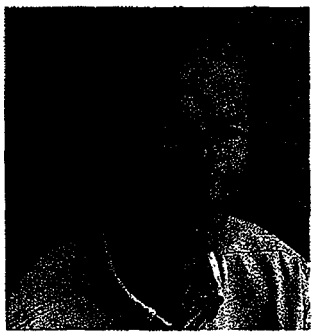
C8 Science Panel

c8sciencepanel.org

Members of the C8 Science Panel:



Dr. Tony Fletcher, London School of Hygiene and Tropical Medicine
Dr. Tony Fletcher is a senior researcher and lecturer at the Public and Environmental Health Research Unit in the London School of Hygiene and Tropical Medicine (LSHTM), London, England, since 1992. He has worked in environmental and occupational epidemiology and human health risk assessment for over 25 years. He is an Adjunct Research Professor in Environmental Health at the School of Public Health at Boston University. He was President of the ISEE International Society for Environmental Epidemiology in 2004-2005. Earlier jobs included work at the World Health Organization's International Agency for Research on Cancer in Lyon, France.

Dr. David Savitz, Mount Sinai School of Medicine
David Savitz received his PhD in Epidemiology from the University of Pittsburgh Graduate School of Public Health in 1982. He moved to the University of North Carolina School of Public Health in 1985, and eventually became chair of the Epidemiology department there. Beginning in January 2006, he has joined the Mount Sinai School of Medicine as Director of the Center of Excellence for Epidemiology and Disease Prevention and the Charles W. Bluhdorn Professor of Community and Preventive Medicine.

Dr. Kyle Steenland, Rollins School of Public Health, Emory University
Dr. Kyle Steenland is an environmental and occupational epidemiologist. He has been a Professor in the Department of Environmental and Occupational Health at the School of Public Health at Emory University in Atlanta, Georgia since 2002. Previously, he worked for 20 years at the National Institute for Occupational Safety and Health (NIOSH/CDC), in Cincinnati, Ohio. Dr. Steenland has written over 60 first-authored articles in peer-reviewed medical journals and has edited two books on environmental and occupational epidemiology. Many of his studies have involved the long-term follow-up of large populations to determine disease occurrence.

C_8 Science Panel

Serum PFOA and PFOS and Pregnancy Outcome

David A. Savitz

Mount Sinai School of Medicine

Scope of Report

- Results of analyses of PFOA (C8) and PFOS (C8S) in famale participants in the C8 Health Project (2005-2006)
- Only PFOA elevated and mandated for evaluation, PFOS of interest as other major fluorocarbon, studied by other researchers
- Reported on pregnancy history and outcomes
- Analysis of relationship between exposure to PFOA and PFOS in relation to several measures of the health of pregnancy

Background

- PFOA and PFOS are chemical pollutants that most Americans are exposed to at some level; detectable in pregnant women
- Animal studies show possible effects on growth, fetal development at high doses
- Previous human studies suggest possible reduction in size at birth, but only studied populations with low exposure

Study Population

- Female participants in the C8 Health Project who provided blood for measurement of PFOA and PFOS; PFOA elevated, PFOS not
- Pregnancies that were singleton (not twins), ended in pregnancy loss or live birth
- Restricted to ensure blood levels would be applicable to the time of pregnancy
  - pregnancies in the 5 years preceding enrollment
  - residents of same water district from time of pregnancy to enrollment in the C8 Health Project

Measurement of Exposure

- PFOA and PFOS laboratory values
- Contrast in risk between the 75th (exposed) and 25th (referent) percentile based on continuous measure
- Grouped at <50th percentile (referent), 50-<75th percentile, 75-90th percentile, >90 percentile

Pregnancy Health Measures

- Miscarriage – loss <20 wks' gestation
- Preeclampsia –complication of pregnancy with high blood pressure and protein in the urine
- Preterm birth – 3+ wks early delivery
- Low birthweight -- <5.5 pounds
- Birth defects – abnormal development

Data Analysis

- 1,845 eligible pregnancies, 1,590 live births included
- Studied association between exposure to PFOA/PFOS as continuous measure and in groups
- Adjustment for mother's age, parity, education, smoking, and PFOA/PFOS using logistic regression

Results for Miscarriage: Adjusted Odds Ratios

	PFOA		PFOS	
	OR	CI	OR	CI
<50th Percentile	1.0		1.0	
50+ Percentile	1.0	(0.7-1.4)	1.0	(0.6-1.7)

Results for Preeclampsia: Adjusted Odds Ratios

	PFOA		PFOS	
	OR	CI	OR	CI
<50th Percentile	1.0		1.0	
50+ Percentile	1.3	(0.9-1.9)	1.4	(1.0-2.0)

Results for Preterm Birth: Adjusted Odds Ratios

	PFOA		PFOS	
	OR	CI	OR	CI
<50th Percentile	1.0		1.0	
50+ Percentile	1.0	(0.7-1.3)	1.0	(0.9-1.5)

Results for Low Birthweight: Adjusted Odds Ratios

	PFOA		PFOS	
	OR	CI	OR	CI
<50th Percentile	1.0		1.0	
50+ Percentile	0.7	(0.5-1.2)	1.6	(1.0-2.6)

Results for Birth Defects: Adjusted Odds Ratios

	PFOA		PFOS	
	OR	CI	OR	CI
<50th Percentile	1.0		1.0	
50+ Percentile	1.0	(0.6-1.7)	1.3	(0.8-2.1)
50-<75th Percentile	1.0	(0.5-1.8)	0.8	(0.4-1.5)
75-90th Percentile	0.7	(0.3-1.6)	1.8	(1.0-3.4)
>90th Percentile	1.7*	(0.8-3.6)	1.8	(0.9-3.6)

*Based on only 12 cases

Summary of Results

- No relationship found for miscarriage, preterm birth
- Both PFOA and PFOS weakly related to preeclampsia
- PFOA not related to low birthweight, PFOS above 50th percentile weakly related to low birthweight
- Both PFOA (>90th percentile) and PFOS (>75th percentile) related to birth defects

Interpretation of Results

- Based only on recent pregnancies from C8 Health Project
- Limited quality of self-reported information
- Positive relationships were weak, little indication of increase in risk with increase in exposure overall
- Most noteworthy are results for birth defects and preeclampsia, with no prior research on those health outcomes

Relation to Previous Studies

- No previous research on humans addressing miscarriage, preeclampsia, or birth defects
- Studies of low-exposure populations suggested possible small effects on fetal growth, not supported by our findings for low birthweight
- ZIP code-level analysis by Nolan et al. (2008) reported no elevation in risk of low birth weight or preterm birth among those living in areas with higher exposure based on birth certificate data

Plans for More Definitive Studies of Reproductive Outcomes

- Use exposure estimates from ongoing project to allow analysis of pregnancies going back much further in time
- Link pregnancies to birth records from Ohio and West Virginia

C_8 Science Panel

C8 Half-Life Study Update

C8 concentrations before and after carbon filtration of public water systems in Little Hocking, OH and Lubeck, WV

Scott M Bartell[1,2], Christopher Lyu[3], P Barry Ryan[2], and Kyle Steenland[2,4]

[1]University of California, Irvine, CA
[2]Emory University, Atlanta, GA
[3]Battelle/Centers for Public Health Research & Evaluation, Durham, NC
[4]C8 Science Panel

C8 Half-Life Study Update: Motivation

- Half-life: the time required for half of the PFOA to be removed from the body
- The half-life of PFOA is critical for estimating
- past serum levels
- Current estimates for half-life is 3.8 years, based on 26 retired PFOA workers age 55+ with no recent PFOA exposures, including only 2 women
  - Half-life may differ among individuals

C8 Half-Life Study Update: Study Design

- In May 2007, The C8 Science Panel initiated a study of how PFOA serum concentrations change over time after exposure ceases
- Currently following 200 Lubeck and Little Hocking public water residents with repeated blood samples and questionnaires, until June 2011
- Public water filtration to remove PFOA began:
  - Lubeck WV: June 2007
  - Little Hocking OH: November 2007

