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Private Drinking Water Wells as a Source of Exposure to PFOA in Communities Surrounding a Fluoropolymer Production Facility

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Key words: drinking water; pharmacokinetic modeling; perfluorooctanoic acid (PFOA, or C8); private wells; serum

List of Abbreviations:

C8 – perfluorooctanoic acid, PFOA

CI – confidence interval

EPA – Environmental Protection Agency

GEE – generalized estimating equations

IQR – interquartile range

LOQ – limit of quantification

MOU – Memorandum of Understanding

PFCs – polyfluoroalkyl chemicals

PFOA – perfluorooctanoic acid, C8

Abstract:

Background: The C8 Health Project was established in 2005 to collect data on perfluorooctanoic acid (PFOA, or C8) and human health in Ohio and West Virginia communities contaminated by a fluoropolymer production facility.

Objective: We assessed PFOA exposure via contaminated drinking water in a subset of C8 Health Project participants using private drinking water wells.

Methods: Participants provided demographic information, and residential, occupational, and medical histories. Laboratory analyses were conducted to determine serum PFOA concentrations. PFOA monitoring data were collected from 2001 to 2005 in 62 private drinking water wells. We examined the relationship between drinking water and serum PFOA levels using robust regression methods. As a comparison to regression models, we used a first-order, single compartment pharmacokinetic model to estimate the serum-to-drinking water concentration ratio at steady-state.

Results: The median serum PFOA concentration in 108 study participants using private wells was 75.7 µg/L, approximately 20 times greater than the US general population levels, but similar to local residents drinking public water. Each µg/L increase in drinking water PFOA is associated with an increase in serum concentrations of 141.5 µg/L (95% confidence interval 134.9-148.1). The serum-to-drinking water concentration ratio for the steady-state pharmacokinetic model is 114.

Conclusions: PFOA contaminated drinking water is a significant contributor to serum levels in this population. Regression methods and pharmacokinetic modeling produced similar estimates of the relationship.

Introduction:

Perfluorooctanoic acid (PFOA, or C8) is a synthetic chemical that is used as a processing aid in the manufacture of fluoropolymers. Products made with fluoropolymers possess unique abilities including oil, stain, grease, and water repellency. These properties led to the wide spread use of fluoropolymers in a number of products including non-stick cookware, weather and stain resistant clothing and textiles, building and construction materials, and electronics (Renner 2001).

The chemical structure of PFOA makes the compound extremely resistant to environmental and metabolic degradation. PFOA has been detected globally in the environment (Lau et al. 2007). It is well established that PFOA is readily absorbed via inhalation and ingestion. Routes of exposure in the general population remain unclear, although research suggests diet is a potentially important source (Trudel et al. 2008). PFOA is detected in the vast majority of serum samples from the US and world populations (Lau et al. 2007). Once absorbed, PFOA is eliminated from the human body very slowly. Estimates of the serum half-life of PFOA range from 2.3 year in residents of a contaminated community to 3.8 years in retired fluorochemical workers (Bartell et al. 2010; Olsen et al. 2007). Although there is some evidence that PFOA concentrations are declining in serum, possibly due to reductions in use, the median serum concentrations remain around 4 µg/L in the US population (Calafat et al. 2007a; Calafat et al. 2007b; Olsen et al. 2007). PFOA exposure has been linked to a variety of health impacts in animals including increased cancer risk, adverse reproductive outcomes, and liver damage (Lau et al. 2007; Lau et al. 2004). Due to a lack of data, health impacts of exposure in humans remain largely unknown (Steenland et al. 2010).

In 2003, the US EPA began an enforceable consent agreement process with industry and other stakeholders to collect additional information for a PFOA risk assessment (US Environmental Protection Agency 2010a). The EPA and DuPont (the maker of Teflon®) entered a memorandum of understanding (MOU) in November of 2005 as part of the risk assessment. Building on an agreement in place between the West Virginia Department of Environmental Protection and DuPont, the MOU required DuPont to conduct environmental sampling, including the monitoring of ground and surface waters around their Washington Works facility in Parkersburg, West Virginia (US Environmental Protection Agency 2004b).

DuPont began using PFOA in the manufacture of Teflon® at their Washington Works plant in the early 1950s. According to data provided by the company, emissions to air and the Ohio river reached a maximum in the late 1990s (Emmett et al. 2009; Paustenbach et al. 2007). The company reported a large reduction in these emissions in recent years (US Environmental Protection Agency 2010b). Previous research indicates that the primary source of exposure for individuals in the surrounding communities is contaminated ground water that is used for drinking water (Emmett et al. 2006; Steenland et al. 2009). The ground water in the area was contaminated via two main routes: PFOA released into the atmosphere was deposited onto soils and eventually leached downward into ground water, and PFOA was released directly into the Ohio River which runs near the facility and is linked to the groundwater supply (Paustenbach et al. 2007).

In 2001, a group of residents in communities surrounding the facility filed a class-action lawsuit against DuPont alleging health damages after PFOA was detected in public drinking water districts. The resulting settlement established the C8 Health Project, a baseline survey

conducted in 2005-2006 to investigate potential links between PFOA and human disease in the area surrounding the facility (Frisbee et al. 2009).

