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Title: An Analysis of the 2000 Fluorochemical (Perfluorooctanoate, PFOA) Medical Surveillance Program at 3M Company's Antwerp (Belgium), Cottage Grove (Minnesota), and Decatur (Alabama) Facilities

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Abstract

The 3M Company has published several periodic medical surveillance studies of its fluorochemical production workers at its Antwerp (Belgium), Cottage Grove (Minnesota) and Decatur (Alabama) manufacturing facilities. These programs have compared clinical chemistry results in relation to serum measurements of perfluorooctanesulfonate (PFOS) and/or perfluorooctanoate (PFOA). Toxicologically, PFOA is a peroxisome proliferator alpha receptor (PPARα) agonist and exerts morphological and biochemical effects characteristic of PPARα agonists including beta-oxidation of fatty acids, increased CPY450-mediated reactions, and inhibition of the secretion of very low-density lipoproteins and cholesterol from the liver in rats and mice. In worker studies there have been no consistent associations with PFOA and various clinical chemistry measurements. A weak positive association between PFOA and serum total cholesterol was reported in an analysis of a the 2000 fluorochemical medical surveillance data for Antwerp and Decatur employees combined but it was considered a spurious finding based on the understanding that a hypolipidemic effect would be the hypothesis to be tested from the toxicological data. A subsequent unpublished brief letter from DuPont reported that total cholesterol, LDL and triglycerides, but not HDL, were positively associated with their employees' serum PFOA concentrations but the authors urged caution as minimum variance was explained in their analyses. In light of these findings, the purpose of this study was to reanalyze the 2000 fluorochemical medical surveillance male employee database (n = 552) which included three facilities: Antwerp, Cottage Grove and Decatur and to stratify the analyses by employees' self-reported cholesterol lowering medication

status concentrating on those individuals (n = 506, 92 percent) who reported they were not taking cholesterol lowering medications.

Using several types of statistical analyses (analysis of variance, analysis of covariance, logistic regression and multiple regression using multiplicative models), there was no evidence that PFOA [adjusted for age, body mass index (BMI) and alcohol] was statistically significantly ($p < .05$) positively or negatively associated with serum total cholesterol or LDL (calculated by the Friedwald formula when serum triglycerides were less than 400 mg/dL) regardless of cholesterol lowering medication status. Although HDL was negatively associated with PFOA for the combined three locations, only one percent of its variance was explained with PFOA and this association was not observed when the data were stratified by location. Thus, the association observed with HDL and PFOA was likely due to residual confounding between the locations themselves rather than to any possible causal association with PFOA. For the combined locations, serum triglycerides were positively associated with PFOA but not consistently by location. Antwerp, the location with the lowest mean triglyceride and PFOA concentrations, showed a positive association whereas Cottage Grove, with the highest mean PFOA and triglyceride levels, showed no association between triglycerides and PFOA. A hypothesis is offered that the inconsistent associations observed for serum triglycerides and PFOA might be due to non-adherence to fasting requirements by night shift production workers since all sample collections occurred in the morning for production and non-production employee participants. The former would have higher serum PFOA concentrations. Also, shift workers, in general, have been reported to have more elevated

serum triglycerides. To clarify an association, if any, between PFOA concentrations and serum triglyceride levels, the methodological questions raised herein merit further inquiry.

Adjusted for the potential confounding factors of age, BMI or triglycerides, and alcohol, the three locations combined did not result in consistent associations with hepatic enzyme tests. Whereas the individual Antwerp and Cottage Grove locations showed no statistically significant associations, weak positive associations were observed in the multiplicative models between alkaline phosphatase, ALT, and GGT with PFOA (adjusted for age, BMI or triglycerides, and alcohol) among the Decatur male employee population which could be due to residual confounding as minimum variance was explained by PFOA in these models. Several epidemiologic research studies of the Decatur workforce have not found statistically significantly increased risks for hepatic disease (malignant or nonmalignant conditions) using a variety of data sources including episodes of care, self-reports, and death certificates. Other worker populations and a community-based PFOA-exposed population have also not reported positive associations between liver enzyme test results and serum PFOA concentrations.

Few individual thyroid-related hormone (TSH, T4, free T4, and T3) results were out-of-reference range. Analyses of the multiplicative models predicted these thyroid-related hormone measurements would be well within their normal reference ranges when PFOA concentrations varied between 0.005 µg/mL (average general population concentration reported) and 100 µg/mL (high range of occupational measurements historically

reported). The lack of an association with clinically relevant thyroid test results has also been reported in other worker and community-based studies of PFOA whose average serum concentrations were at or below those reported in the present study.

Introduction

The 3M Company has published several periodic medical surveillance studies of its fluorochemical production workers at its Antwerp (Belgium), Cottage Grove (Minnesota) and Decatur (Alabama) manufacturing facilities (Ubel 1980; Gilliland and Mandel 1996; Olsen et al. 1998; 1999; 2000; 2003a; 2003b). These programs have compared clinical chemistry results in relation to serum measurements of perfluorooctanesulfonate (PFOS) and/or perfluorooctanoate (PFOA).

Serum PFOS concentrations measured in these 3M employees have been routinely compared with serum total cholesterol levels as a decline in the latter has been a consistent early reliable measure of clinical response reported in laboratory animal studies (3M Company 2003; Haughom and Spydevold 1992; Seacat et al. 2002; 2003). No association between PFOS and cholesterol has been observed in these fluorochemical medical surveillance programs, and is likely due to the fact that the serum PFOS concentrations measured (average approximately 1 to 2 μg/mL, maximum < 14 μg/mL) were below those measured in laboratory animals where effects have been reported (Olsen et al. 1999; 2003a; 2003c). Among cynomolgus monkeys fed PFOS in the diet for 6 months, statistically significant decreases in cholesterol from predose values occurred in the high dose group (0.75 mg/kg/day) that had serum PFOS concentrations above 100 ppm (Seacat et al. 2002). This serum PFOS concentration in the high dose group corresponded to 50 mg/kg and 34 mg/kg cumulative doses in males and females, respectively. Seacat et al. (2002) considered this decrease in serum total cholesterol the

earliest reliable measure of clinical response to PFOS in these cynomolgus monkeys. Lowered HDL values were also reported in the 0.75 mg/kg/day dose group. However, a lack of prestudy and interim HDL values in a lower dose group (0.15 mg/kg/day) made this interpretation more problematic. In a sub-chronic dietary toxicity of PFOS in rats, Seacat et al. (2003) did not report strong evidence for hepatocellular peroxisomal or cellular proliferation at the doses tested (0, 0.5 2.0 5. 0 and 20 parts per million in diet) Lowered serum cholesterol was observed although decreased glucose among male animals at the high dose at 4 weeks (but not at 14 weeks or with females at 4 or 14 weeks) and elevated alanine transaminase levels (ALT) at 14 weeks in males (but not females) were also reported. The mode of action for serum cholesterol reduction is uncertain but may be due, in part, to PFOS acting as a peroxisome proliferator alpha receptor (PPARα) agonist.

PFOA is a PPARα agonist and exerts morphological and biochemical effects characteristic of PPARα agonists including beta-oxidation of fatty acids, increased CPY450-mediated reactions, and inhibition of the secretion of very low-density lipoproteins and cholesterol from the liver in rats and mice (Haughom and Spydevold 1992; DePierre 2002; Kennedy et al. 2003; Xie et al. 2003). These effects resulted in a reduction of serum cholesterol and triglycerides in rats and mice. Xie et al. (2003) have shown that severe adipose tissue atrophy occurs upon dietary treatment of mice with PFOA but is rapidly reversed after termination of treatment. Hepatomegaly, however, was much more persistent after dose termination. Unlike rats and mice, there was no reduction in serum cholesterol in cynomolgus monkeys dosed with PFOA (ammonium

salt) for 6 months (Butenhoff et al. 2002). PFOA was statistically significantly positively associated with triglycerides in the high-dose (30/20 mg/kg) group whose steady state serum PFOA concentration was 158 μg/mL ± 10 μg/mL (range 20 to 467 μg/mL). This association between PFOA and serum triglycerides was observed in measurements taken after one month of dosing at which time the group mean triglyceride level was significantly higher than control values as well as within group pretreatment values. At the end of the study the mean triglyceride was elevated compared to time related controls but not to the animals' pretreatment values. However, only two primates were evaluated in the high-dose group at end of study. Inspection of individual values for PFOA serum concentration and serum triglyceride values did not reveal a meaningful association between these two parameters (John Butenhoff, personal communication; see Olsen et al. 2003a).

In worker studies there have been no consistent associations with PFOS or PFOA and various clinical chemistry measurements (Gilliland and Mandel 1996; Olsen et al. 1998; 1999; 2000; 2003a; 2003b). Gilliland and Mandel (1996) did report that PFOA (measured as the surrogate serum total organic fluorine) may negatively modulate the effect alcohol has on high-density lipoprotein (HDL) levels and exacerbate the effect that obesity has on hepatic enzyme tests. However, three subsequent analyses of this employee population that measured specifically for PFOA did not find that it modulated hepatic responses to either obesity or alcohol consumption (Olsen et al. 2000).