C8 Half-Life Study Update: Enrollment Restrictions

- PFOA serum concentration measurement of 50 ng/mL or greater during the C8 Health Project
  - about 10 times higher than average among general US population
- Did not report growing vegetables at home
- Never been employed by DuPont Company
- No other job working worked with PFOA since 2000

C8 Half-Life Study Update: Enrollment Restrictions

- Consented to allow C8 Health Project data to be shared with the C8 Science Panel
- Public-water drinkers reported primary use of public water for drinking at home, both in C8 Health Project and in May 2007
- Bottled-water drinkers reported primary use of bottled water for drinking at home, both in the C8 Health Project and in May 2007
- Willing to participate for four years
  - 197 participants remained enrolled throughout the first year

C8 Half-Life Study Update: Study Participants

	Lubeck		Little Hocking	
	Public	Bottled	Public	Bottled
Number enrolled	132	17	40	11
Proportion female	49%	59%	50%	55%
Age (yrs)	55.8 (15)	52 (16)	51.8 (14)	53 (15)
PFOA blood concentration (ng/mL)	122 (81)	58 (36)	424 (333)	180 (193)
Proportion provided with public water at work	33%	29%	45%	9%

C8 Half Life Study Update: Interim Results

- Average serum PFOA concentrations as filtration started
  - Lubeck public water drinkers, 122 ng/mL in June 2007
  - Lubeck bottled water drinkers, 58 ng/mL in June 2007
  - Little Hocking public water, 368 ng/mL in Dec. 2007
  - Little Hocking bottled water, 140 ng/mL in Dec. 2007
- Average decrease in serum PFOA by June 2008
  - Lubeck public water drinkers, by 32 ng/mL (26%)
  - Lubeck bottled water drinkers, by 16 ng/mL (28%)
  - Little Hocking public water, by 39 ng/mL (11%)
  - Little Hocking bottled water, by 28 ng/mL (20%)

C8 Half-Life Study Update: Preliminary Half Life Estimates

- Estimated average rate of decrease in PFOA after water filtration for all four groups is 26% per year
- Preliminary estimate of average PFOA serum half-life using these data is 2.3 years
  - At this rate about 95% of PFOA would be removed from the body 10 years after exposure ended

- Individual estimated half-lives varied widely in our study; most were between 1.5 and 4.6 years

C8 Half-Life Study Update: Interpretation

- PFOA serum concentrations were already decreasing over time in Little Hocking before public water filtration began, but average rate of decrease was about 60% faster after filtration started.
- Public water filtration appeared to effectively decrease serum PFOA concentrations, even for bottled water drinkers
- Bottled-water drinkers may have routinely used public water for cooking, coffee, etc., or may have been exposed at work or other locations

C8 Half-Life Study Update: Interpretation

- Long half-lives cannot always be accurately calculated from shorter studies
- We will request two more blood samples from each participant, in June 2009 and June 2011
- We expect to report more precise half-life estimates in 2012 when this study is completed

C8 Half-Life Study Update: Acknowledgements

This study would not have been possible without the assistance of Antonia Calafat and Kayoko Kato at the US Centers for Disease Control, nor without our tireless study participants.

Parkersburg: March 26, 2009

C8 and immune markers in adults in the Mid-Ohio Valley

Fletcher, Tony[1] **for the C8 Science Panel**

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom.

Why look at immune system?

- Animal tests indicate C8 disturbs normal immune function
- Immune system important in protecting against disease
- Almost no human data (one Italian study of only 56 workers, looking at only two markers. IgG, IgM: no evidence of change in C8 linked to change in these markers)

Data used for immune analyses

- Analysis of data already collected in the C8 Health Project
- Serum and questionnaire data collected in July 2005-July 2006
- Final data, after checking and repeated lab analyses, turned over to Science Panel by Brookmar mid 2008
- Data cleaning and analyses underway, working in partnership with WVU on joint reports
- Results here focus on adults, analyses are ongoing on children

Analyses done

- All adults 18+ in C8 health project 29,272 Female, 26,536 Male
- Data available on 6 immune markers
- 4 Immunoglobulins, 1 autoimmune disease marker, 1 inflammation marker
- Analyses take into account other factors which may hide or mislead associations: age, sex, ethnicity, obesity, smoking, drinking.

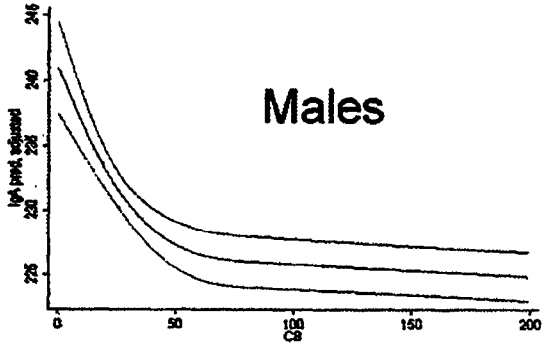
Results

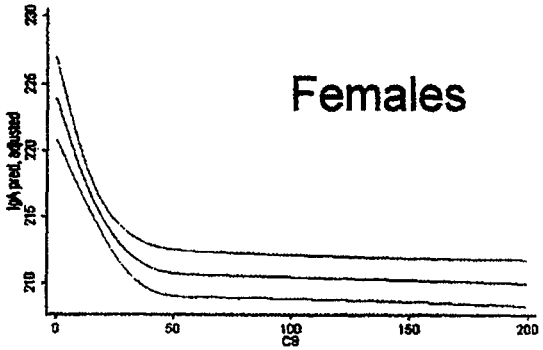
For each marker we looked at:

1. Is there a trend of change of marker with changing levels of C8?
2. What is the shape of the relationship?
3. If there is a change, is it a big change?
4. Is there any difference between men and women?
5. Show results as graphs to reveal trends.