Previous studies observed a significant association between living in an area with contaminated public drinking water and increased serum PFOA levels using water-district-level data (Emmett et al. 2006; Holzer et al. 2008; Steenland et al. 2009; Vieira et al. 2008b). These studies are partially ecologic in that the exposure variable is assigned at the group level while other variables are assigned at the individual level (Webster 2000, 2002; Björk and Strömberg 2002). In particular, the previous studies provide information on serum concentration in relation to average exposure for populations serviced by the same water supply, but there is a lack of data investigating the relation between private household well contamination and serum levels. In the current analyses, we examine the relationship between serum and drinking water PFOA concentrations using data collected from private drinking water wells contaminated by industrial emissions. By using private well data, we are able to quantify PFOA levels in C8 Health Project participants' drinking water at the individual level. We assess the relationship using standard regression approaches, and, for comparison, we also use a pharmacokinetic model to explore the association between PFOA in drinking water and serum levels. Simple, single compartment, first-order models have been applied previously to estimate the serum concentration following exposure from diet and drinking water (Fromme et al. 2007; Vieira et al. 2008b). In the current analyses, we utilize updated estimates of pharmacokinetic parameters to predict the serum-to-drinking water concentration ratio. We compare the association between drinking water and serum PFOA concentrations from regression models to those obtained in pharmacokinetic analyses.

Methods:*Study Population*

The C8 Health Project was a cross-sectional study of approximately 69,000 adults conducted by Brookmar Inc. from August 2005 to August 2006 (Frisbee et al. 2009). Participants lived in one of six public water districts in West Virginia and Ohio that surround DuPont's Washington Works facility: Belpre, Little Hocking, Lubeck, Mason County, Pomeroy and Tappers Plains-Chester (Figure 1). Data were collected from each participant using questionnaires and clinical examinations to obtain demographic information and residential, occupational, and medical histories (Frisbee et al. 2009). Concentrations of 10 perfluorinated compounds, including PFOA, were also determined in serum samples taken once from each participant between August 2005 and August 2006. Detailed analytic methods were described previously (Kuklennyik et al. 2004). Briefly, serum samples were analyzed using automated solid-phase extraction coupled to reversed-phase high-performance liquid chromatography. Participants provided informed consent to have their data used for research purposes.

Water monitoring was conducted by DuPont in public and private wells surrounding the Washington Works facility beginning in 2001. Private well monitoring reports contained PFOA measurements as well as the primary use of each well and the names and address of each well's owner. These reports are available through the EPA docket EPA-HQ-OPPT-2004-0113 (US Environmental Protection Agency 2004a). We linked well monitoring data for 62 private wells used primarily for drinking water to C8 Health Project participants based on name and address. We also identified family members using well water as individuals having the same last name and address as the well owner for a total of 115 participants. The number of samples taken in each well prior to the collection of serum samples varied. Although the majority of wells were

sampled just once, 11 of the 62 private wells were sampled multiple times.. The Institutional Review Board of Boston University Medical Center approved this research.

Statistical Analysis

In preliminary analyses we identified several participants with serum PFOA concentrations or well PFOA concentrations that were much greater than the other participants. For data with outliers, using standard least squares estimation is both inefficient and biased; regression coefficients are pulled toward outliers and estimates of the variance are artificially inflated which can obscure outliers (Hampel et al. 1986). As such we used robust regression methods to assess the relationship between serum and drinking water PFOA concentrations. Robust regression provides stable results by limiting the influence of outliers and is generally less subject to bias than standard least squares estimation methods (Hampel et al. 1986). Robust regressions were performed using Yohia's MM-estimator which possesses high statistical efficiency and provides stable estimates of regression parameters when data include a relatively large percentage of outliers (Yohai 1987).

Additionally, because multiple individuals from the same family were included in analyses, which violates the assumption of independence for linear regression, we used generalized estimating equations (GEEs) in a second set of analyses to predict serum PFOA concentrations from drinking water PFOA concentrations. Using GEEs, we account for possible residual within-family correlation and investigate the sensitivity of our results from the robust regression that include multiple individuals from the same family in the analyses. GEEs and robust regressions were performed in SAS version 9.1.

Age and sex have been previously associated with serum PFOA levels in the population surrounding the Washington Works facility as well as in other populations (Emmett et al. 2006; Holzer et al. 2008; Steenland et al. 2009). Additionally, working at the Washington Works plant and growing one's own vegetables were linked to increased PFOA levels in serum (Emmett et al. 2006; Steenland et al. 2009). We included these *a priori* variables in all statistical models. A number of other variables including body weight, bottled water consumption (modeled as yes or no), cigarette smoking, and alcohol consumption, which have been previously linked to serum PFOA level, were also assessed (Emmett et al. 2006; Steenland et al. 2009). Only the *a priori* variables were included in the final models as the others did not materially alter the association between serum and well PFOA levels (did not cause a change greater than 10% in the predicted contribution of drinking water to serum).

For wells with multiple PFOA sampling events, we used the arithmetic average PFOA concentration in each well to predict serum levels in regression models. This method provided an estimate of the serum-to-drinking water concentration ratio that is readily comparable to the results of steady-state pharmacokinetic model which assumes that the concentration of PFOA in drinking water is constant over time (discussed in following section). We also performed an analysis using time-weighted water concentrations based on a non-steady state pharmacokinetic model. In main analyses we included all individuals regardless of how long they had lived at their current residence. We also performed analyses investigating the sensitivity of our results to the residential duration at a particular well. By restricting the sample to long-term residents (greater than 15 years) we ensure that participants had been exposed to water from a specific well for a period of time long enough for their serum levels to have reached steady state.

Pharmacokinetic Models

Regression provides us with an estimate of the change in serum concentrations per unit change in water concentration, adjusting for other factors. For comparison with the regression analyses we also predicted the ratio of serum-to-drinking water PFOA concentration using a simple first-order, single compartment pharmacokinetic model. Bartell et al. (2010) previously demonstrated that the pharmacokinetics of PFOA in humans are consistent with first-order elimination. Based on data which suggested that the duration of exposure to PFOA-contaminated drinking water in the study population is on the order of decades (Paustenbach et al. 2007), we assumed that levels of PFOA in serum had reached a steady-state concentration. The ratio of steady-state serum PFOA concentration, C_s ($\mu\text{g/L}$), to water concentration, C_w ($\mu\text{g/L}$) was modeled using the following equation (Bartell 2003):

$$\frac{C_s}{C_w} = \frac{f \cdot Q}{k \cdot V_d} \quad [1]$$

where f is the fraction of PFOA absorbed, Q is the daily water intake (L/day), k is the first-order rate constant for PFOA elimination (day^{-1} , $k=0.693/t_{1/2}$ where $t_{1/2}$ is the half-life), and V_d is the apparent volume of distribution (L).