Previous analyses of the most recently published fluorochemical medical surveillance data conducted at the 3M Antwerp and Decatur facilities (conducted in 2000) primarily concentrated on PFOS analyses although data were also presented for PFOA. In these PFOA-specific analyses, Olsen et al. (2003a) reported a positive association with serum cholesterol and triglycerides with PFOA. They attributed this to be a spurious finding given the toxicological evidence would suggest a hypolipidemic (not hyperlipidemic) effect, along with the fact that minimum variation was explained in the statistical models (partial R^2 for PFOA in the models was <0.01 (cholesterol) and 0.03 (triglycerides), respectively) used in the analyses. In the same published paper, Olsen et al. (2003a) also provided a longitudinal analysis of 174 Antwerp and Decatur male employees who participated in at least two of three fluorochemical medical surveillance programs between 1994 and 2000 and found PFOA to also be positively associated with cholesterol as well as triglycerides. This association was primarily attributed to 21 Antwerp employees whose mean serum PFOA levels increased over a six-year period of time from 1.32 ppm to 2.06 ppm. During the same time period, their mean cholesterol values increased from 208 mg/dL to 229 mg/dL and their triglyceride levels increased from 85 mg/dL to 123 mg/dL. Their BMIs, however, also increased from 23.4 to 24.3 during this same time period. No statistically significant associations were reported between PFOA and either serum cholesterol or triglycerides for the Cottage Grove male employees who participated in the 2000 fluorochemical medical surveillance program (Olsen et al. 2003a). Analyses of prior fluorochemical medical surveillance programs at Cottage Grove (1993, 1995 and 1997) showed mean serum triglyceride levels were highest among the Cottage Grove PFOA production workers with the highest (>= 10 ppm) PFOA

serum concentrations although controlling for potential confounders did not provide consistent results as well as the fact that several of the observations in the high exposure category were repeated measurements from the same individuals.

Based on the possibility of a positive association between PFOA and serum cholesterol and/or triglycerides that was not supported by laboratory (toxicological) data and was therefore considered a spurious association (Olsen et al. 2003a), others have since provided nonpublished data (Costa 2004; Leonard 2005). Costa (2004) provided cursory analyses of approximately 35 Italian fluorochemical production workers and reported a "slight increase of total cholesterol in workers exposed to PFOA." There was no increase of other lipids, such as triglycerides, but the fraction of non-HDL cholesterol appeared elevated. Costa suggested his findings might be consistent with the hypothesis that PFOA might influence cholesteryl ester transfer protein (CETP). CETP is a plasma glycoprotein that facilitates the transfer of cholesteryl esters from HDL (apolipoprotein A-containing lipoprotein) to apolipoprotein B-containing lipoproteins (e.g., LDL) (Brousseau et al. 2004). Inhibition of CETP has been shown to markedly elevate plasma levels of HDL and apolipoprotein A1. However, there did not appear to be a decrease in HDL in the Costa analysis. Several additional caveats also existed in the Costa data analysis as outlined by Kaplan (2005) including: 1) the Costa data set was a small and arbitrary collection of subjects; 2) there were no pre-employment/baseline lipid levels for historical reference; 3) concomitant exposure to other chemicals was unknown; and 4) inadequate adjustment for important confounding factors. In addition, many of these

individuals were the same subjects over time and no repeated measures analysis was conducted.

Leonard et al. (2005) have provided to the U.S. EPA an unpublished one page report that briefly summarized a cross-sectional analysis of 782 male and 243 female (combined eligible population 1,863) DuPont workers with potential exposure to PFOA at the Parkersburg, West Virginia facility. Of the 62 clinical chemistry and hematology endpoints measured, Leonard et al. found most were well within normal ranges and not associated with serum PFOA levels. Measured PFOA concentrations were reported as high as 10 μg/mL (parts per million, ppm) but the average was less than 1 μg/mL (Leonard, personal communication). No statistically significant associations were observed for PFOA and serum liver enzymes or any hematology measures and PFOA. EKGs and C-reactive protein were not associated with PFOA. Statistically significant positive associations were identified for total cholesterol, LDL and triglycerides with serum PFOA levels adjusted for BMI, alcohol and age in both males and females although the percent variation explained was generally low. The potential change in total cholesterol at the highest serum PFOA level was approximately 10 percent. No effect, however, was seen in the HDL fraction. Small, but statistically significant increases in uric acid and iron were also reported with the highest PFOA blood levels. A suggested role for PFOA to enhance CETP activity, as discussed by Costa, however, was not supported by the much larger Leonard et al. analyses since the latter investigators showed no association between PFOA and HDL. Leonard et al. offered no hypotheses or suggested causal models (Hernán et al. 2002) to explain their observations. Because

PFOA has been shown to bind to blood albumin in the rat, monkey and human (Han et al. 2003; Kerstner-Wood et al., 2003), a positive correlation, and not a causal association, between lipoproteins (binding) and PFOA is a possibility.

Re-examination of the Olsen et al. analyses conducted of the 2000 fluorochemical medical surveillance program at the Antwerp and Decatur facilities (Olsen et al. 2001a; 2001b; 2001c; 2001d; 2003a) and the Cottage Grove facility (Olsen et al. 2003b) suggested some limitations of these data analyses as they may relate to testing a hypothesis that PFOA is positively associated with total cholesterol and its fraction, LDL. First, all male subjects were included in the original analysis regardless of their cholesterol lowering medication status. A positive association may be masked by inclusion of subjects whose serum cholesterol levels have been reduced by medication if such an increase was, in part, associated with higher PFOA concentrations. Second, LDL analyses were not restricted to those instances where serum triglycerides were 400 mg/dL or less. The potential for bias steadily increases with higher triglyceride levels (Nakanishi et al. 2000). Third, the Antwerp and Decatur facility study (Olsen et al. 2003a) concentrated primarily on PFOS and not PFOA. Both PFOS and PFOA have been shown to result in hypolipidemia in rats at high concentrations and thus the causal model hypothesized in these earlier analyses concentrated on testing for this effect, not hyperlipidemia. Olsen et al. (2003a) did not show a causal association between PFOS and lowered cholesterol at the serum concentrations measured in these workers. Direct comparison with PFOA from the Olsen et al. (2003a) report is not possible since the many of the tabular analyses (e.g., Table 2 of Olsen et al. 2003a) were PFOS-specific.

Although the employees' PFOS and PFOA concentrations were correlated, the categorical analyses of PFOS did result in overlapping of employees' PFOA concentrations. Fourth, there was no combined analysis of the three manufacturing facilities, Antwerp, Cottage Grove and Decatur, as the Cottage Grove analysis has historically been reported separately (Ubel et al. 1980; Gilliland and Mandel 1996; Olsen et al. 2000; 2003a). Those sites that were combined (Antwerp and Decatur) may have resulted in unmeasured and/or residual confounding since the two locations were distinctly different with some potential confounding variables, most especially alcohol consumption and BMI (Olsen et al. 1999; 2003a).

With the above limitations in mind, the purpose of this study was to reanalyze the 2000 fluorochemical medical surveillance program data in order to examine the hypothesis that PFOA may be positively associated with increased cholesterol, LDL levels and triglyceride levels. To address some of the above limitations, the three manufacturing facilities were analyzed separately and jointly. Analyses concentrated on those male employees who self-reported that they were not taking cholesterol lowering medications in order to minimize any unexplained bias. Because PFOS concentrations were not previously associated with lowered serum cholesterol (Olsen et al. 2003), it (PFOS) was not considered an important potential confounding variable in these reanalyses for PFOA. Three covariates were: age, BMI and alcohol. Age is known to be positively associated with serum cholesterol. BMI is positively associated with serum triglycerides (and to some degree cholesterol) and alcohol consumption (e.g., red wine) has been positively associated with increased HDL. In addition to the lipid variables analyzed, liver enzyme

and thyroid tests were also reanalyzed. Although liver enzymes, in particular gamma glutamyl transferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) can be positively associated with heavy alcohol consumption, liver enzymes can also be due to obesity and dyslipidemia (Collantes et al. 2004; Mofrad and Sanyal 2003; Ruhl and Everhart 2003) as nonalcohol fatty liver disease has substantially increased in prevalence in the United States population, as indicated by the third National Health and Nutrition Examination Survey (NHANES) (Clark et al. 2003). Whereas the majority of elevated aminotransferase activity in NHANES could not be explained by alcohol consumption, viral hepatitis or hemochromatosis, unexplained aminotransferase enzyme elevation was significantly associated with higher BMI, waist circumference, triglycerides, fasting insulin, and lower HDL (Clark et al. 2003). Clark et al. (2004) concluded that unexplained aminotransferase elevation was strongly associated with adiposity and other features of the 'metabolic syndrome', and thus may represent nonalcoholic fatty liver disease. [Note: The metabolic syndrome includes abdominal obesity, atherogenic dyslipidemia (elevated triglyceride, small LDL particles, low HDL cholesterol), raised blood pressure, insulin resistance (with or without glucose intolerance) , and prothrombotic and proinflammatory states (Expert Panel 2001). Clinical identification of the metabolic syndrome in men includes any three of the following: waist circumference > 40 inches (surrogate BMI >= 30); triglycerides 150 mg/dL; HDL < 40 mg/dL; blood pressure 130/85 mmHg; and fasting glucose 110 mg/dL.] As they relate to the present study, the NHANES findings indicate BMI and serum triglycerides are important predictors of liver enzyme values and therefore should be controlled in any analyses that examine the relationship between PFOA and liver

enzyme tests (e.g., ALT, GGT), as was done previously with analyses with serum PFOS concentrations in this employee population (Olsen et al. 2003a).