3 with clear trends

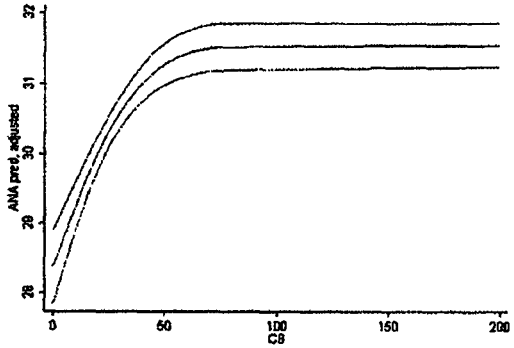
IgA Immunoglobulin A

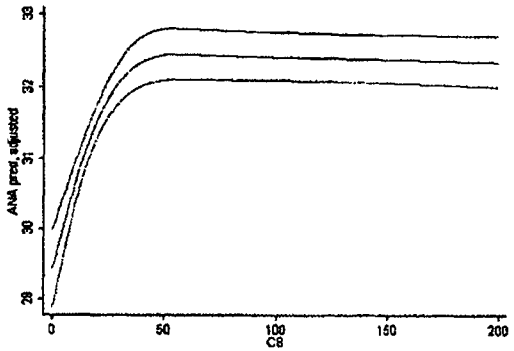




Downward trend suggesting immune suppression

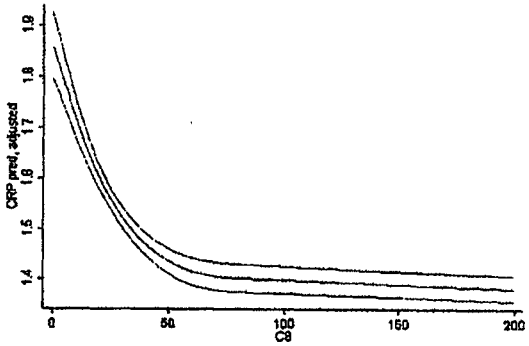
Antinuclear Antibodies ANA

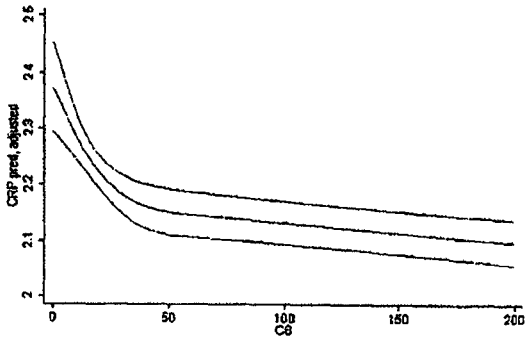




Upward trend of indicator of auto-immune disease

C Reactive protein CRP



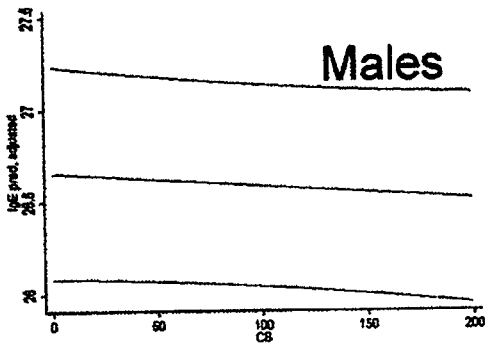


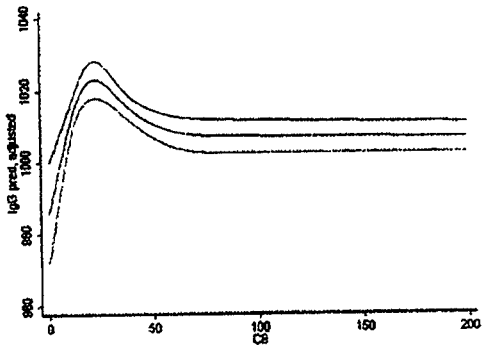
Reducing trend for marker of inflammation

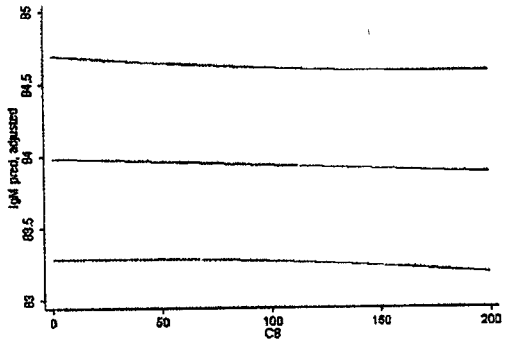
* Adjusted for age, bmi, ethnicity, smoking, alcohol

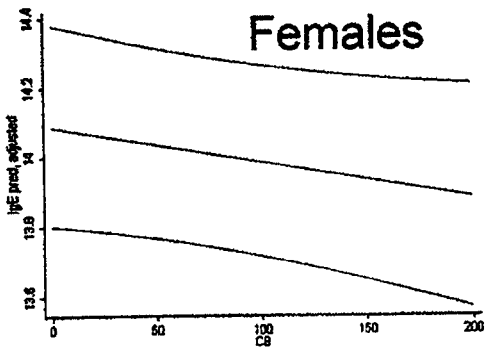
Little or no consistent relationships for 3 other immune markers

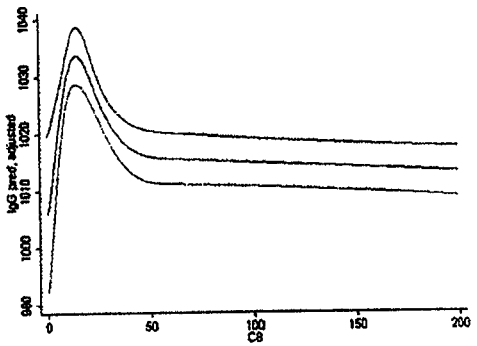
Immunoglobulin IgE | IgG | IgM

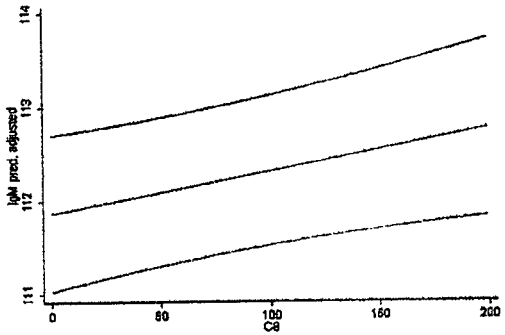












Trend for females may be due to chance

Trends rising and falling difficult to interpret

Males and females more or less flat

* Adjusted for age, bmi, ethnicity, smoking, alcohol

Summary of results

Strong statistical association, consistency between sexes:

- Significant +ve relationship with ANA
- Significant –ve relationship with IgA
- Significant –ve relationship with CRP

Weak statistical association:

- Females only, fall in IgE with PFOA

No relationship or no consistent relationship

- IgM, IgG

Ongoing work 1

Present these results for open scrutiny:

- Status report filed with Court
- Summary of results presented today to press and public
- Presented last week at meeting of immune specialists at Society of Toxicology
- Preparation and publication of detailed technical report

Future work will collect more data to deal with uncertainties in these results

Ongoing work 2

Science panel study will carry out additional interview and blood sampling in a sample of the population (800)

Several Components:

- Repeated measures over time of clinical markers
- Collection of data on infectious disease incidence
- Additional markers of immune status
- Assessment of modification of vaccination efficacy

Science Panel communications

New newsletter will provide rapid updates on these and future outputs of science panel work.

C8 Science Panel

Newsletter

C8 Science Panel Newsletter #1

March 26 2009

Contents: C8 Science Panel News

1 Science Panel launches e-Newsletter
2 Birth outcomes and C8
3 Clearance of C8 after stopping exposure
4 Immune markers and C8
5 Science panel closes new consents

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Predictors of PFOA Levels in a Community Surrounding a Chemical Plant

Kyle Steenland, Chuangfang Jin, Jessica MacNeil, Cathy Lally, Alan Ducatman, Veronica Veiera and Tony Fletcher

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Online 23 March 2009

NIEHS
National Institute of Environmental Health Sciences

National Institutes of Health
U.S. Department of Health and Human Services

Predictors of PFOA Levels in a Community Surrounding a Chemical Plant

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Running header: PFOA levels in a community

Key words: PFOA, serum levels, water contamination

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Article descriptor: exposure assessment

Abbreviations

BMI	Body mass index
CI	Confidence interval
EPA	Environmental Protection Agency
PFOA	Perfluorooctanoic acid
ng/ml	nanogram/milliliter

Outline:

Introduction

Methods
- Study participants
- Statistical analysis
- Laboratory methods for PFOA

Results

Discussion

References

Tables

Figure Legends

Figures

Abstract

Background: Perfluorooctanoic acid (PFOA) is considered a probable human carcinogen by the U.S. EPA. It does not exist in nature, but has been used widely since World War II. It is present in the serum of most Americans at about 4-5 ng/ml, although the routes of exposure remain unknown. Here we examine predictors of PFOA in mid-Ohio valley residents living near a chemical plant, which until recently released large quantities of PFOA into the environment, contaminating drinking water.

Methods: We studied 69,030 residents in six contaminated water districts, who participated in a 2005-2006 survey involving a questionnaire and blood sample. Of these, 64,251 had complete data on PFOA and covariates. We also analyzed a subset (71%) for whom we had occupational history. Linear regression models were run to determine serum PFOA predictors.

Results: Mean PFOA serum level was 83.0 ng/ml (median 28.2). The most important predictors were current (median all districts 38.4, highest district 224.1) and past (median 18.6) residence in contaminated water districts, and current (median 147.8) and past (median 74.9) employment at the chemical plant (R-square model 0.55). PFOA was higher for males, those consuming local vegetables, and those using well water rather than public water, and lower for those using bottled water. PFOA was higher at younger and older ages.

Conclusions: PFOA levels in this population varied with distance of residence from the plant and employment at the plant. Effects of age and gender reflected prior findings. Effects of other demographic and lifestyle covariates were relatively weak.