Values for each parameter were obtained from a review of available animal and human PFOA pharmacokinetic data (Table 1). We assumed that 100% of ingested PFOA was absorbed based on animal data (Butenhoff et al. 2004; Gibson and Johnson 1979; Hundley et al. 2006). Similar estimates of the fraction of PFOA absorbed in humans that are highly exposed to PFOA have been used previously (Thompson et al. 2010; Trudel et al. 2008). In previous pharmacokinetic analyses of PFOA (Vieira et al. 2008b), we utilized a serum half-life of 3.8 years (1388 days) based on a small study of retired fluorochemical production workers (Olsen et al. 2007). In the current analyses, we applied a more recent estimate of 2.3 years (840 days)

based on data from Bartell and colleagues collected in a subset of C8 Health Project participants (Bartell et al. 2010). The volume of distribution (V_d) is a proportionality constant in pharmacokinetic modeling that relates the total amount of a chemical in the body to the concentration in plasma. We used a V_d for PFOA of 181 ml/kg and 198 ml/kg for males and females respectively based on results from cynomolgus monkey experiments (Butenhoff et al. 2004). Thompson et al. proposed a similar V_d (170 ml/kg) using data from residents of two chronically exposed communities around DuPont's Washington Works facility (2010). As the goal of our regression analysis was to use the serum and water data to estimate a steady state ratio, and not the V_d , we used the Butenhoff estimate from monkeys in the pharmacokinetic model rather than the Thompson estimate from the same community. We scaled the V_d to the sex and body weight of study participants and used the median of the study population in pharmacokinetic models. Because water consumption data were unavailable, we used the EPA's recommended average tap water intake rate for adults of 1.4 L/day which includes water consumed from the tap as a beverage or used in the preparation of foods and beverages (US Environmental Protection Agency 1997).

Results:

Linking well monitoring data to C8 Health Project Participants, we were able to identify 115 individuals using 62 different private wells for drinking water. Of these, 4 (3.5%) individuals were missing data (PFOA levels in serum: $n = 1$, body weight: $n = 2$, race: $n = 1$). We also excluded vegetarians ($n=2$) and non-white participants ($n=1$) as the numbers of each were too small to adequately control for these variables. Our final sample consisted of 108 participants. Serum PFOA levels ranged from 0.9 to 4751.5 $\mu\text{g/L}$ with a median concentration

of 75.7 $\mu\text{g/L}$ (mean=177.3 $\mu\text{g/L}$ and standard deviation=499.7 $\mu\text{g/L}$). As reported previously in the larger C8 Health Project sample (Steenland et al. 2009), individuals growing their own vegetables and employed at DuPont had higher median serum PFOA concentrations (Table 2). PFOA concentrations were higher in older and heavier participants, but differences were not statistically significant (Table 2).

Well locations and the corresponding average PFOA concentration are shown in Figure 1. The number of participants using each well ranged from 1 to 4. The median PFOA concentration in drinking water wells included in our analyses was 0.2 $\mu\text{g/L}$ (mean=0.8 $\mu\text{g/L}$ and standard deviation=1.9 $\mu\text{g/L}$), much greater than the US EPA provisional health advisory level of 0.04 $\mu\text{g/L}$ (US Environmental Protection Agency 2009). There was considerable variability between wells, with PFOA concentrations ranging from below the limit of quantification (LOQ=0.006 $\mu\text{g/L}$) furthest from the Washington Works facility to 13.3 $\mu\text{g/L}$ closest to the facility. One sample was reported below the limit of quantification and was assigned the LOQ 0.006 $\mu\text{g/L}$ in analyses. Multiple samples were taken in 11 wells which were used by 19 study participants. In general there did not seem to be an overall trend from 2001 to 2005 in the concentrations of PFOA in private drinking water. Although PFOA concentrations in each well appeared to fluctuate by season, these differences may be due to seasonal changes in precipitation. PFOA concentrations measured in 2004 and 2005 for a subset of wells measured seasonally are shown in Supplemental Material, Figure 1.

Regression Results

We examined the shape of the relationship between serum PFOA concentration and average drinking water PFOA concentration using a locally weighted regression smoother

(LOESS) in S-Plus. Visual inspection of a plot of the smoothed data indicated that the association between serum and drinking water PFOA levels could be estimated as a linear trend (data not shown), as suggested by the pharmacokinetic model (equation 1). We therefore included the average drinking water PFOA concentration as a linear predictor of non-transformed serum PFOA concentrations in regression models. In the adjusted robust regression models each $\mu\text{g/L}$ increase in drinking water PFOA concentration was associated with a 141.5 $\mu\text{g/L}$ (95% confidence interval (CI) = 134.9-148.1) increase in serum concentrations. Effect estimates for other variables included in the model are presented in Table 3. Growing one's own vegetables, male gender, and employment at DuPont were associated with elevated serum PFOA levels; however, associations did not reach statistical significance at the 0.05 level. The estimated background serum level in this population after accounting for known sources was 7.4 $\mu\text{g/L}$ (Table 3). Additionally, we investigated differences in the serum-to-drinking water concentration ratio in males and females. Stratifying by sex we observed very similar ratios in both sexes. Accordingly, including an interaction term in models, we did not observe a significant ($p\text{-value} < 0.05$) sex by water concentration interaction (data not shown).