Methods

The following clinical chemistry variables were considered dependent variables for reanalysis of the 2000 fluorochemical medical surveillance program data: alkaline phosphatase (IU/L), gamma glutamyl transferase (GGT, IU/L), aspartate aminotransferase (AST, IU/L), alanine aminotransferase (ALT, IU/L), total and direct bilirubin (mg/dL), blood glucose (mg/dL), cholesterol (mg/dL), low density cholesterol (LDL, mg/dL), high density cholesterol (HDL, mg/dL), and triglycerides (mg/dL). These measurements were performed at Allina Laboratories (St. Paul, MN). LDL was an indirect calculation using the Friedwald formula [LDL = total cholesterol – (triglycerides/5)]. Presented in this report are LDL values where serum triglycerides did not exceed 400 mg/dL. LDL was also calculated when serum triglycerides did not exceed 250 mg/dl as well as for all triglyceride levels. Results were not substantially different for LDL regardless of formula used. Thyroid stimulating hormone (TSH; μIU/mL); serum thyroxine (T4; μg/dL); free thyroxine (free T4; ng/dL) and serum triiodothyronine (T3; pg/mL) were also re-examined. These thyroid related hormones were measured by LabCorp (Kansas City, MO). Thyroid hormone analyses excluded the five individuals who were already diagnosed with thyroid-related conditions and likely taking medication. Analyses did not substantially differ with these individuals included.

Details of the method validation including matrix extraction and analytical measurement procedures used to determine serum PFOA and PFOS can be found elsewhere (see U.S. EPA docket AR226-1208, AR226-1209, AR226-1210). The analytical method consisted of a liquid:liquid extraction procedure followed by evaporation and reconstitution of the extract residue with 30:70 20 mM ammonium acetate in water:20 mM ammonium acetate in methanol (v/v). The samples were analyzed by liquid chromatography/tandem mass spectrometry using a PE Sciex API 3000. The instrument was operated in the multiple reaction monitoring (MRM) mode under optimized conditions for detection of PFOS and PFOA for detection of negative ions formed by turbo ionspray ionization. Laboratory analyses were conducted at Tandem Laboratories, Salt Lake City, UT (formerly Northwest Bioanalytical Laboratory Inc.). All employee serum values (μg/mL) for PFOA (and PFOS) were above the lower limit of quantitation (LOQ).

Statistical analyses included both univariate and multivariable methods (analysis of variance, analysis of covariance, logistic regression, multiple regression) using JMP (Cary, NC) and Stata (College Station, TX) software. Age, BMI and alcohol (drinks per day) were considered as covariates in multivariable models. For analysis of hepatic enzyme tests in these models, triglycerides were also considered in place of BMI. Distributions were examined to assess normality using nontransformed and transformed (log, square root, inverse) variables. In general, log transformations improved normality assumptions of response and explanatory variables and thus multiplicative models were considered applicable (T. Church, personal communication). For the log transformation of alcohol, 0.1 was added to drinks per day to prevent the log of 0. Residual plots were

examined to detect model inadequacies including homoscedasticity. Goodness of fit statistics were examined including R^2 and adjusted R^2. Multicollinearity in the models was assessed by the inverse of tolerance (Variation Inflation Factor). Crude and adjusted odds ratios for PFOA categorized by deciles were determined via logistic regression analyses for reference range values of the response variable.

A review of the 2000 Cottage Grove database used in the Olsen et al. (2003b) report found eight male employees had missing BMI and/or alcohol information. For the present study, a review of the subjects' Cottage Grove medical records by the plant nurse provided these data and was generally within two years of the 2000 Cottage Grove medical surveillance program.

Graphical analyses were performed to examine patterns of association (see Appendix A) for PFOA. Graphs in Appendix A include nontransformed as well as transformed (natural log) variables. Density ellipses are also provided in Appendix A for PFOA. A density ellipsoid was considered a good graphical indicator of the correlation between two variables. The ellipsoid collapses diagonally as the correlation between two variables approaches either 1 or -1. The ellipsoid is more circular (less diagonally oriented) if the two variables were uncorrelated.

Results

A total of 196 (95%) of the 206 Antwerp male employee participants, 122 (93%) of the 131 Cottage Grove male employee participants and 188 (87%) of the 215 Decatur male

employee participants were included in the primary reanalyses of the 2000 fluorochemical medical surveillance program (Table 1). These 506 (92%) participants represent those who did not self-report taking choleseterol lowering medications.

The mean PFOA concentration was statistically significantly ($p < .05$) higher among Cottage Grove than either Antwerp or Decatur male employee participants but the median PFOA concentration for Decatur was somewhat higher than either Antwerp or Cottage Grove participants (Table 2). [Note: Decatur also had a slightly higher mean concentration for PFOS than Antwerp or Cottage Grove employee participants, with the median value approximately twice that of Antwerp or Cottage Grove.] As has been reported before (Olsen et al. 1999; 2003a), Antwerp employees were statistically significantly younger, had lower BMIs, and consumed more alcohol than their counterparts at Decatur, and in the present analysis, also Cottage Grove. Whereas mean cholesterol and LDL were not statistically significantly different between the three locations, mean HDL levels were statistically significantly higher among Antwerp employees whereas their triglyceride and blood glucose levels were significantly lower. Mean (arithmetic) liver enzyme tests were statistically significantly lower for Antwerp compared to Cottage Grove and Decatur employees except for total and direct bilirubin. Antwerp employees had a statistically significantly lower mean TSH than Decatur employees and y higher mean T3 than the Cottage Grove or Decatur employees. These mean thyroid values, however, were well within the reference range.

The number and percent of employees by reference points for demographic factors and clinical chemistry results are presented in Table 3. As expected based on the data presented in Table 2, there were substantially fewer Antwerp employees (5%) who would be categorized as obese (BMI $\geq$ 30) compared to Cottage Grove (44%) or Decatur (32%) employees. More than 40% of Antwerp and Cottage Grove employees reported drinking 1 alcohol beverage per day compared to only 1% of Decatur employees. Statistically significant differences between the three locations were seen for blood glucose, HDL, triglycerides, ALT, and total bilirubin. There was only 1 percent of the Antwerp employees who were categorized as having the 'metabolic syndrome' compared to 20% and 13% among the Cottage Grove and Decatur employees, respectively. The present study definition of the metabolic syndrome included any three of the following four: BMI $\geq$ 30; triglycerides $\geq$ 150 mg/dL; HDL $<$ 40 mg/dL; and fasting glucose $\geq$ 110 mg/dL.

Presented by PFOA quartile ranges are the data for Antwerp (Table 4), Cottage Grove (Table 5) and Decatur (Table 6). Quartiles were divided to allow for a defined break in PFOA concentrations. Among Antwerp employees, the mean value in the first PFOA quartile was statistically significantly different than the fourth PFOA quartile for PFOA, PFOS, age, blood glucose, triglycerides and T3. Among Cottage Grove employees, the mean value in the first PFOA quartile was statistically significantly different (higher) than the fourth PFOA quartile for PFOA and AST. Among Decatur employees, the mean value in the first quartile was statistically significantly different (lower) than the fourth PFOA quartile for PFOA, PFOS, ALT, AST/ALT ratio, total bilirubin and T3. The

AST/ALT ratio is a useful index for distinguishing nonalcoholic fatty liver (steatohepatitis) disease (AST/ALT less than one) from alcoholic liver disease (AST/ALT greater than one). It should be noted that those locations (Cottage Grove and Decatur) with the highest obesity (as measured by BMI which is not necessarily as good of a measurement as waist/hip circumference ratio) had the lowest AST/ALT ratio.

The 506 employees from the three locations were combined and categorized into PFOA deciles in Table 7. Mean PFOA decile concentrations ranged from decile 1 of 0.06 μg/mL (range 0.007 – 0.13 μg/mL) to decile 10 of 12.15 μg/mL (range 3.71 – 92.03 μg/mL) with corresponding median values of 0.06 μg/mL and 4.94 μg/mL, respectively.

The distributions of demographic factors by PFOA decile are presented in Table 8. There was an uneven distribution of employees by location in these deciles. If there was a proportional distribution across deciles by location, then there would be 39% Antwerp, 24% Cottage Grove, and 37% Decatur employees in each decile. Instead, as seen in Table 8, there are higher percentages of Antwerp employees in the first 3 deciles and lower percentages in the highest two deciles (9 and 10). Likewise, there are lower percentages of Decatur employees in the first three deciles and higher percentages in the upper deciles (six through 10), in particular decile 9. Cottage Grove employees have higher than expected percentages in decile 1 and decile 10. Because of these uneven distributions, mean BMI values are greater in the upper deciles and alcohol consumption is lower, reflecting the demographic differences seen across the three facilities.

The mean and median PFOS concentrations by PFOA decile are presented in Table 9. In general PFOS concentrations increased by decile but not consistently. Deciles 7 through 10 are all statistically significantly higher than deciles 1 through 5.