Introduction

Perfluorooctanoic acid (PFOA, or C8) does not occur in nature. It is used as a polymerization aid in the manufacture of several types of fluoropolymers, which are used in a wide variety of industrial and consumer products. It has been used extensively in the manufacture of Teflon, for example. PFOA does not break down once in the environment, leading to widespread buildup and bioaccumulation. The half-life of PFOA in human serum has been estimated to be about 4 years (Olsen et al 2007). Most people in the US have measurable PFOA in their serum, with a median of 4 ng/ml in 2003-2004 (Calafat et al. 2007b), although the exact sources of this exposure are not clear.

PFOA causes cancer of the testicles, liver, and pancreas in rodents, and there is some evidence it also causes breast cancer in rodents (EPA 2005). It also causes fetal loss and low birthweight in mice (EPA 2005), and there are immunotoxic and hepatoxic effects in rodents (EPA 2005). Health effects in humans are not well established. There have been some reports of associations with lower birthweight (Apelberg et al. 2007, Fei et al. 2007), higher cholesterol (Sakr et al. 2007a, Sakr et al. 2007b), and impaired liver function (Olsen et al. 2007), but these effects are usually modest, and the literature is sparse. Mortality studies of workers have shown increases in some causes of death but have not been consistent and have been based on relatively small numbers of deaths (Gilliland and Mandel 1993, Leonard et al. 2008).

PFOA has been used in the manufacturing of fluoropolymers at a chemical plant in Washington, West Virginia since 1951, with use peaking in the late 1990s. PFOA is used a surfactant in the polymerization of trifluoroethylene to make Teflon. It entered the groundwater via both air emissions, which were deposited on the soil around the plant and leached downward, and emissions into the Ohio river, which then entered the groundwater which communicates with

the river. Public drinking water comes from wells pumping from the groundwater, which are located close to the river. Some local landfill sites may have also contributed to groundwater contamination. Emissions have been sharply reduced in the past few years. There is evidence that that drinking water is the primary route of exposure for the population living in these water districts (Emmett et al. 2006).

In 2001, a group of residents from the Ohio and West Virginia communities in the vicinity of the plant filed a class-action lawsuit, alleging health damage due to contamination of human drinking water supplies with PFOA. The settlement of the class action lawsuit led to a baseline survey, called the C8 Health Project, which was conducted in 2005-2006 and gathered data from 69,000 Ohio and W. Virginia residents who lived in six contaminated water districts surrounding the chemical plant. The C8 Health Project included blood draws and subsequent measurement of serum PFOA (WVU 2009). The current study is an analysis of these data to study factors associated with PFOA level.

Methods

Study participants

The C8 Health Project began data collection in August 2005 and completed it in August 2006. The purpose of the C8 Health Project was to collect health data from class members through questionnaires and a battery of blood tests, including a test to ascertain the concentration of PFOA in the serum.. Subjects were eligible to participate in the C8 Health Project if they had consumed drinking water for at least one year before December 3, 2004 supplied by Little Hocking Water Association (Ohio), City of Belpre (Ohio), Tuppers Plains Chester Water District (Ohio), Village of Pomeroy (Ohio), Lubeck Public Service District (West Virginia), Mason

County Public Service District (West Virginia), or private water sources within these areas that have been contaminated with PFOA. Subjects were also eligible if they could document that they had either worked in a contaminated water district or went to school there for at least one year. Figure 1 shows the six water districts. Subjects were compensated $400 if they filled out the extensive questionnaire and came to local survey stations to donate a blood sample. A full description of the C8 Health Project is in preparation.

The C8 Health Project collected data on 69,030 subjects. It is not known what percentage of the eligible population participated, because the eligible population was not enumerated (the past populations of the water districts themselves are not known, nor are the number eligible who lived outside the water districts but went to school or worked there). Nonetheless, it is believed that the majority participated, given the widespread public interest and the financial incentive. We have estimated the participation rate among current residents in 2005-2006 among adults age 20 and older using census data (the population age 18 and older, as studied here, was not available from the census). Estimates of the population of the six water districts were made based on population estimates for census block groups in 2005. Block groups are smaller than census tracts but larger than census blocks. To find the population of each water district, we determined which block groups were entirely within the water district. We then determined which block groups intersected the boundaries of the water districts. For those which intersected, we then calculated the ratio of water district area to block group area within each block group and multiplied the ratio by the block group population. We then summed the populations for the entire water district and then summed across all six water districts. Finally we determined the numbers of current residents (63% of total participants) in the water districts who participated in the C8 Health Project in 2005-2006, and divided these

residents (33,001) by the population (40,721) to find a participation rate of 81% among current residents age 20 and older.

Statistical Analysis

It was expected a priori that water district would play an important role in predicting exposure, with subjects in water districts more distant from the plant likely to have lower serum levels. Subjects in the C8 Health Project were required to document past or present consumption of contaminated public water from one of the six contaminated water districts (either via living in the water district for at least one year, or by working or going to school there for at least one year)(n=68,873), or from having drunk from private wells with documented contamination (n=157). This documented water district of exposure is called the 'qualifying' water district. Sixty-three percent of the population reported currently drinking public water (as their main water source) in one of the six water districts. We classified water district into twelve groups, six for currently (2005-2006) drinking public water in one of the six contaminated water districts, and six for not-currently-drinking-public water but having previously been exposed by drinking water in one of the six water districts (ie, using their 'qualifying water district). Among those classified by their qualifying water district, 73% of these had a record of having lived or worked in the past in their 'qualifying water district', with the remainder presumably having gone to school there (no data were available on school history). Hereafter we loosely describe these variables as "current" (2005-2006) and "past" exposure, since the majority of those not currently drinking contaminated public water qualified for the study due to having drunk contaminated water in the past.

Besides age, race, sex, and water district, other a priori variables of interest were having worked at the chemical plant, growing your own vegetables, and drinking bottled water (Emmett et al. 2006). Detailed employment history was only available for 71% of adult study subjects who consented to make available identifiable information to the authors as part of future follow-up studies. Analyses using a variable for current or past employment at the chemical plant were restricted to that subset. Our initial model was based on including these a priori variables found to be important in previous studies, as well as the variables for water district. The initial model then included current or past water district, occupational exposure (for the subset with available data), eating local vegetables, use of bottled water, age, sex, and race (white vs. non-white).

We included the entire population (n=69,030) in analyses using the above regression model (absent occupational exposure, available on a subset), to which we added a large number of other potentially important variables, ultimately retaining those which had a significant association (at $p<=0.05$) with PFOA. Because the population is so large and any variable only slightly associated with PFOA may be statistically significant, this strategy of model building led to inclusion in the final model of a variables statistically associated with PFOA levels but without any important contribution to explaining the overall variance of PFOA. We adopted this strategy partly because of the exploratory nature of this analysis and the minimal prior data on factors associated with PFOA in the general population.

All regression models used the natural log transformation of PFOA because the log transform was more normally distributed; residuals were checked for normality.

Laboratory method for PFOA

Analyses were conducted by a large commercial lab (Exygen). PFOA is customarily measured in the serum, where virtually all PFOA in whole blood may be found (Ehresman et al.

2007). The analytical method for measurement of PFOA in the serum, which was used in this study, has been described in detail previously (Flaherty et al. 2005, Longnecker, et al. 2008). Briefly, the method utilizes liquid chromatography separation with detection by tandem mass spectrometry. The approach allows for rapid throughput using a 96-well plate and can handle large numbers of samples. Extraction of the serum or plasma samples is done using acetonitrile. Chromatography on the extract was done using a quaternary pump and vacuum degasser. The mobile phases consisted of two systems: a 2mM ammonium acetate solution and methanol with gradients set up to ensure both rapid and complete separation. The lab used ^{13}C-PFOA at a concentration of 1ng/ml as their internal standard. Mass spectrometry was done in selected reaction monitoring mode with m/z=413 → 369 as the principal ion monitored for PFOA (m/z=370 for the ^{13}C internal standard. Fortification recoveries using rabbit serum or plasma as the matrix for PFOA were generally within the 90-110% levels. The coefficient of variation based on multiple samples between batches was generally at or less than 0.10 over the range of 0.5 ng/mL to 40 ng/mL with a more precise relative coefficient of variation of approximately 0.01 for highly fortified (10,000 ng/mL) samples (Flaherty et al. 2005).