Robust regression analyses revealed 6 outliers (observations for which the standardized residual was larger than three). For these individuals, the predicted values for serum PFOA concentrations using regression parameters under or over estimated observed concentrations (standardized residuals 3.0 to 44.5). In analyses using GEEs, we observed a small within-families correlation of serum PFOA levels of 0.1. Compared to results of the robust regression, GEE analyses excluding outliers produced a very similar estimate of effect (β) for each $\mu\text{g/L}$ increase in drinking water PFOA concentration ($\beta = 141.8 \mu\text{g/L}$; 95% CI = 134.3-149.4). When outliers were included in the GEE, the estimate of the association between serum and drinking

water PFOA levels was much larger. The inclusion of one participant in particular, with the highest serum and drinking water PFOA concentrations in the population, increased the estimate of effect to 232.7 $\mu\text{g/L}$ (95% CI=200.9-264.5). We could not identify a plausible explanation for this participant's extreme serum concentration using available data (the participant did not report being employed in the fluorochemical industry). Increased water consumption in this individual may have resulted in the extreme concentration, however data were not available to evaluate this hypothesis.

When we restricted to individuals with a residency duration greater than 15 years results were similar (β =140.2 $\mu\text{g/L}$; 95% CI = 132.1-148.4; n=67). We considered other residential duration restrictions (2, 5, 10, and 20 years), but restrictions had little effect on the magnitude of the association between serum and drinking water. We also excluded participants who were ever employed at the Washington Works facility, as these individuals may have had other significant sources of exposure. Again, the association between drinking water levels and serum was similar when these individuals were excluded. Additionally, excluding participants who reported consuming bottled water (N=6) from analyses had little effect on the magnitude of the association between serum and drinking water.

Comparison of Pharmacokinetic and Regression Results

Using the simple steady-state first-order pharmacokinetic model (equation 1) with a median V_d of 15,000 mL in the study population after scaling for the body weight and sex of study participants, we obtained a serum-to-drinking water concentration ratio of 114. This is similar to the estimate derived from regressing serum concentrations vs. water concentrations, 141.5.

Discussion:

Serum PFOA concentrations in private well users in the area surrounding DuPont's Washington Works facility were much greater than those observed in the general US population and were comparable to what has been observed in the study area previously (Emmett et al. 2006; Steenland et al. 2009; Vieira et al. 2008b). Private drinking water wells in the area were contaminated with PFOA, with levels in some wells being much greater than those observed in public drinking water supplies in the same area which ranged from 0.03 µg/L in Mason County to 3.5 µg/L in Little Hocking (Emmett et al. 2006; Steenland et al. 2009). Using private well data, we had a large number of individual exposure levels and were able to assess a wide range of exposures to PFOA via drinking water.

Results of regression analyses are consistent with a strong association between serum PFOA levels and drinking water PFOA concentrations. There was little difference in the association between serum and drinking water PFOA concentration when we limited analyses to 67 individuals that were long-term residents.

The serum-to-drinking water concentration ratio of 141.5 estimated using regression was similar to ratios obtained in previous partially ecologic analyses. In our previous work in the study area we found serum-to-drinking water concentration ratios in public water districts ranging from 59 to 411 (Vieira et al. 2008a). In Little Hocking, Ohio, near the Washington Works facility, Emmett and colleagues estimated a water concentration ratio of 105 in an analysis of public water consumers (Emmett et al. 2006). Additionally, in a small sample of private well users (n=6), serum to water concentration ratios ranged from 142 to 855 (Emmett et al. 2006).

The steady-state serum-to-drinking water concentration ratio of 114 obtained from pharmacokinetic modeling was close to the estimate of effect (141.5) obtained from regression analyses, suggesting that the pharmacokinetic model provides a reasonable estimate. We used a serum PFOA half-life based on data that Bartell and colleagues collected in a subset of C8 Health Project participants with exposure levels and patterns similar to the participants in these analyses (Bartell et al. 2010). Using the half-life estimate from Olsen et al. (2007) of 3.8 years increased the serum-to-drinking water ratio to 188. Other pharmacokinetic parameters that we used were more uncertain, particularly the volume of distribution which was estimated based on animal data (Butenhoff et al. 2004). A recent study by Thompson et al. estimated a very similar V_d (170 ml/kg) based on data from community residents (2010). Using the V_d from Thompson produced a similar serum-to-drinking water concentration ratio of 126. Based on data from sub-chronic monkey studies however, Washburn et al. (2005) recommend the use of a volume of distribution a factor of 10 higher than the Butenhoff et al. ratio that we used in analyses (Butenhoff et al. 2004); using this ratio would have reduced our ratio by an order of magnitude. Further research is needed on the volume of distribution of PFCs in humans. Additionally, in the absence of consumption data for each individual, we used the EPA estimated average daily tap water consumption value of 1.4 L/day; however, water consumption in the study population likely varies (US Environmental Protection Agency 1997). We believe that the difference in serum-to-drinking water concentration ratio estimates from regression and pharmacokinetic models may be explained by these uncertainties.

As reported previously for C8 Health Project participants, we observed a positive association between serum PFOA levels and growing one's own vegetables after adjusting for water concentration suggesting consuming locally-grown food may be an important source of

exposure in this population (Steenland et al. 2009, Bartell et al. 2010). The background serum PFOA concentration predicted in regression analyses (7.4 $\mu\text{g/L}$) is greater than background levels previously reported in the US population [geometric mean 3.8 $\mu\text{g/L}$ (Calafat et al. 2007b); arithmetic mean 4.3 $\mu\text{g/L}$ (Centers for Disease Control and Prevention, 2007)]. These results suggest that there may be other sources of PFOA exposure in the C8 Health Project population that were not included in the model or that random exposure misclassification may be inflating the predicted background levels for this population. Other potentially important sources of PFOA exposure in this population include water consumption at work, school, or religious and social organizations frequented by study participants. Although the release of PFOA from the Washington Works facility has been reduced (US Environmental Protection Agency 2010b), PFOA may still be present in indoor environments and may contribute an additional source of exposure for residents. Data were not available to test hypotheses on these exposure sources.