Presented in tables 10 through 13 are the analyses for cholesterol, LDL, HDL and triglycerides. Table 10 is the univariate analysis by PFOA decile. Table 11 presents the mean decile values adjusted for age, BMI and alcohol using analysis of covariance. Table 12A presents adjusted odds ratios and 95% confidence intervals of the deciles by reference range cutoff points listed in the table using decile 1 as the reference. Odds ratios were adjusted for age, BMI and alcohol. Table 12B presents crude and adjusted (for location) odds ratios and 95% confidence intervals of the deciles by reference points for HDL and triglyceride. Table 13 presents non-adjusted and adjusted PFOA coefficients with cholesterol, LDL, HDL and triglycerides adjusted for age, BMI and alcohol in the multiplicative models. Analyses included all locations as well as presented individually for each location by itself.

Based on the analyses presented in Tables 10 through 13, cholesterol and LDL were not statistically significantly associated with PFOA whether across the combined three locations or each location analyzed separately. Adjusted mean HDL levels were lower in the highest (10^{th}) PFOA decile compared to deciles 1 through 4 (Table 11). The crude odds ratio was 3.0 (95% CI 1.2-7.5) for HDL < 40 mg/dL in decile 10 compared to decile 1 (Table 12B). However, this was reduced to an adjusted odds ratio of 1.5 (95% CI 0.6-4.0) when location was considered a covariate. Similar results were observed for

triglycerides (Table 12B). The adjusted PFOA coefficient in the multiplicative model for HDL was statistically significant at p = .01 (Table 13) but only explained 1 percent of the HDL variance in the full model ($R^2 = 0.26$), which was primarily attributable to BMI and alcohol. This finding with PFOA was also attributed to the decile disproportionate distribution of subjects as shown previously with the much greater proportion of Cottage Grove and Decatur employees in the highest two PFOA deciles. Multiplicative models stratified for each of the three locations showed no statistically significant findings between PFOA and HDL (Table 13).

Mean serum triglyceride levels were highest in decile 10 whether unadjusted or adjusted (Tables 12A and 12B). Odds ratios for triglyceride levels ≥ 150 mg/dL were highest for deciles 8 through 10. The multiplicative model for the combined three locations indicated a statistically significant coefficient ($p < .0001$) for PFOA (Table 13) which explained approximately 4 percent of the variance of the response variable. Stratified by location, however, showed only Antwerp to produce a statistically significant coefficient although Decatur had a marginal nonstatistically significant coefficient for PFOA (p = .07). No association (p = .38) was found between PFOA and triglycerides for Cottage Grove in the multiplicative models (Table 18). Cottage Grove had the highest PFOA concentrations of the three locations. As seen in Tables 2 and 3, serum triglyceride levels were considerably lower among Antwerp than Cottage Grove or Decatur employees.

Presented in tables 14 through 18 are the analyses for alkaline phosphatase, AST, ALT, AST/ALT ratio, GGT, and total and direct bilirubin. Table 14 is the univariate analysis

by PFOA decile. Table 15A presents the mean decile values adjusted for age, BMI and alcohol using analysis of covariance. Table 15B presents the mean decile values adjusted for age, triglycerides and alcohol using analysis of covariance. Table 15C presents the adjusted AST/ALT ratios. Table 16 presents the percent of employees by PFOA decile that were above reference range for these liver clinical chemistry tests. Tables 17A and 17B present adjusted odds ratios and 95% confidence intervals of the deciles by different reference range cutoff points for ALT and GGT provided in table 16 using decile 1 as the reference. These odds ratios were non-adjusted (crude), adjusted for age, BMI and alcohol, and adjusted for age, triglycerides and alcohol. Table 18 presents non-adjusted and adjusted PFOA coefficients of these liver enzymes using either age, BMI and alcohol or age, triglycerides and alcohol (natural logs) as covariates in the multiplicative models. Analyses in Table 18 included all locations as well as presented individually for each location.

Overall, the mean non-adjusted ALT is statistically significantly higher in deciles 9 and 10 compared to deciles 1 through 6 (Table 14) but this association is not evident upon adjustment of the mean values in Tables 15A or 15B. Odds ratios for values above the reference range are only calculated for ALT and GGT (Tables 17A and 17B) because these were the only liver clinical chemistry tests that had more than a few employees outside the reference range (Table 16). There were no statistically significant odds ratios (non-adjusted or adjusted) for ALT or GGT when compared to decile 1 (Table 17A). Analysis of a lower cutoff reference point ($\geq$ 40 IU) did not substantially alter the findings (Table 17B). Analyses did not result in any statistically significant associations

when all locations were included in the multiplicative models, except for total bilirubin (negatively associated) (Table 18). Stratified by location, Decatur had marginally statistically significant positive coefficients for alkaline phosphatase, ALT, GGT and a negative log coefficient for total bilirubin in the models. The amount of variance of the hepatic response variables explained by PFOA in these models was minimal ranging from <1 to 3 percent. These hepatic enzyme associations with PFOA were not observed for the individual Antwerp or Cottage Grove analyses.

Presented in tables 19 through 22 are the PFOA analyses with TSH, T4, free T4 and T3. Table 19 is the univariate thyroid analyses by PFOA decile. The mean TSH value in the 4^{th} decile (3.41 μIU/mL) is influenced by one subject whose TSH value was 65.28 μIU/mL. If removed from analysis, the mean of the 4^{th} decile became 2.15 μIU/mL and not statistically significant from any other decile. Table 20 presents the mean values adjusted for age, BMI and alcohol using analysis of covariance which includes the outlier in decile 4. The adjusted decile 10 of mean free T4 was statistically significantly lower than that of the first decile (Table 20). Table 21 presents the percent of employees by PFOA decile that were above reference range for these thyroid tests. Adjusted odds ratios and 95% confidence intervals are not presented in a separate table because of the few subjects whose thyroid tests were above or below the reference range as shown in Table 21. Only two of the 18 subjects in Table 21, that had TSH values above the upper reference range, had another thyroid related hormone result out of reference range (Table 22). One individual had a T4 value below reference range (with the highest TSH value in the analysis) and the other was above the reference range for T4 (Table 22). The former

was likely a clinically diagnosed hypothyroid individual (subject 45 in Table 22) who also had a low T4 just above the reference range. Table 23 presents non-adjusted and adjusted coefficients (natural log) of PFOA in the multiplicative models. For all locations combined, there were no statistically significant adjusted coefficients in the models except for free T4 (negative coefficient for PFOA) and T3 (positive coefficient for PFOA). However, the full multiplicative models (4 independent variables) explained only 5 and 2 percent of the variance of free T4 and T3, respectively. There were also positive PFOA coefficients for T3 in the individual Antwerp and Decatur locations (Table 23). Percent variances explained in these models were 9 and 7 percent, respectively. Because so few values were out-of-reference range (Table 21), the results presented in Table 23 are not suggestive of clinically relevant findings as the predicted results from these models (Table 24) were well within normal reference ranges for these thyroid parameters. Predicted serum PFOA concentrations, up to 100 µg/mL in Table 24, were 5 orders of magnitude greater than the average PFOA concentration reported in the general population (approximately 0.005 µg/mL). As shown in Table 24, these predicted PFOA concentrations resulted in TSH, T4, free T4, and T3 all within their normal reference ranges.

There was no association observed between metabolic syndrome, as categorized in this study, and PFOA, as shown in Table 24 which presents the number of people defined with metabolic syndrome and non-adjusted and adjusted (age) odds ratios and 95% confidence intervals by PFOA decile.

In addition to the analyses that focused solely on those male subjects who self-reported they were not taking cholesterol lowering medications as shown in Tables 1 through 24, other analyses examined those subjects (n = 46) who self-reported cholesterol lowering medication usage (See Appendix B, Tables B1 through B4). These 46 subjects were significantly older, and had tended to have higher mean BMI, serum glucose, triglycerides and liver enzyme tests than the 506 subjects who did not report cholesterol lowering medications. As seen previously, the Cottage Grove and Decatur employees were significantly more likely to have higher BMI values than Antwerp employees. Multiplicative models did not indicate, however, PFOA to be associated with the independent variables presented in Table B4, including cholesterol, LDL, HDL and triglycerides.

Appendix C (Tables C1 through C9) contains the combined (N = 552) analyses of the 506 male employees who did not report cholesterol lowering medications (Table 1 through Table 24) and the 46 who did (Tables B1 through B4 in Appendix B). Analyses were not substantially different whether they excluded (Tables 1 – 24) or included those employees who self-reported cholesterol lowering medications (Tables C1 through C8). For each analysis presented in Appendix C for the 552 male employees, there is a comparable analysis for those employees who did not take cholesterol lowering medications. For example, Table C1 is the PFOA decile distribution analysis for all 552 employees, regardless of cholesterol lowering medication status. The 46 employees who took cholesterol lowering medication are included in the deciles used for those employees who did not take such medication. See Table 7 for the comparable analysis for only

those employees (n = 506) who did not self report cholesterol lowering medications. Findings did not differ. Presented in Tables C2 and C3 are the odds ratios by decile for the lipid out-of-reference range values for all male employee participants (N = 552) regardless of cholesterol lowering medication status. See Tables 12A and 12B for the 506 employees who did not self-report cholesterol lowering medications. Results were comparable. Table C4 presents the odds ratios by PFOA decile for ALT and GGT values out-of-reference range for all male employee participants (N = 552) Comparable analyses for the more restricted subset of 506 employees who did not take cholesterol lowering medications are found in Table C7. Findings did not differ. Tables C4 through C6 contain both the non-prescribed (n = 506) and all male participants (n = 552) regression coefficients for the lipid (Table C4), liver enzyme (Table C6), and thyroid (Table C7) analyses. Analyses from the multiplicative models were not substantially different whether all male employee participants, or only those who did not self report cholesterol lowering medication usage, are included. The few employees among all participants (n = 552) who had out-of-reference range thyroid tests are presented in Table C8 (see Table 21 for comparison purposes for the 506 employees who did not take cholesterol lowering medications). Table C9 (as was previously done in Table 24 for Table 22) are the predicted thyroid test values for the regression model coefficients that were shown in Table C7. These results in Table C9 again showed that an increase in serum concentrations of PFOA, as high as 100 μg/mL, would not result in out-of-reference range thyroid clinical chemistry tests.