The limit of detection for PFOA was 0.5 ng/ml. Only 0.06% of observations were below the limit of detection, and these were assigned 0.25 ng/ml.

Results

Descriptive data for the population are given in Table 1. Figure 2 shows the distribution of PFOA. The log of PFOA is more normally distributed than PFOA, and use of it in the regression model for the full population led to residuals which were approximately normally distributed (Figure 3). The theoretical 2.5% tails of the distribution of the studentized residuals

(>1.96, or <-1.96) contained 2.76% and 2.60% of the data, respectively, conforming reasonably to what was expected.

Table 2 shows the results of the final model for the entire population, without inclusion of a variable for working at the chemical plant (R-square model 0.55). Five additional variables (date of testing divided into bi-monthly intervals, alcohol consumption in the last 3 days, being a vegetarian, body mass index (BMI), and regular exercise) were added to variables of a priori interest in the initial model, based on each being significantly associated with PFOA ($p<0.05$) when added to the initial model.

There are strong effects of water district seen in Table 2, with current residence in water districts closest to the plant having the highest PFOA levels. Figure 4 shows the data graphically. Currently drinking public water in Little Hocking or Lubeck is associated with the highest levels of PFOA. The well field for Little Hocking public water is located directly across the river from the plant, and the plant itself is located in Lubeck. Current residence in Belpre and Tupper Plains water districts had the next highest levels. These districts are slightly further away (Belpre is also upstream). Residents of districts furthest away (Mason, Pomeroy) had the lowest levels. Past consumption of water in Little Hocking or Lubeck ('qualifying water district') is also associated with elevated levels, although less than those currently residing in these water districts. The median level for current residents of any water district was 38.4 ng/ml, while the median for past residents was 18.6 ng/ml.

Table 2 indicates that PFOA levels show a J-shaped curve with age; Figure 5 illustrates this. Male gender is strongly associated with increased PFOA levels. Besides water district, age, and gender, other variables explain less of the variation in PFOA level.

Growing one's own vegetables is associated with increased PFOA, while drinking bottled water is associated with decreased PFOA. Drinking well water, current smoking, and drinking alcohol in the last three days are positively associated with an increase in PFOA. The alcohol finding could reflect some unknown aspect of increased liver activity (protein and lipid production).

Table 2 shows an approximate 30% decrease in levels over the year of testing (2005-2006), which results largely from residents outside the six water districts (37%) who were no longer exposed and whose blood levels were dropping as PFOA was excreted. Note that the 34% decrease over time contrasts with the much sharper decrease seen in the unadjusted data in Table 1; that greater decrease reflects the greater participation of residents from low exposure areas toward the end of the year-long study, which is not seen in the adjusted results in Table 2, based on the model in which water district is included as variable.

High BMI is associated with lower PFOA levels. White race slightly increases PFOA but is not statistically significant. Socio-economic status (SES) was not included in the model. There was a weak positive trend between household income and PFOA concentration, and a stronger (contradictory) negative trend between years of schooling and PFOA for those age 30 and over. These conflicting results do not lend themselves to any simple conclusion regarding an association of PFOA and SES.

Further analyses were conducted restricting the data set to the 71% of the population with employment history, and adding a variable for working at the chemical plant to the model in Table 2. Overall the R-square for the model for this subset was 58%, similar to the R-square of 55% for the model with all subjects. Currently working at the plant was associated with a much higher level of PFOA (coefficient 1.41, standard error 0.03, $p<0.0001$, partial R-square 0.06),

equivalent to a 309% increase in PFOA over someone who had never worked at the plant Prior work at the plant was also associated with a higher level (coefficient 0.44, standard error 0.02, $p<0.0001$, partial R-square 1%), equivalent to a 55% increase in PFOA compared to someone who never worked at the plant. Coefficients for other variables remained largely unchanged, with the exception of the coefficient for white vs non-white, which increased from 0.020 to 0.064 (standard error 0.023, $p=0.005$). Working at the chemical plant was slightly less common for whites than non-whites (odds ratio adjusted for age, 0.79, 95% CI 0.62-1.00), such that inclusion of a variable for working at the plant may have made the estimate of race more accurate (ie, occupational exposure was a negative confounder for the effect of white vs non-white).

By way of sensitivity analysis, we re-ran the model in Table 2 after eliminating the top 1% and bottom 1% of the distribution of studentized residuals, to consider the possible influence of outliers. This analysis, with 98% of the original data, increased the R-square of the model from 55% to 63%, as might be expected. However, this led to little change in most model coefficients, especially the most important predictors. All the same variables were statistically significant or not statistically significant, as in the original analysis, with the exception of race, which became statistically significant without the outliers. The coefficients for age, gender, current water district, BMI (>30), prior water district, date of testing, growing your own vegetables, being a vegetarian, current alcohol consumption, and using well water changed by 10% or less. The coefficients for race, current and former smoking, BMI (first two categories), and using bottled water changed by more than 10%, indicating they were more affected by outliers. They were among the least important predictors, none of which had a partial correlation coefficient more than 1%; the coefficients for race, BMI (first two categories), and former smoking were not statistically significant in the full model.

Similarly, for sensitivity analysis we restricted the analysis to 50% of the data, after generating a uniform random number and taking those in the lower half. The model R-square was again 55%. In this analysis, however, there was more variation in the estimated model coefficients. Ten of 35 coefficients changed more than 20%, although all had the same sign (positive or negative). Those that changed were among the least stable; 7 of the 10 were not significant at the 0.05 level in the split sample, and six of these had not been significant in the original complete data analysis. Overall, all coefficients all had the same direction (ie, were consistently positive or negative in the full and 50% split sample).

Discussion

PFOA is an important new chemical introduced after WWII and now found in virtually the entire US population. The routes of exposure in the general population are not known. PFOA is known to have some toxic properties in animals but no human health effects have been well established.

Data remain sparse on factors associated with serum levels of PFOA. Two prior studies of the general population (NHANES population, 1999-2000, and NHANES 2003-2004) found that males had higher levels, that there was little trend with age, that whites had higher levels than Hispanics and blacks, and that increased education was associated with higher levels (Calafat et al 2007a, Calafat et al 2007b). R-squares for regression models were not reported. These findings sometimes failed to reach statistical significance and sometimes were apparent only in certain age groups. Both studies were restricted to adults. Further research using NHANES data for children has shown that children had higher PFOA levels than adults (personal communication, Antonia Calafat, May 2008). PFOA levels in the US may be

decreasing in the past several years since several manufacturers have stopped using or drastically reduced the use of PFOA (Calafat et al. 2007b, Olsen et al. 2007).

Olsen et al. (2007) studied 140 Red Cross donors in 2000 and 2005 with background levels of exposure, and found that men had significantly higher serum levels than women but there were no trends with age. Kannan et al (2004) studied 473 serum samples from many countries and found that PFOA was present in most samples from industrialized countries, but found no significant differences by sex or age. Emmett et al. (2006) has studied 371 highly-exposed subjects drinking PFOA contaminated water (with a median level about 354 ng/ml), residing near the same plant under study here. They found a J-shaped relationship with age (high exposure at young and old ages). They also found that eating locally grown vegetables increased PFOA levels, while drinking bottled water decreased levels. Work at the nearby plant sharply increased levels. Holzer et al. (2007) studied 355 exposed and 236 non-exposed community subjects in Germany. The exposed subjects were drinking water contaminated with fluoropolymers, predominantly PFOA; the average PFOA serum level was approximately 25 ng/ml. Factors significantly associated with higher PFOA levels were male sex, higher age, drinking larger quantities of public water, eating local vegetables, and residing in the exposed vs nonexposed area.

Here we have studied such factors in by far the largest population to date. This population has been exposed to PFOA primarily through drinking water contamination from a nearby plant, similar to the population of 600 studied in Germany (Holzer et al. 2008).