Our analyses are limited by our steady-state assumption and reliance on a single measurement of serum levels and, in most cases, a single measurement of drinking water PFOA levels. For a small number of individuals with multiple well measurements, we considered variability in well measurements in a sensitivity analysis using a time weighted well concentration rather than an arithmetic average to predict serum PFOA concentrations (see Supplemental Material). Although there was some seasonal variability from 2001 to 2005, on average well PFOA concentrations were fairly stable, and there was no long-term trend during this time period. Consequently, predicted serum concentrations that accounted for variation in PFOA concentrations in wells were similar to those obtained using simple steady-state models (data not shown).

Despite these limitations, our analyses have a number of strengths. We were able to link drinking water PFOA measurements to a relatively large number of individual study participants consuming private well water. The extensive questionnaire administered as part of the C8 Health Project allowed us to consider a number of potential confounders in the association between serum and drinking water PFOA levels (including age, sex, growing one's own vegetables, body weight, bottled water consumption, cigarette smoking, and alcohol consumption). Unlike previous assessments which used water-district-level water samples, participant's drinking water well measurements were used, increasing the variability of exposure measures. Additionally, available residential history information allowed us to consider differences in long and short term residents using contaminated wells for drinking water.

Conclusions:

Private drinking water wells in West Virginia and Ohio communities surrounding the DuPont Washington Works facility are contaminated with PFOA. Concentrations in private wells are, in some cases, much greater than those observed in area public water districts. For private well users, adjusted regression analyses indicate that PFOA levels in drinking water are a significant predictor of serum levels. The regression analysis predicted a 141.5 µg/L increase in serum levels for each µg/L increase in drinking water PFOA, very similar to the 114 µg/L in serum for each µg/L predicted in steady-state pharmacokinetic models. These results may also be applicable in other areas with point-source PFOA contamination.

References:

- Bartell S. 2003. Statistical methods for non-steady state exposure inference using biomarkers. [PhD Dissertation]. Davis, CA: University of California, Davis.
- Bartell SM, Calafat AM, Lyu C, Kato K, Ryan PB and Steenland K. 2010. Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. *Environ Health Perspect* 118(2): 222-228; doi: 10.1289/ehp.0901252. [Online 4 February 2010].
- Björk J, and Strömberg U. 2002. Effects of systematic exposure assessment errors in partially ecologic case-control studies. *Int J. Epidemiol* 31: 154-160.
- Butenhoff JL, Kennedy GL, Jr., Hinderliter PM, Lieder PH, Jung R, Hansen KJ, et al. 2004. Pharmacokinetics of perfluorooctanoate in cynomolgus monkeys. *Toxicol Sci* 82(2): 394-406.
- Calafat AM, Kuklenyik Z, Reidy JA, Caudill SP, Tully JS and Needham LL. 2007a. Serum concentrations of 11 polyfluoroalkyl compounds in the U.S. population: data from the national health and nutrition examination survey (NHANES). *Environ Sci Technol* 41(7): 2237-2242.
- Calafat AM, Wong LY, Kuklenyik Z, Reidy JA and Needham LL. 2007b. Polyfluoroalkyl chemicals in the U.S. population: data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and comparisons with NHANES 1999-2000. *Environ Health Perspect* 115(11): 1596-1602.
- Centers for Disease Control and Prevention. 2007. National Health and Nutrition Examination Survey: 2003-2004 Laboratory Files. Available: http://www.cdc.gov/nchs/nhanes/nhanes2003-2004/lab03_04.htm [accessed 16 August 2010].
- Emmett EA, Shofer FS, Zhang H, Freeman D, Desai C and Shaw LM. 2006. Community exposure to perfluorooctanoate: relationships between serum concentrations and exposure sources. *J Occup Environ Med* 48(8): 759-770.
- Frisbee SJ, Brooks AP, Jr., Maher A, Flensburg P, Arnold S, Fletcher T, et al. 2009. The C8 health project: design, methods, and participants. *Environ Health Perspect* 117(12): 1873-1882.
- Fromme H, Schlummer M, Moller A, Gruber L, Wolz G, Ungewiss J, et al. 2007. Exposure of an adult population to perfluorinated substances using duplicate diet portions and biomonitoring data. *Environ Sci Technol* 41(22): 7928-7933.
- Gibson S and Johnson J. 1979. Absorption of FC - 143-14C in rats after a single oral dose.: Riker Laboratories, Inc. Subsidiary of 3M Company. St Paul, MN. AR-226-0455.