PFOA and PFOS serum concentrations were highly correlated among these employee participants of the 2000 fluorochemical medical surveillance program (Appendix A). For purposes of brevity, PFOS-related graphs are presented in Appendix D for the 506 employees who self-reported they did not take cholesterol lowering medications. Also, found in Appendix E are the coefficients from the multiplicative models examining the association for PFOA, as was done previously for PFOA for lipids (Table E1), liver enzymes (Table E2) and thyroid tests (Table E3) for the combined three facilities (Antwerp, Cottage Grove, and Decatur) as well as each facility separately. As seen with PFOA, there was a positive association with PFOS and triglycerides which is inconsistent with the known toxicological effects of PFOS. This association was likely due to the fact that higher PFOS concentrations were observed among the Cottage Grove and Decatur employees than Antwerp employees, the latter had the lower serum triglyceride values. No association with PFOS and triglycerides was seen when Cottage Grove and Decatur employees were analyzed separately as shown in Table E1. A positive association was observed with triglycerides and PFOS among Antwerp workers only, similar to what has already been reported for PFOA in this subgroup of workers (Olsen et al. 2003a). Inconsistent findings were observed for ALT and PFOS as there was a statistically significant negative association with Antwerp employees and a positive association with Decatur employees (Table E2). Other liver enzyme tests provided no consistent patterns of association. Thyroid related tests also provided no consistent measures of association in the multiplicative models presented in Table E3.

Discussion

Based on an analysis of 506 male participants of the 2000 fluorochemical medical surveillance program offered at the Antwerp, Cottage Grove, and Decatur facilities who self-reported that they did not take cholesterol lowering medications, there was no indication that these employees' serum PFOA concentrations were positively or negatively associated with serum total cholesterol or LDL.

A weak negative association was observed with HDL that was likely due to uncontrolled (i.e., residual) confounding, based on lower HDL values observed among the Cottage Grove and Decatur workers than the Antwerp workers and their markedly different demographic factors (e.g., BMI). When the analyses were stratified by location, no statistically significant associations were observed between HDL and PFOA. In another occupational study, Leonard (2005) did not report an association between HDL and serum PFOA concentrations. Neither did Emmett (2004) in a community-based study. To further clarify any possible association with HDL, the A apolipoproteins, which form the major proteins found in HDL, could be measured although this was not part of the present study. Apolipoprotein A-I was not associated with serum PFOA of comparable concentrations in a small analysis of Italian production workers (Giovanni Costa, personal communication).

Serum triglyceride levels were positively associated with PFOA but it is likely that this association was also due, at least partially, to residual confounding as a consequence of the a disproportionate number of Cottage Grove and Decatur employees with slightly

higher PFOA concentrations than the Antwerp employees. The same positive association was also observed between PFOS and serum triglycerides which are entirely inconsistent given the well-established hypolipidemia reported in PFOS-related toxicological studies whose concentrations were much higher than the present study (Seacat et al. 2002; 2003).

Of the four lipid measurements used in this study, serum triglycerides have approximately 3 times more intraindividual biological variation than either total cholesterol, LDL, or HDL (Stein and Myers 1994). Serum triglycerides may also be influenced by obesity, alcohol intake, and inattention to fasting requirements for blood collection. We hypothesize that the associations observed for serum triglycerides and PFOA in these workers might be the consequence of the non-adherence to fasting requirements by some shift production workers and/or the effect of postprandial metabolic responses in shift workers. Our explanation follows. First, production workers would be more likely to have higher PFOA concentrations than non-production workers (e.g., administrative, laboratory, engineers). This has been shown to be the situation at all three facilities: Antwerp (Olsen et al. 2001c); Cottage Grove (Olsen et al. 2003b) and Decatur (Olsen et al. 2001d; 2003). Second, only production workers engage in shift work. Third, required fasting blood collection occurred only during the morning for all participants. Fourth, it is conceivable that the night shift production workers, compared to day shift production workers as well as non-production workers, could have been less compliant with fasting requirements as well as consumed caffeinated beverages prior to their morning blood collection. Fifth, several studies have indicated postprandial serum triglyceride levels are higher among night shift workers (Al-Naimi et al. 2004; Morgan et

al. 2003; 1998; Karlsson et al. 2001; Lund et al. 2001; Sopowski et al. 2001). Therefore if a subset of subjects (production workers with higher PFOA serum concentrations) who worked night shift were less likely to adhere to the fasting requirements and/or have postprandial metabolic profiles of night shift workers, then a non-causal positive association between PFOA concentrations and serum triglycerides could be observed when all subjects are included in the analysis. At the time of data blood collection we did not obtain shift status information and therefore within this database we are unable to further address this methodological question. Countering this possible hypothesis is the fact that blood glucose, also requiring a fasting sample, was not associated with PFOA at any site. However, hyperglycemia has not been consistently associated with night shift workers (Al-Naimi et al. 2004; Karlsson et al. 2003). Also, the association between serum triglycerides and PFOA was not observed at the Cottage Grove site which had both production and non-production workers. Nevertheless, a positive association between serum triglycerides and PFOA was reported by Leonard et al. (2004) whose study population also consisted of production (shift workers) and nonproduction (nonshift workers) participants. To further clarify possible association, if any, between workers' PFOA concentrations and serum triglyceride levels, adjustment for shift work becomes a methodological necessity in the data analyses.

Adjusted for BMI and/or serum triglycerides, which are important potential confounders in the analysis of liver enzymes as they are associated with the increasingly prevalent nonalcohol fatty liver disease observed in the United States (Clark et al. 2003), there was no indication that the measured liver enzymes (alkaline phosphatase, AST, ALT, GGT

and total bilirubin) were causally associated with employees' serum PFOA concentrations. A weak positive association between alkaline phosphatase, ALT and GGT with PFOA was observed among the Decatur male employees, however, several epidemiologic research studies of this workforce, past and present, have not reported associations with hepatic disease (malignant or nonmalignant conditions) using a variety of data sources including death certificates (Alexander et al. 2003), episodes of care (Olsen et al. 2004) and self-reports (Alexander and Grice 2006). Neither have other worker populations (Leonard et al. 2004) or a community-based PFOA-exposed population (Emmett 2004) reported positive associations between liver enzyme test results, liver disease and serum PFOA concentrations measured at or below those reported in the present study. For example, in the Emmett study (a presentation is available at http://www.lhwc8study.org/index.htm), the median serum PFOA concentration measured in this community-based study was 0.34 μg/mL. Individuals older than 60 years had significantly higher levels of PFOA compared to all groups except those less than six years of age. There was no relationship between the blood levels of PFOA and the results for cholesterol, liver function tests (serum protein, albumin, bilirubin, serum alkaline phosphatase, AST, ALT and GGT), kidney function tests (BUN, creatinine) and TSH. Furthermore, there was no relationship between PFOA serum concentrations and being treated for or informed by a physician that a community participant had liver disease (cirrhosis, hepatitis, and any other liver condition).

In the present study, there were no consistent associations with TSH, T4, free T4 or T3 with PFOA (or PFOS) across the individual facility locations. For the combined location

analyses, adjusted PFOA coefficients that were statistically significant were the result of models whose range of predictions for serum PFOA concentrations (up to 100 μg/mL) were well-within the normal reference ranges for these thyroid related tests. This was not unexpected as few thyroid-related tests were out-of-reference range. The lack of thyroid related hormone associations is also consistent with the worker data reported by Leonard et al. (2004) and a population-based study by Emmett (2004) that included thyroid-related conditions (hyperthyroidism, hypothyroidism, goiter). In rats the presence of PFOS or fatty acids such as oleic acid in serum appeared to compete with free T4 for protein bindings, and their presence in serum resulted in a negative bias in analog free T4 measurements (Tanaka et al. 2005). PFOS, however, did not reduce either free T4 by equilibrium dialysis radioimmunoassay (ED-RIA) or the liver response to thyroid hormones [e.g., malic enzyme and uridinediphosphate-glucuronsyltransferase (UGT1A)]. These observations therefore suggested that prior reports of reduced free T4 in the presence of PFOS may have been artifacts of the analog methods. It is conceivable this negative bias of the assay could also effect measurement of PFOA.