We have found that markedly higher levels of PFOA were associated with working at the chemical plant which was the source of the contamination. Workers who no longer worked at the plant had much higher levels (median 75) than non-workers (median 24), but lower levels

than those who continued working there (median 148), consistent with a gradual excretion of PFOA from the body after ending high exposure. Other occupational data (Sakr et al. 2007a,) have shown that 1000 workers at the plant in 2004 had a mean serum level of 428 ng/ml. This is virtually identical to the mean serum level we have found in our data for the subset of workers currently at the plant (427 ng/ml) in 2005-2006 (the PFOA distribution among workers was highly skewed, accounting for difference between the mean and median serum levels, 427 vs 147 ng/ml for current workers).

The other main factor influencing PFOA levels in the population studied here were the distance of residence from the plant. Current residence in water districts near the plant (eg. Little Hocking and Lubeck) was associated with the highest levels. Those with prior residence near the plant also had high levels, but much less than those living there currently, again consistent with the gradual excretion of PFOA once high exposure ceases. This analysis via distance of water district from the plant is crude; a more comprehensive analysis using geocoding of past and present addresses, as well as estimates of annual emissions from the plant, is underway.

Demographic and other environmental factors played much less important roles. Male sex was the most important demographic factor associated with higher levels. Age showed a J-shaped relationship with serum PFOA, with higher levels in the young and the old, similar to what has been found previously by Emmett et al. (2007) and Calafat et al. (personal communication 2008). The reasons for these demographic patterns are not known. We also found a trend of decreasing levels of PFOA over time during this one year study, which was primarily due to decreasing levels among people no longer living in the six water districts and therefore no longer exposed.

In conclusion, PFOA levels are far above background in this population which has consumed contaminated drinking water. Further studies are underway to determine whether PFOA is associated with health effects in this population.

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Table 1. Descriptive statistics of mid-Ohio valley residents exposed to PFOA (n=69030)

Variable*	N(%)	Median PFOA (ng/ml)
Blood PFOA in 2005-6	69,030 (100%)	28.2**
Age:		
0-9 years	4,915 (7.1)	32.8
10-19 years	9,658 (14.0)	26.6
20-29 years	10,073 (14.6)	21.0
30-39 years	10,547 (15.3)	22.7
40-49 years	12,113 (17.6)	28.0
50-59 years	10,515 (15.2)	33.6
60-69 years	6,881 (10.0)	42.9
>70 years	4,328 (6.3)	40.1
Gender:		
Male	33,242 (48.2)	33.7
Female	35,788 (51.8)	23.7
Race		
White	66,989 (97%)	28.1
Non-white	2,041 (3%)	29.5
BMI:		
<24	18,849 (28.1)	27.9
24-26	12,501 (18.6)	29.1
27-29	11,800 (17.6)	30.8
>30	24,005 (35.8)	26.1
Worked at chemical plant:***		
Yes – current	1,171 (2.4)	147.8
Yes – previous	1,447 (2.9)	74.9
No	45,276 (94.9)	24.3
Grow own vegetables:		
Yes	16,015 (23.2)	34.1
No	53,015 (76.8)	26.7
Currently resident in water district:		
Belpre	5,388 (7.8)	35.0
Tupper Plains	9,703 (14.1)	37.2
Little Hocking	8,390 (12.2)	224.1
Lubeck	8,289 (12.0)	66.9
Mason County	10,066 (14.6)	12.4
Pomeroy	1,560 (2.3)	12.1
Previously resident or worked in water district		
Prior Belpre	3,387 (4.9)	17.3

Prior Tupper Plains	4,359 (6.3)	13.6
Prior Little Hocking	4,465 (6.5)	33.7
Prior Lubeck	8,552 (12.4)	28.4
Prior Mason County	2,711 (3.9)	10.5
Prior Pomeroy	2,016 (2.9)	11.0
Vegetarian:		
Yes	502 (0.7)	24.5
No	68,528 (99.3)	28.2
Consumed alcohol in last 3 days:		
Yes	8,883 (13.1)	33.4
No	59,029 (86.9)	27.6
Current smoking:		
Yes	14,847 (21.5)	25.3
No	54,088 (78.5)	29.3
Former smoking:		
Yes	14,697 (21.3)	31.2
No	54,280 (78.7)	27.5
Regular exercise:		
Yes	22,072 (32.0)	30.3
No	46,958 (68.0)	27.3
Bottled water:		
Yes	3,728 (5.4)	31.3
No	65,302 (94.6)	28.0
Well water:		
Yes	4,434 (6.4)	21.7
No	64,596 (93.6)	28.7
Date of testing:		
First two months	10,284 (14.9)	48.9
Second two months	14,046 (20.4)	39.9
Third two months	15,524 (22.4)	28.8
Fourth two months	14,948 (21.7)	23.8
Fifth two months	8,756 (12.7)	17.8
Last two months	5,472 (7.9)	14.7

* 2,120 subjects missing PFOA values, 1,875 subjects missing BMI, 1,118 subjects missing alcohol use, 95 subjects missing current smoking, 53 subjects missing former smoking, 8,649 subjects missing household income, and 144 subjects missing water district.
** Mean 83.6 ng/ml, geometric mean 32.9 ng/ml
*** Data on working at chemical plant available for only 71% of the population

Table 2. Multiple linear regression model for the log of PFOA level in all six water districts*

Variable	Predicted % change in PFOA versus referent group	Regression coefficient (change in log PFOA) (95% CI)	P-value	Percent Variance PFOA explained (partial R^2)
Age: 0-9 years	Referent			
10-19 years	-15%	-0.16 (-0.20,-0.12)	<.0001	<1%
20-29 years	-24%	-0.28 (-0.32, -0.24)	<.0001	<1%
30-39 years	-16%	-0.17 (-0.21, -0.13)	<.0001	<1%
40-49 years	-2%	-0.02 (-0.06, 0.02)	0.24	<1%
50-59 years	12%	0.11 (0.07, 0.15)	<.0001	<1%
60-69 years	23%	0.21 (0.17, 0.25)	<.0001	<1%
>70 years	26%	0.19 (0.11, 0.27)	<.0001	<1%
Gender: female	Referent			
Male	35%	0.30(0.29, 0.31)	<.0001	2.9%
BMI <24	Referent			
24-26	2%	0.02 (-0.01, 0.03)	0.13	<1%
27-29	2%	0.02 (-0.01, 0.03)	0.18	<1%
>30	-4%	-0.04 (-0.05, -0.01)	<.0001	<1%
Grow vegetables: no	Referent			
Yes	11%	0.10 (0.08, 0.12)	<.0001	<1%
Currently resident water district:				
Belpre	203%	1.11 (1.07, 1.15)	<.0001	3.7%
Tupper Plains	200%	1.10 (1.06, 1.14)	<.0001	4.1%
Little Hocking	1612%	2.84 (2.80, 2.88)	<.0001	21.5%
Lubeck	421%	1.61 (1.61, 1.69)	<.0001	8.2%
Mason County	9%	0.09 (0.05, 0.13)	<.0001	<1%
Pomeroy	3%	0.03(-0.03, 0.09)	0.27	<1%
Previously lived/worked In water district				
Prior Belpre	62%	0.48 (0.44, 0.52)	0.005	<1%
Prior Tupper Plains	36%	0.29 (0.25, 0.33)	<.0001	<1%
Prior Little Hocking	246%	1.22 (1.18, 1.26)	<.0001	4.3%
Prior Lubeck	169%	0.88 (0.84, 0.92)	<.0001	3.2%
Prior Mason County	-2%	-0.01 (-0.05, 0.04)	0.57	<1%
Prior Pomeroy	Referent			
Vegetarian: no	Referent			
Yes	-10%	-0.10 (-0.18 -0.02)	0.01	<1%
Consumed alcohol in last 3 days: No	Referent			
Yes	7%	0.06 (0.04, 0.08)	<0.001	<1%
Smoking: never	Referent			

Current	6%	0.06 (0.04, 0.08)	<.0001	<1%
Former	-1%	-0.01(-0.03, 0.01	0.18	<1%
Bottled water: no	Referent			
Yes	-6%	-0.06 (-0.08, -0.04)	<.0001	<1%
Well water: no	Referent			
Yes	12%	0.11 (0.09, 0.13)	<.0001	<1%
Race: non-white	Referent			
White	2%	0.02 (-0.02, 0.06)	0.31	<1%
Time of blood draw				
First two months	Referent			
Months 3-4	6%	0.06 (0.04, 08)	<0.0001	<1%
Months 5-6	-11%	-0.12 (-014, -00)	<0.0001	<1%
Months 7-8	-14%	-0.15 (-0.17 -013)	<0.0001	<1%
Months 9-10	-22%	-0.25 (-0.27, -0.23)	<0.0001	<1%
Months 11-12	-29%	-0.34 (-0.38, -0.30)	<0.0001	<1%

* Model, R-square=0.55, n=64251

Figure Legends

Figures

Figure 1. Six contaminated water districts

Figure 2. Distribution of PFOA (ng/ml)*.