- Hampel FR, Ronchetti EM, Rousseeuw PJ, and Stahel WA. 1986. Robust Statistics: The Approach Based on Influence Functions. New York: Wiley.
- Holzer J, Midasch O, Rauchfuss K, Kraft M, Reupert R, Angerer J, et al. 2008. Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanoate-contaminated drinking water. *Environ Health Perspect* 116(5): 651-657.
- Hundley SG, Sarraf AM and Kennedy GL. 2006. Absorption, distribution, and excretion of ammonium perfluorooctanoate (APFO) after oral administration to various species. *Drug Chem Toxicol* 29(2): 137-145.
- Kuklennyik Z, Reich JA, Tully JS, Needham LL and Calafat AM. 2004. Automated solid-phase extraction and measurement of perfluorinated organic acids and amides in human serum and milk. *Environ Sci Technol* 38(13): 3698-3704.
- Lau C, Anitole K, Hodes C, Lai D, Pfahles-Hutchens A and Seed J. 2007. Perfluoroalkyl acids: a review of monitoring and toxicological findings. *Toxicol Sci* 99(2): 366-394.
- Lau C, Butenhoff JL and Rogers JM. 2004. The developmental toxicity of perfluoroalkyl acids and their derivatives. *Toxicol Appl Pharmacol* 198(2): 231-241.
- Olsen GW, Mair DC, Reagen WK, Ellefson ME, Ehresman DJ, Butenhoff JL, et al. 2007. Preliminary evidence of a decline in perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations in American Red Cross blood donors. *Chemosphere* 68(1): 105-111.
- Paustenbach DJ, Panko JM, Scott PK and Unice KM. 2007. A methodology for estimating human exposure to perfluorooctanoic acid (PFOA): a retrospective exposure assessment of a community (1951-2003). *J Toxicol Environ Health A* 70(1): 28-57.
- Renner R. 2001. Growing concern over perfluorinated chemicals. *Environ Sci Technol* 35(7): 154A-160A.
- Steenland K, Jin C, MacNeil J, Lally C, Ducatman A, Vieira V, et al. 2009. Predictors of PFOA levels in a community surrounding a chemical plant. *Environ Health Perspect* 117(7): 1083-1088.
- Steenland K, Fletcher T, Savitz DA. 2010. Epidemiologic evidence on the health effects of perfluorooctanoic acid (PFOA). *Environ Health Perspect* 118(8): doi:10.1289/ehp.0901827.
- Thompson J, Lorber M, Toms LM, Kato K, Calafat AM and Mueller JF. 2010. Use of simple pharmacokinetic modeling to characterize exposure of Australians to perfluorooctanoic acid and perfluorooctane sulfonic acid. *Environ Int* 36(4): 390-397; doi:10.1016/j.envint.2010.02.008 [Online 20 March 2010].

- Trudel D, Horowitz L, Wormuth M, Scheringer M, Cousins IT and Hungerbuhler K. 2008. Estimating consumer exposure to PFOS and PFOA. *Risk Anal* 28(2): 251-269.
- US Environmental Protection Agency. 1997. Exposure Factors Handbook (Final Report), U.S. Environmental Protection Agency, Washington, DC, EPA/600/P-95/002F a-c.
- US Environmental Protection Agency. 2004a. DuPont PFOA site-related monitoring and environmental assessment at Washington, West Virginia EPA-HQ-OPPT-2004-0113
- US Environmental Protection Agency. 2004b. Memorandum of understanding between the US Environmental Protection Agency and E. I. DuPont De Nemours and Company for a Perfluorooctanoic acid (PFOA) site-related environmental assessment program. EPA-HQ-OPPT-2004-0113-0002.
- US Environmental Protection Agency. 2009. Provisional health advisories for perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS). EPA-HQ-OW-2007-1189-0183.
- US Environmental Protection Agency. 2010a. Perfluorooctanoic acid (PFOA) and fluorinated telomers: Enforceable consent agreement (ECA) process to generate additional information. Available: <http://www.epa.gov/opptintr/pfoa/pubs/eca.html> [accessed 16 August 2010].
- US Environmental Protection Agency. 2010b. Perfluorooctanoic Acid (PFOA) and Fluorinated Telomers: 2009 annual progress reports. Available: <http://www.epa.gov/opptintr/pfoa/pubs/stewardship/preports3.html#2008>. [accessed 16 August 2010].
- Vieira V, Webster T, Bartell S, Steenland K, Savitz D and Fletcher T. 2008a. PFOA community health studies: Exposure via drinking water contaminated by a Teflon manufacturing facility. *Dioxin 2008 - 28th International Symposium on Halogenated Persistent Organic Pollutants (POPs)*, Birmingham England UK.
- Vieira V, Webster T, Bartell S, Steenland K, Savitz D and Fletcher T. 2008b. PFOA community health studies: Exposure via drinking water contaminated by a Teflon manufacturing facility. *Organohalogen Compounds* 70 730-732.
- Washburn ST, Bingman TS, Braithwaite SK, Buck RC, Buxton LW, Clewell HJ, et al. 2005. Exposure assessment and risk characterization for perfluorooctanoate in selected consumer articles. *Environ Sci Technol* 39: 3904-3910.
- Webster TF. 2000. Bias in ecologic and semi-individual studies. [PhD Dissertation] . Boston, MA: Boston University.
- Webster, TF. 2002. Commentary: Does the spectre of ecologic bias haunt epidemiology? *International Journal of Epidemiology* 31:161-162.

Yohai VJ. 1987. High breakdown-point and high efficiency robust estimates for regression. Ann Statist 15(2): 642-656.

Table 1: Pharmacokinetic parameter values and sources.

Parameter	Symbol	Value	Data Source
Water intake	Q	1.4 L/day	US EPA1997
Fraction of PFOA absorbed ^a	f	100%	Gibson and Johnson 1979
Half-life	$t^{1/2}$	2.3 years, 840 days	Bartell et al. 2010
Volume of distribution ^a	Vd	male 181 ml/kg Female 198 ml/kg, multiplied by individual body weight	Butenhoff et al. 2004

^a based on animal data

Table 2: Selected population characteristics (number (%)), serum PFOA concentrations ($\mu\text{g/L}$) (median serum concentration and interquartile range (IQR)), and statistical significance of difference (p-value).