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Table 1. Number (percent) of Male Employees Who Self-Reported Cholesterol Lowering Medications, By Location, 2000 Fluorochemical Medical Surveillance

	Cholesterol Lowering Medication		
Location	Yes (%)	No (%)	Total
Antwerp	10 (5)	196 (95)	206
Cottage Grove	9 (7)	122 (93)	131
Decatur	27 (13)	188 (87)	215
Total	46 (8)	506 (92)	552

Table 2. Mean, Standard Deviation, Median and Range of PFOA, PFOS, Demographic Factors and Clinical Chemistry Results, By Location, 2000 Fluorochemical Medical Surveillance Program

	Antwerp (N=196)				Cottage Grove (N=122)				Decatur (N=188)			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
PFOA	1.02[2]	1.06	0.65	0.01-7.04	4.63[1, 3]	12.53	0.95	0.01-92.03	1.89[2]	1.61	1.51	0.04-12.70
PFOS	0.95[3]	0.97	0.55	0.04-6.24	0.86[3]	0.98	0.45	0.03-4.79	1.29[1, 2]	0.92	1.00	0.06-4.17
Age	37[2, 3]	8	36	21-58	41[1]	9	40	24-67	42[1]	9	43	26-63
BMI	24.7[2, 3]	3.0	24.5	17.5-34.7	29.9[1, 3]	4.8	29.5	19.7-52.1	28.6[1, 2]	4.4	27.5	17.2-50.1
Alcohol	1.1[2, 3]	1.1	0.9	0.0-6.4	0.7[1, 3]	0.7	0.5	0.0-3.0	0.1[1, 2]	0.3	0.0	0.0-2.0
Glucose	84[2, 3]	17	87	31-131	100[1, 3]	23	95	59-259	93[1,2]	14	91	74-184
Cholesterol	217	41	216	105-331	210	39	206	130-311	214	41	211	121-319
LDL	139[2]	37	134	43-235	130[1]	32	125	37-208	136	36	133	47-225
HDL	55[2, 3]	15	53	26-121	46[1]	11	45	18-77	44[1]	10	42	24-82
Triglycerides	120[2, 3]	83	100	34-731	187[1]	139	142	24-725	182[1]	110	164	32-796
Alk Phos	60[2, 3]	14	61	21-113	65[1, 3]	15	63	28-107	73[1,2]	20	69	26-160
AST	23[2, 3]	6	22	13-58	25[1]	8	24	10-54	26[1]	8	25	13-69
ALT	23[2, 3]	10	21	8-71	34[1]	17	29	13-95	34[1]	16	30	6-103
AST/ALT	1.04[2, 3]	0.12	1.02	0.81-1.47	0.94[1]	0.09	0.92	0.70-1.25	0.95[1]	0.11	0.93	0.75-1.82

Table 2
(Continued)

	Antwerp (N=196)				Cottage Grove (N=122)				Decatur (N=188)			
	Mean	(SD)	Med	Range	Mean	(SD)	Med	Range	Mean	(SD)	Med	Range
GGT	23[2, 3]	17	18	6-111	31[1]	32	22	7-314	30[1]	17	27	7-144
Total Bil	1.0[2, 3]	0.3	1.0	0.4-2.3	0.9[1, 3]	0.3	0.8	0.4-2.3	0.7[1, 2]	0.2	0.7	0.3-1.5
Direct Bil	0.1[3]	0.05	0.1	0.0-0.4	0.1	0.02	0.1	0.0-0.2	0.1[1]	0.07	0.1	0.0-0.7
TSH	2.0[3]	1.6	1.7	0.03-19.4	2.4	14	2.0	0.03-9.4	2.8[1]	5.2	1.9	0.03-65.3
T4	8.2	1.4	8.2	4.2-12.0	7.9[3]	1.1	7.9	4.9-11.6	8.4[2]	1.4	8.5	4.6-11.4
Free T4	1.1[3]	0.2	1.1	0.6-1.6	1.1	0.1	1.1	0.8-1.8	1.1[1]	0.2	1.1	0.6-1.5
T3	131[2, 3]	19	130	87-85	125[1]	30	121	78-300	125[1]	22	120	86-196

1. Statistically significantly ($p < .05$) different than Antwerp
2. Statistically significantly ($p < .05$) different than Cottage Grove
3. Statistically significantly ($p < .05$) different than Decatur

Table 3. Number and Percent of Employees by Location for Reference Points of Demographic Factors and Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program

	Antwerp (N=196)		Cottage Grove (N=122)		Decatur (N=188)		
	N	(%)	N	(%)	N	(%)	p value*
BMI ≥ 30	9	(5)	54	(44)	61	(32)	.0001
Alcohol ≥ 1 drink/day	92	(47)	49	(40)	2	(1)	.0001
Glucose ≥ 110 mg/dL	10	(5)	22	(18)	16	(9)	.001
Cholesterol ≥ 200 mg/dL	119	(61)	69	(57)	114	(61)	.72
Cholesterol ≥ 240 mg/dL	60	(31)	32	(26)	50	(27)	.60
HDL < 40 mg/dL	16	(8)	36	(30)	72	(38)	.0001
LDL ≥ 130 mg/dL	106	(55)	53	(48)	100	(55)	.40
Triglycerides ≥ 150 mg/dL	46	(23)	58	(48)	103	(55)	.0001
Alk Phos ≥ 120 IU/L	0	(0)	0	(0)	5	(3)	.01
AST ≥ 50 IU/L	1	(1)	4	(3)	2	(1)	.11
ALT ≥ 50 IU/L	2	(1)	20	(16)	22	(12)	.0001
GGT ≥ 50 IU/L	13	(7)	15	(12)	16	(9)	.22
Total Bil > 1.5 mg/dl	13	(7)	1	(1)	0	(0)	.0001
Direct Bil > 0.4 mg/dl	0	(0)	0	(0)	2	(1)	.18
TSH							
<0.35 µIU/mL	1	(1)	1	(1)	1	(1)	.92
>5.5 µIU/mL	5	(3)	5	(4)	8	(4)	.60
T4							
< 4.5 µg/dL	1	(1)	0	(0)	0	(0)	.46
>12.0 µg/dL	0	(0)	0	(0)	0	(0)	1.0
Free T4							
<0.70 ng/dL	1	(1)	0	(0)	2	(1)	.49
>1.53 ng/dL	3	(2)	1	(1)	1	(1)	.60
T3							
< 60 ng/dL	0	(0)	0	(0)	0	(0)	1.0
>181 ng/dL	2	(1)	3	(3)	2	(1)	.46
"Metabolic Syndrome"[1]	2	(1)	24	(20)	25	(13)	.0001

* chi square test of significance

1. See text for description

Table 4. Mean, Standard Deviation, Median and Range of PFOA, PFOS, Demographic Factors and Clinical Chemistry Results, By PFOA Quartile, 2000 Medical Fluorochemical Surveillance Program for Antwerp (N = 196)

	Quartile 1 (N=49)				Quartile 2 (N=49)				Quartile 3 (N=49)				Quartile 4 (N=49)			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
PFOA	0.11[2, 3, 4]	0.07	0.10	0.01-0.25	0.41[1, 3, 4]	0.10	0.40	0.26-0.64	1.07[1, 2,4]	0.24	1.10	0.67-1.53	2.49[1, 2, 3]	1.06	2.23	1.56-7.04
PFOS	0.34[3, 4]	0.37	0.25	0.04-2.19	0.80[3, 4]	0.88	0.52	0.25-5.19	1.07[1,4]	0.57	1.03	0.06-2.35	1.59[1, 2, 3]	1.32	1.25	0.18-6.24
Age	40[2, 3, 4]	10	40	23-58	36[1]	7	36	25-53	36[1]	8	35	21-53	35[1]	7	35	22-50
BMI	25.0	3.1	24.6	19.2-34.7	25.2[3]	3.0	24.9	20.2-33.9	24.1[2]	3.1	24.2	17.5-32.3	24.5	2.6	24.2	19.5-30.9
Alcohol	1.0	0.9	0.7	0.0-4.3	1.0	1.2	0.7	0.0-6.4	1.2	1.1	1.0	0.0-5.0	1.2	1.1	1.1	0.0-4.3
Glucose	91[2, 3, 4]	15	92	60-131	82[1]	18	85	48-115	81[1]	20	86	31-120	82[1]	16	84	49-117
Chol	220	42	215	140-331	211	40	216	122-286	213	43	213	105-300	225	40	221	145-316
LDL	145	36	142	68-224	131	34	129	59-205	136	40	128	43-235	144	37	141	54-226
HDL	54	13	55	26-96	57	20	53	29-121	56	12	53	37-88	53	12	51	36-85
Trig	105[4]	62	87	37-348	123	104	99	36-731	108	53	198	41-287	145[1]	98	128	34-546
Alk Phos	61	15	63	30-96	59	13	58	36-94	56[4]	13	58	21-84	64[3]	16	64	34-113
AST	24	6	22	13-36	24[3]	7	24	13-49	21[2, 4]	4	21	15-31	25[3]	8	24	15-58
ALT	24	10	21	10-61	23	8	21	11-45	20[4]	8	19	8-46	24[3]	12	22	9-71
AST/ALT	1.02	0.10	1.01	0.81-1.23	1.03	0.11	1.02	0.83-1.37	1.06	0.14	1.02	0.87-1.42	1.04	0.14	1.01	0.85-1.47
GGT	22	14	18	8-80	25	20	20	6-111	20	12	17	7-53	26	20	22	8-89
Total Bil	1.0	0.3	1.0	0.5-2.0	1.0	0.4	1.0	0.5-2.3	1.0	0.3	1.0	0.5-2.2	1.0	0.3	1.0	0.4-2.0
Direct Bil	0.1	0.04	0.1	0.0-0.2	0.1	0.06	0.1	0.0-0.3	0.1	0.06	0.1	0.0-0.4	0.1	0.03	0.1	0.0-0.2
TSH	1.8	1.1	1.7	0.4-5.4	1.8	0.9	1.6	0.03-4.3	1.9	1.1	1.8	0.5-6.1	2.4	2.7	1.8	0.6-19.4