*405 observations over 1000 ng/ml not shown

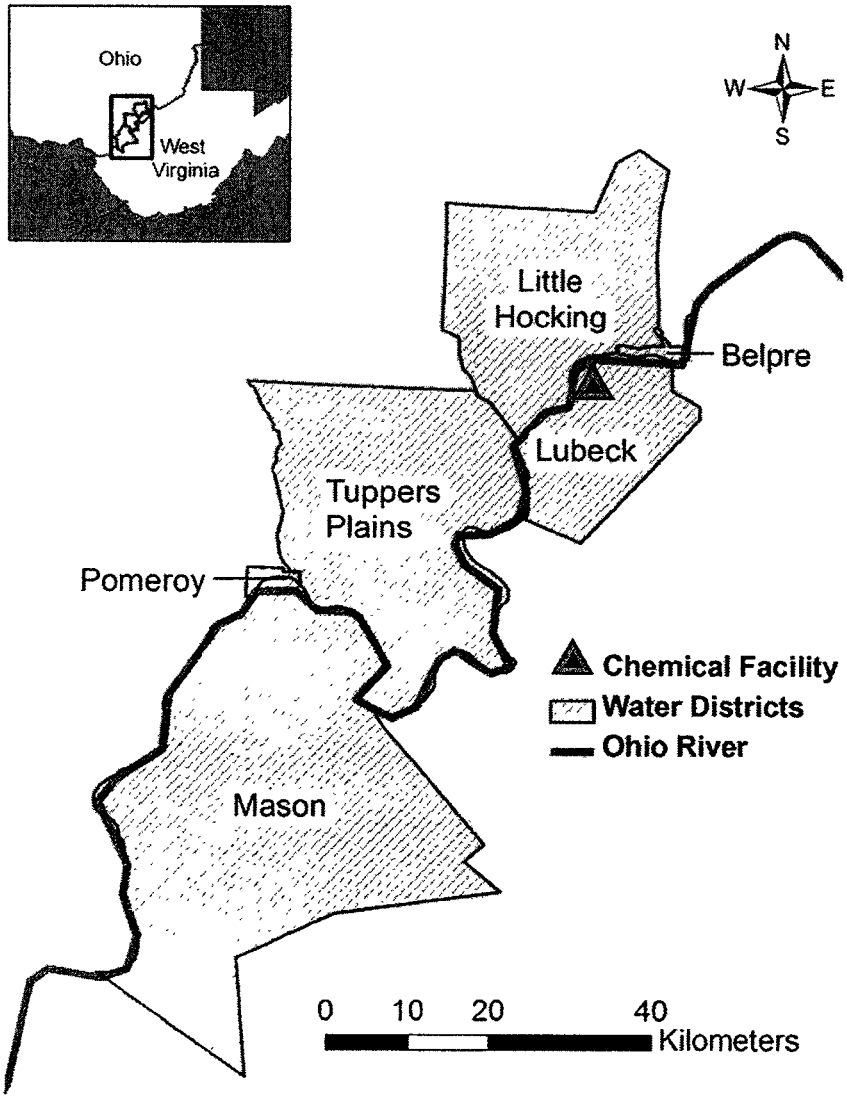
Figure 3. Distribution of residuals from regression model (Table 2).

Figure 4. PFOA level (geometric mean) by current and former water district*

* Current water district refers to living in exposed water district in 2005-2006 at time of blood draw, Prior water district refers to having either lived, worked, or gone to school for at least at year in one of the six exposed water districts . Model prediction compared to observed median value of 11.50 ng/ml for prior Pomeroy.

Figure 5. Predicted PFOA serum level (geometric mean) by age*

* Model prediction compared to observed median value of 32.0 ng/ml for age group 0-9.



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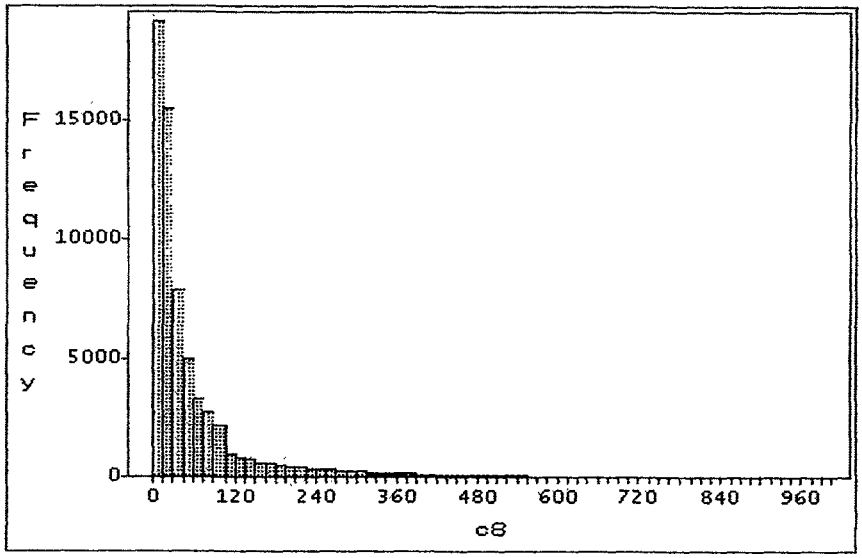

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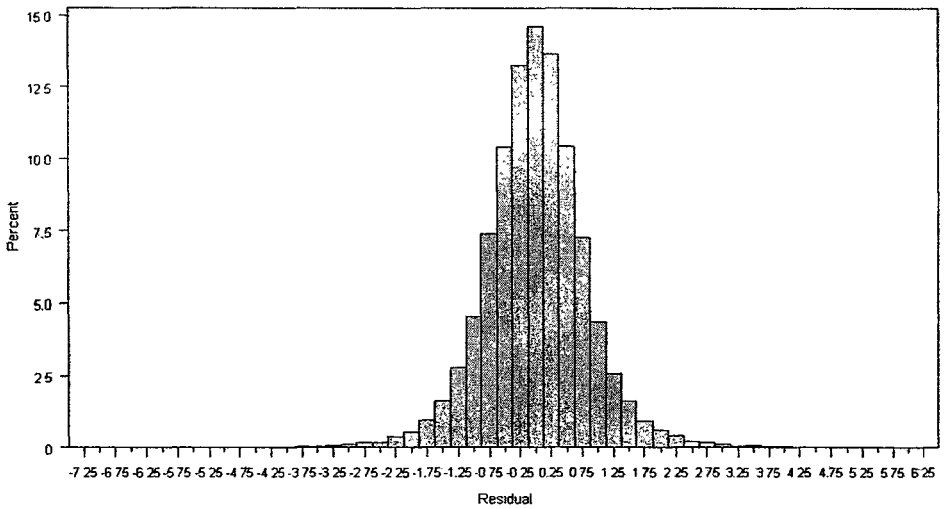