Characteristic	N (%)	Median serum PFOA (IQR)	p-value
Total Population	108 (100 %)	75.7 $\mu\text{g/L}$ (31.5-130.5)	
Male	51 (47.2 %)	82.2 $\mu\text{g/L}$ (45.9-164.3)	0.10
Female	57 (52.8 %)	68.1 $\mu\text{g/L}$ (21.0-115.5)	
Grow own vegetables			
No	64 (59.3 %)	50.7 $\mu\text{g/L}$ (24.9-107.3)	<0.001
Yes	44 (40.7 %)	91.2 $\mu\text{g/L}$ (57.0-145.2)	
Employed at DuPont			
No	94 (87.0 %)	67.6 $\mu\text{g/L}$ (72.2-102.4)	0.11
Yes	14 (13.0 %)	87.1 $\mu\text{g/L}$ (27.4-145.1)	
Age			
=< 65 Years	63 (58.3%)	59.8 $\mu\text{g/L}$ (20.6-115.9)	0.35
> 65 Years	45 (42.7%)	84.9 $\mu\text{g/L}$ (49.0-145.1)	
Body Weight			
=< 80 kg	50 (46.3%)	63.5 $\mu\text{g/L}$ (31.5-107.7)	0.64
> 80 kg	58 (53.7%)	81.2 $\mu\text{g/L}$ (30.1-177.4)	

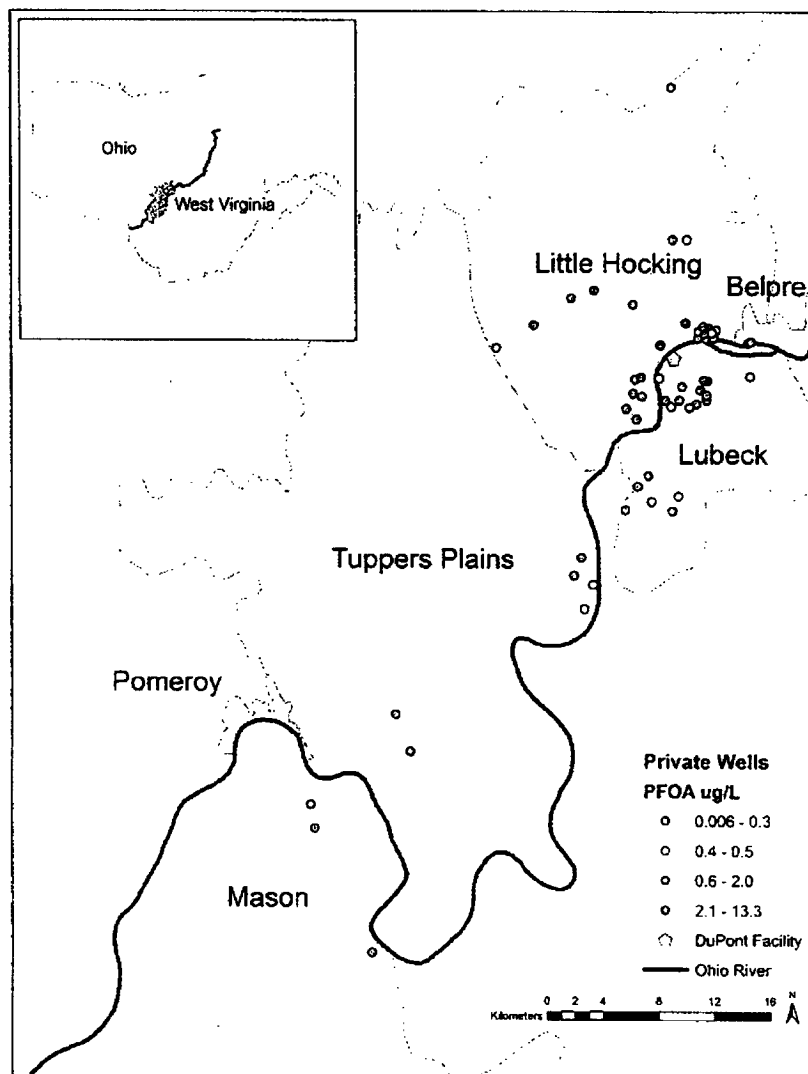
Table 3: Adjusted^a robust regression model of serum PFOA µg/L.

Covariate	Beta	(95% CI)
Intercept	7.4	(-9.8 to 24.4)
Well PFOA µg/L	141.5	(134.9 to 148.1)
Males	18.8	(-1.6 to 39.1)
Age > 65 Years	-4.2	(-24.2 to 15.9)
Grow Own Vegetables	18.4	(-1.3 to 38.1)
Employed at DuPont	5.9	(-24.1 to 36.2)

^a The inclusion of other covariates (body weight, bottled water consumption, cigarette smoking, and alcohol consumption) did not alter the main associations.

Figure Legend:

Figure 1: Water districts included in the C8 Health Project and the locations of private drinking water wells. The average PFOA concentration ($\mu\text{g/L}$) in each private well is shown.



215x279mm (500 x 500 DPI)

Supplemental Material

Private Drinking Water Wells as a Source of Exposure to PFOA in Communities Surrounding a Fluoropolymer Production Facility