Table 4.
(Continued)

	Quartile 1 (N=49)				Quartile 2 (N=49)				Quartile 3 (N=49)				Quartile 4 (N=49)			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
T4	8.4	1.5	8.5	5.0-11.5	8.1	1.4	7.9	4.2-12.0	8.0	1.4	8.0	5.0-11.1	8.3	1.5	8.5	4.7-10.7
Free T4	1.1	0.2	1.1	0.9-1.5	1.2[3]	0.2	1.2	0.9-1.5	1.1[2]	0.2	1.1	0.6-1.6	1.1	0.1	1.1	0.8-1.6
T3	125[4]	18	124	91-166	130	19	131	87-171	132	20	132	97-185	135[1]	18	132	102-184

1. Statistically significantly ($p < .05$) different than 1st quartile
2. Statistically significantly ($p < .05$) different than 2nd quartile
3. Statistically significantly ($p < .05$) different than 3rd quartile
4. Statistically significantly ($p < .05$) different than 4th quartile

Table 5. Mean, Standard Deviation, Median and Range of PFOA, PFOS, Demographic Factors and Clinical Chemistry Results, by PFOA Quartile, 2000 Fluorochemical Medical Surveillance Program for Cottage Grove (N = 122)

	Quartile 1 (N=31)				Quartile 2 (N=28)				Quartile 3 (N=33)				Quartile 4 (N=30)			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
PFOA	0.12[4]	0.08	0.11	0.01-0.30	0.51[4]	0.17	0.46	0.30-0.87	1.60[4]	0.47	1.67	0.91-2.49	16.50[1, 2, 3]	21.48	6.64	2.51-92.03
PFOS	0.62[2]	0.83	0.15	0.02-2.64	1.18[1]	1.22	0.83	0.12-4.79	0.90	0.92	0.55	0.02-4.22	0.78	0.88	0.48	0.12-4.31
Age	37[3]	8	37	24-61	39[3]	9	38	26-61	45[1, 2, 4]	9	44	27-67	41[3]	9	41	28-59
BMI	29.4	5	28.8	19.7-40.1	30.1	4.7	29.2	23.4-39.9	29.9	5.6	29.1	23.6-52.1	30.0	3.6	30.6	22.0-37.3
Alcohol	0.5	0.5	0.5	0.0-2.0	0.8	0.8	0.5	0.0-3.0	0.7	0.8	0.5	0.0-3.0	0.7	0.6	0.5	0.0-2.0
Glucose	101	31	95	73-259	99	28	92	77-222	102	13	103	79-143	97	14	95	59-126
Chol	207	38	196	146-278	214	40	210	142-289	206	34	205	151-293	214	44	205	130-311
LDL	128	32	125	58-189	133	31	124	80-201	129	32	118	82-208	129	35	135	37-180
HDL	47	11	46	29-77	46	11	44	23-69	46	11	46	25-68	43	10	44	18-62
Trig	168	115	132	24-503	180	124	155	55-542	174	129	136	50-715	227	179	159	38-725
Alk Phos	65	11	65	44-90	65	15	63	28-101	66	17	63	32-107	62	15	63	37-100
AST	27[4]	10	25	14-52	26	7	25	15-47	25	10	23	10-54	23[1]	5	22	14-38
ALT	35	17	30	14-84	37	20	30	16-95	33	19	27	13-87	32	11	29	15-56
AST/ALT	0.96	0.09	0.95	0.84-1.25	0.93	0.09	0.93	0.75-1.10	0.94	0.09	0.91	0.80-1.24	0.92	0.09	0.92	0.70-1.13
GGT	37	56	22	7-314	32	22	22	10-97	27	16	24	7-83	28	16	24	10-84
Total Bil	0.9	0.2	0.8	0.4-1.5	0.9	0.3	0.9	0.6-2.3	0.8	0.2	0.8	0.4-1.4	0.9	0.3	0.8	0.4-1.5
Direct Bil	0.1	0.03	0.1	0.0-0.2	0.1	0.03	0.1	0.1-0.2	0.1	0.0	0.1	0.1-0.1	0.1	0.02	0.1	0.0-0.1
TSH	2.4	1.1	2.2	0.8-5.0	2.3	1.2	2.0	0.9-6.0	2.2	1.3	1.9	0.6-7.5	2.5	1.8	2.0	0.03-9.4

Table 5
(Continued)

	Quartile 1				Quartile 2				Quartile 3				Quartile 4			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
T4	8.1	1.4	8.2	5.1-11.6	8.0	1.2	7.9	4.9-10.0	7.9	0.8	7.8	6.7-9.7	7.7	1.0	7.8	5.6-9.8
Free T4	1.1	0.2	1.1	0.8-1.8	1.1	0.1	1.1	0.9-1.4	1.1	0.1	1.1	0.9-1.4	1.1	0.1	1.1	0.8-1.3
T3	123	34	119	78-277	123	19	123	87-158	127	30	124	85-270	123	36	118	81-300

1. Statistically significantly ($p < .05$) different than 1st quartile
2. Statistically significantly ($p < .05$) different than 2nd quartile
3. Statistically significantly ($p < .05$) different than 3rd quartile
4. Statistically significantly ($p < .05$) different than 4th quartile

Table 6. Mean, Standard Deviation, Median and Range of PFOA, PFOS, Demographic Factors and Clinical Chemistry Results, by PFOA Quartile, 2000 Fluorochemical Medical Surveillance Program for Decatur (N = 188)

	Quartile 1 (N=48)				Quartile 2 (N=51)				Quartile 3 (N=42)				Quartile 4 (N=47)			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
PFOA	0.36[2, 3, 4]	0.18	0.36	0.04-0.69	1.21[1, 3, 4]	0.24	1.24	0.73-1.59	2.15[1, 2, 4]	0.32	2.15	1.61-2.70	3.97[1, 2, 3]	1.69	3.67	2.72-12.70
PFOS	0.51[2, 3, 4]	0.32	0.45	0.06-1.64	1.03[3, 4]	0.51	0.98	0.18-2.53	1.32[1,2, 4]	0.75	1.18	0.29-3.55	2.35[1, 2, 3]	0.85	2.42	0.67-4.17
Age	44[4]	11	46	27-63	43[4]	8	45	26-61	41	8	43	26-57	39[1, 2]	9	38	27-60
BMI	27.9	4.1	27.0	21.7-40.8	29.4	4.9	27.6	24.0-50.1	28.8	3.5	28.2	22.7-35.1	28.5	4.9	28.3	17.2-45.5
Alcohol	0.2	0.4	0.0	0.0-2.0	0.1	0.3	0.0	0.0-0.8	0.1	0.2	0.0	0.0-0.8	0.1	0.2	0.0	0.0-0.8
Glucose	92	14	90	75-166	95	18	91	74-184	96	12	94	75-135	91	12	87	75-129
Cholesterol	204[2]	41	197	137-305	224[1]	42	223	146-308	214	42	211	121-297	214	38	208	151-319
LDL	127[2]	35	122	76-205	147[1]	37	148	80-222	133	39	140	47-199	135	30	133	69-225
HDL	46	12	43	29-82	43	9	42	24-70	44	10	42	29-68	42	8	41	28-75
Trig	152[2]	82	139	38-399	209[1]	146	155	32-633	183	67	175	85-379	183	115	166	39-796
Alk Phos	68[3]	18	69	26-117	74	20	68	52-160	77[1]	24	73	39-142	74	19	68	44-122
AST	26	8	24	15-48	25	7	24	13-51	26	6	26	16-42	27	10	25	15-69
ALT	30[4]	15	26	12-91	30[4]	14	29	17-103	35	13	34	10-63	40[1, 2]	19	33	6-99
AST/ALT	0.98[4]	0.10	0.97	0.82-1.30	0.95	0.09	0.95	0.75-1.11	0.94	0.09	0.93	0.76-1.23	0.92[1]	0.15	0.89	0.78-1.82
GGT	28[3]	18	25	7-119	26[3]	13	21	11-87	36[1, 2]	22	31	12-144	32	14	29	10-80
Total Bil	0.8[4]	0.2	0.8	0.3-1.5	0.8	0.2	0.7	0.4-1.2	0.7	0.2	0.7	0.4-1.2	0.7[1]	0.2	0.7	0.4-1.3
Direct Bil	0.1	0.06	0.1	0.0-0.2	0.1	0.06	0.1	0.0-0.2	0.1	0.10	0.1	0.0-0.7	0.1	0.09	0.1	0.0-0.6
TSH	3.5	9.3	1.9	0.03-65.3	2.6	2.6	1.9	0.7-18.8	2.3	1.6	1.8	0.2-8.6	2.7	3.3	2.2	1.0-23.2

Table 6
(Continued)