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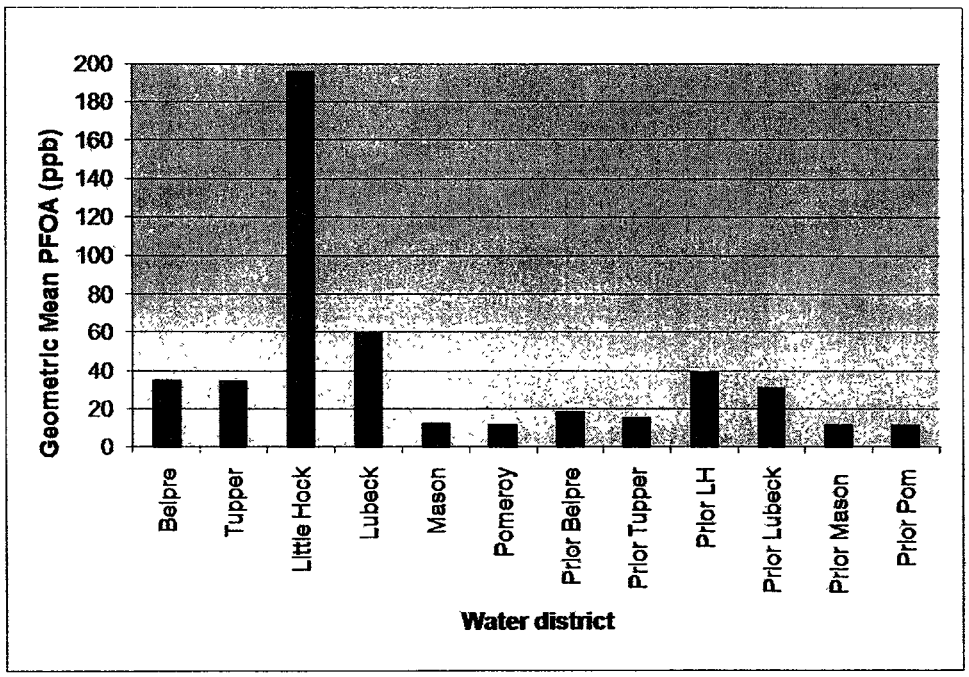

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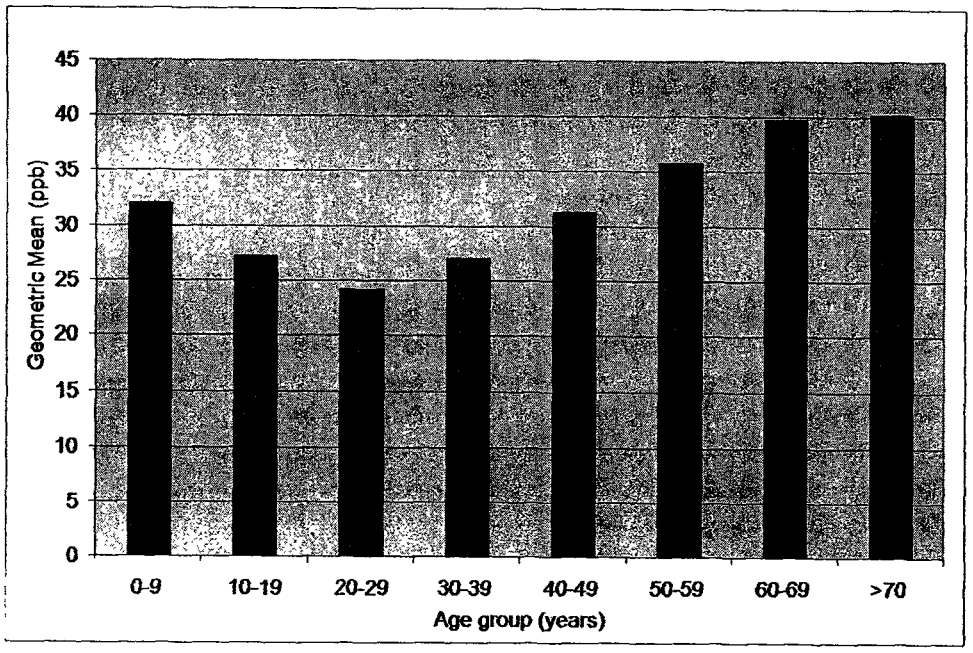

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta, GA 30333

February 10, 2009

Barbara Taylor, Director
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Bureau for Public Health
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Dear Ms. Taylor:

This letter is in response to your request to the Agency for Toxic Substances and Disease Registry (ATSDR) for an evaluation of the public health issues related to using water contaminated with perfluorooctanoate (PFOA) to reconstitute baby formula. This evaluation additionally considers the more general issue of water consumption by communities in the area around the Washington Works Facility (Wood County, West Virginia). As you are aware, since your request (letter dated January 18, 2006 and our subsequent response dated February 7, 2006), we have been engaged in ongoing health education and technical review activities. Much of the information contained in this letter has been communicated previously through verbal updates with your staff.

Completed and ongoing studies involving area residents have shown that communities near the Washington Works Facility have elevated serum levels of PFOA. These elevated PFOA levels are primarily a result of using contaminated drinking water.

Defining a safe health-based level of PFOA in the water near the Washington Works Facility has been very difficult. A number of issues contribute to this problem, including: (1) an incomplete characterization of the exposures leading to elevated PFOA levels in the area residents, (2) limited research on the health effects of PFOA in humans, and (3) difficulties relating the pharmacokinetic data obtained from test animals to humans. Due to the scientific limitations and uncertainties, ATSDR has not established a health-based guidance value, a "Minimal Risk Level" that may be used to help define a safe level of PFOA in drinking water.

Occupational studies have reported that highly exposed workers, with serum PFOA levels similar to or higher than those seen in area residents, did not show obvious clinical abnormalities associated with the PFOA exposures. However, effects in young children have not been adequately studied. We note that local children and elderly persons living in areas near the Washington Works Facility have higher PFOA levels than do middle-aged adults who live in the community. Two recent studies reported that background level exposures to PFOA were associated with lower birth weights in infants. However a third study of births from the general area north of the Washington Works Facility could not confirm those findings. While the scientific debate on these studies continues, we must remain open-minded about potential associations between PFOA exposures and developmental endpoints in humans. At the present time, ATSDR considers developmental effects to be the most sensitive adverse response to PFOA exposures.

Based on our evaluation, ATSDR provides the following site-specific recommendations:

Because of concerns for potential adverse effects in vulnerable groups, persons such as pregnant women, women of child-bearing age, children, and the elderly living in the vicinity of the Washington Works Facility should reduce local water exposures to levels that are as low as reasonably achievable.

In addition, ATSDR concurs with previous verbal advice given by the West Virginia Department of Public Health; that it is prudent public health practice for caregivers in the area near the Washington Works Facility to reduce drinking water exposures to infants by using premixed baby formula.

We note that efforts to mitigate the possible effects associated with PFOA exposures in the area of the Washington Works Facility have included: (1) providing bottled water to area residents; (2) filtering PFOA from publicly-supplied water; and (3) installation of at-home filter systems for households supplied by PFOA-contaminated wells. We understand that all publicly-supplied water in the area is currently filtered to reduce PFOA to extremely low levels. EPA has recently confirmed that the vast majority of, if not all, private drinking water well owners in the affected area have been contacted to conduct well water testing, and to install filters if needed. It is important that monitoring of the effectiveness of these drinking water treatment systems be continued. In addition, educational campaigns for both physicians and area residents have raised awareness of the potential problems, and have provided information about how to reduce exposures to PFOA.

Because of the site-specific data gaps and the scientific limitations and uncertainties in the toxicological and epidemiological studies of PFOA, the advice presented in this letter may be revised when new data or study results become available.

ATSDR will work with the State of West Virginia to provide area residents with information about the local drinking water issues. ATSDR will also work with the State of West Virginia to ensure that well water users in the vulnerable groups are aware of the potential risks as well as the measures to reduce/eliminate those potential risks.

Clement Welsh, ATSDR Headquarters, and Lora Werner, ATSDR Region 3, will assist the West Virginia Department of Public Health in ensuring that area residents understand the public health recommendations provided in this letter. Please contact Lora Werner, ATSDR Region 3 at (215)-814-3141, with any questions regarding information presented in this letter.

Sincerely,

Howard Frumkin. M.D., Dr. P.H.
Director, National Center for Environmental Health/
Agency for Toxic Substances and Disease Regis try

cc:
Lora Werner, Region III
Bill Cibulas, DHAC
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