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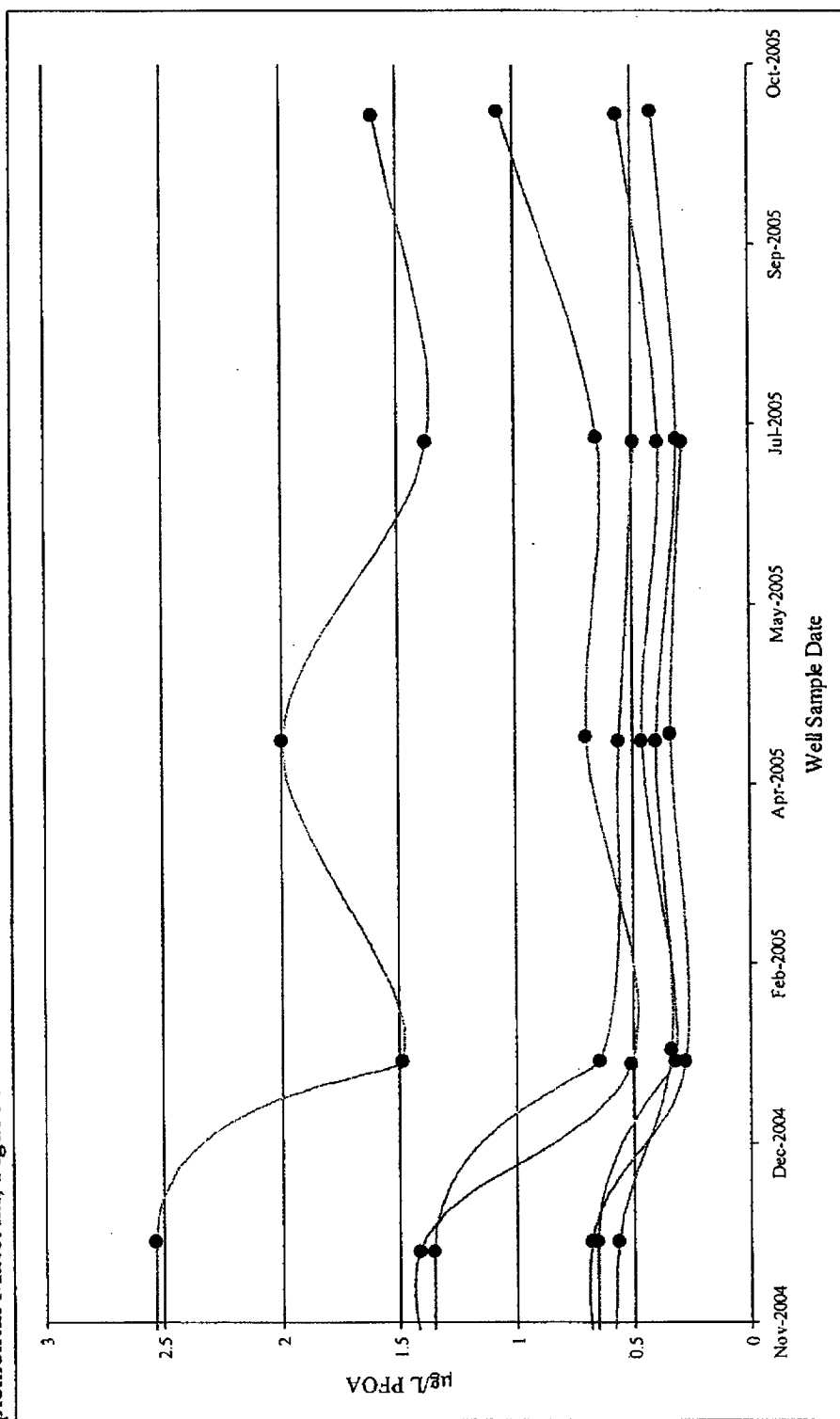
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Supplemental Material, Figure 1:



Supplemental Material, Figure 1: Time variation in well PFOA concentration. PFOA concentration (µg/L) in a subsample of 6 wells measured at least 4 times between November 2004 to October 2005 (other wells had fewer measurements during this time period). Black circles indicate sampling points. We have connected the points to make it easier to distinguish measurements taken in the same well; these lines may not represent the actual well PFOA concentration.

The time-weighted water concentration $\overline{C}_w$ computed using the weights α_j is given by:

$$\overline{C}_w = \sum_{j=1}^q \alpha_j C_{wj} \quad [3]$$

The weight during each time point is give by:

$$\alpha_j = \left(1 - e^{-k(t_j - t_{j-1})}\right) e^{-k(t_q - t_j)} \quad [4]$$

We included the time weighted PFOA concentration in well in regression models based on these equations. PFOA concentrations in each well varied by season, but in general there did not seem to be a long-term trend from 2001 to 2005 in the concentrations in each well; the arithmetic and time-weighted concentrations were very similar. Consequently, using either method produced a similar estimate of the ratio of serum to drinking water PFOA concentrations.

References:

Bartell S. 2003. Statistical methods for non-steady state exposure inference using biomarkers. [PhD Dissertation]. Davis, CA: University of California, Davis.

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Non-steady state pharmacokinetics:

For participants on a private well with PFOA levels that varied over time, steady-state models could provide inaccurate estimates of serum PFOA levels. Although data on the changes in PFOA concentrations over time were not collected in all wells, multiple measurements of PFOA were taken in 11 wells during the study period. We therefore performed another regression model using time-weighted well concentrations (rather than arithmetic average as before). The time-weighted concentration was derived from the non-steady state model given by (Bartell 2003):

$$C_s(t_q) = \sum_{j=1}^q \frac{fQ C_{wj}}{kV_d} \cdot (1 - e^{-k(t_j - t_{j-1})}) \cdot e^{-k(t_q - t_j)} \quad [1]$$

where $C_s(t_q)$ is the serum PFOA concentration at time q , Q is the daily water intake (L/d), C_{wj} is the concentration of PFOA present in drinking water during time period j ($\mu\text{g/L}$), f is the fraction of PFOA absorbed, k is the first-order rate constant for PFOA elimination (day^{-1}), and V_d is the apparent volume of distribution (L).

Bringing the constants out from within the summation, equation 1 the blood concentration (C_s) is given as a function of the constants (f , Q , k and V_d) and the time-weighted water concentration ($\overline{C_w}$):

$$C_s(t_q) = \frac{fQ}{kV_d} \sum_{j=1}^q \alpha_j C_{wj} = \frac{fQ}{kV_d} \overline{C_w} \quad [2]$$