	Quartile 1				Quartile 2				Quartile 3				Quartile 4			
	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range	Mean	SD	Median	Range
T4	8.4	1.5	8.7	4.6-11.0	8.4	1.4	8.3	5.9-11.4	8.2	1.6	8.6	3.3-11.1	8.6	1.4	8.5	5.1-11.4
Free T4	1.1	0.1	1.1	0.6-1.3	1.1	0.2	1.1	0.8-1.4	1.1	0.2	1.1	0.4-1.5	1.1	0.2	1.1	0.8-1.3
T3	119[4]	19	116	86-180	124	20	119	93-186	125	23	120	93-196	131[1]	23	128	87-177

1. Statistically significantly ($p < .05$) different than 1st quartile
2. Statistically significantly ($p < .05$) different than 2nd quartile
3. Statistically significantly ($p < .05$) different than 3rd quartile
4. Statistically significantly ($p < .05$) different than 4th quartile

Table 7. Number of Employees, Mean, 95% Confidence Interval, Median and Range by PFOA Decile Distribution , 2000 Fluorochemical Medical Surveillance Program for Antwerp, Cottage Grove and Decatur (N = 506)

PFOA Decile	N	PFOA			
		Mean	95% C.I.	Median	Range
1	51	0.06[8-10]	0.05-0.07	0.06	0.007-0.13
2	51	0.20[9,10]	0.19-0.21	0.19	0.13-0.29
3	51	0.36[9,10]	0.35-0.37	0.36	0.30-0.44
4	50	0.55[9,10]	0.53-0.57	0.54	0.44-0.71
5	51	0.91[10]	0.87-0.94	0.91	0.72-1.10
6	49	1.26[10]	1.23-1.28	1.25	1.11-1.40
7	50	1.64[10]	1.60-1.67	1.63	1.42-1.85
8	54	2.17[1,10]	2.12-2.23	2.18	1.86-2.50
9	49	3.0[1-4,10]	2.90-3.10	2.96	2.51-3.69
10	50	12.15[1-9]	7.21-17.10	4.94	3.71-92.03

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or10

Table 8. Distribution of Demographic Factors by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program (N = 506)

PFOA Decile	Location			Age	BMI	BMI >= 30	Drinks/day	>= 1 Drink/day
	Antwerp	Cottage Grove	Decatur	Mean (SD)	Mean (SD)	N (%)	Mean (SD)	N (%)
1	28 (55)	17 (33)	6 (12)	39 (11)	27.1 (4.8)	13 (25)	0.7 (0.7)[9]	21 (41)
2	25 (49)	13 (26)	13 (25)	41 (9)	26.7 (4.1)[9]	7 (14)	0.7 (0.9)[9]	17 (33)
3	28 (55)	11 (22)	12 (23)	38 (8)	26.4(3.9)[9, 10]	8 (16)	0.7 (1.0)[9]	15 (29)
4	20 (40)	13 (26)	17 (34)	38 (10)	27.8(4.3)	13 (26)	0.7 (1.0)[9]	13 (26)
5	22 (43)	11 (22)	18 (35)	40 (10)	27.2(5.0)	8 (17)	0.7 (1.0)[9]	16 (32)
6	21 (43)	7 (14)	21 (43)	40 (9)	27.4(4.8)	12 (24)	0.7 (1.0)[9]	14 (29)
7	20 (40)	9 (18)	21 (42)	39 (9)	26.9(3.9)[9]	10 (20)	0.7 (0.9)[9]	14 (28)
8	18 (33)	11 (20)	25 (46)	41 (10)	27.5(5.4)	17 (31)	0.6 (0.9)[9]	16 (30)
9	9 (18)	7 (14)	33 (67)	39 (9)	28.9(4.9)[2,3, 7]	21 (43)	0.3 (0.5)[1-8]	5 (10)
10	5 (10)	23 (46)	22 (44)	39 (9)	28.3(4.0)[3]	15 (30)	0.5 (0.7)	12 (24)
		p<.0001[11]				p < .03[12]		p < .14[13]

[1-10] Statistically significantly ($p < .05$) different than PFOA decile 1, 2, 3 . . . 10.

[11, 12, 13] p value associated with chi square test for location, BMI distribution and ≥ 1 drink/day, respectively.

Table 9. Mean, 95% Confidence Interval , Median and Range of PFOS Serum Concentrations by PFOA Decile Distribution, 2000 Fluorochemical Medical Surveillance Program (N = 506)

PFOA Decile	N	PFOS			
		Mean	95% C.I.	Median	Range
1	51	0.30[3-10]	0.15-0.46	0.13	0.02-2.64
2	51	0.61[6-10]	0.38-0.84	0.35	0.02-5.19
3	51	0.86[7-10]	0.59-1.13	0.52	0.13-4.79
4	50	0.78[7-10]	0.62-0.94	0.58	0.12-3.41
5	51	0.89[1, 7-10]	0.74-1.04	0.82	0.06-2.21
6	49	1.12[1, 2, 9, 10]	0.90-1.33	0.98	0.02-4.22
7	50	1.27[1-5, 9]	1.07-1.48	1.21	0.18-3.25
8	53	1.41[1-5, 9]	1.10-1.73	1.03	0.20-6.24
9	49	1.74[1-8]	1.43-2.06	1.83	0.12-4.86
10	50	1.58[1-6]	1.23-1.94	1.06	0.14-4.31

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 10. Mean and Standard Deviation of Serum Lipid Clinical Chemistry Results by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	Cholesterol Mean (SD)	LDL Mean (SD)	HDL Mean (SD)	Triglycerides Mean (SD)
1	215 (43)	137 (39)	50 (13)[10]	142 (101)[10]
2	213 (42)	137 (33)	52 (13)[9, 10]	120 (66)[8-10]
3	208 (37)	128 (31)	52 (14)[9, 10]	144 (121)[10]
4	210 (41)	132 (34)	50 (19)[10]	147 (101)[10]
5	218 (39)	141 (35)	49 (12)[10]	161 (117)[10]
6	219 (42)	141 (41)	49 (12)[10]	161 (104)[10]
7	214 (40)	133 (37)	50 (11)[9, 10]	154 (106)[10]
8	216 (43)	136 (40)	47 (13)	175 (109)[2]
9	218 (40)	138 (31)	45 (11)[2, 3, 7]	174 (93)[2]
10	214 (42)	132 (35)	43 (9)[1-7]	214 (168)[1-7]

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 11. Adjusted* Mean and 95% Confidence Intervals for Lipid Clinical Chemistry Results by PFOA Decile

PFOA Decile	Cholesterol		LDL		HDL		Triglycerides	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
1	214	203-225	137	127-147	50[10]	46-53	145[10]	116-173
2	211	199-222	135	125-145	51[10]	48-54	124[8,10]	95-153
3	209	198-220	128	118-138	51[10]	48-54	153[10]	124-182
4	210	199-222	133	123-143	50[10]	46-53	145[10]	116-175
5	217	206-228	140	130-150	48	45-51	162	133-191
6	218	206-229	141	130-151	48	45-51	160[10]	131-190
7	214	203-225	133	123-143	50[10]	47-53	158[10]	128-187
8	215	204-226	136	126-146	47	44-50	172[2]	144-201
9	221	210-233	140	130-150	48	44-52	165[10]	135-194
10	216	204-227	133	123-144	44[1-4,7]	41-47	208[1-7,9]	179-238

*Adjusted for age, BMI and alcohol using analysis of covariance

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 12A. Adjusted[1] Odds Ratios (O.R.) and 95% Confidence Interval (95% C.I.) for Lipid Clinical Chemistry Reference Points, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	Chol >= 200 mg/dL		Chol >= 240 mg/dL		LDL >= 130 mg/dL		HDL<= 40 mg/dL		Triglycerides >= 150 mg/dL	
	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.
1	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-
2	0.4	0.2-1.0	1.3	0.5-3.1	0.7	0.3-1.6	1.1	0.4-3.2	0.7	0.3-1.8
3	0.9	0.4-2.0	0.9	0.3-2.2	0.7	0.3-1.6	0.5	0.1-1.5	1.0	0.4-2.4
4	0.9	0.4-2.1	1.1	0.4-2.7	0.8	0.4-1.8	2.0	0.8-5.4	1.3	0.5-3.1
5	1.7	0.7-4.0	1.6	0.7-3.9	1.4	0.6-3.1	1.0	0.4-2.9	1.2	0.5-3.0
6	1.0	0.4-2.2	1.1	0.5-2.8	0.9	0.4-2.0	1.7	0.7-4.7	1.7	0.7-4.0
7	0.8	0.4-1.9	1.2	0.5-2.9	0.7	0.3-1.5	0.6	0.2-1.8	0.9	0.4-2.2
8	1.0	0.4-2.2	1.2	0.5-2.9	1.1	0.5-2.4	1.4	0.5-3.7	2.7	1.2-6.5
9	1.4	0.6-3.3	1.5	0.6-3.7	1.2	0.5-2.7	0.9	0.3-2.4	2.4	1.0-5.9
10	1.1	0.5-2.6	1.0	0.4-2.5	1.2	0.5-2.8	2.6	1.0-6.8	2.4	1.0-5.8

1. Adjusted for age, BMI and alcohol

Table 12B. Nonadjusted and Adjusted Odds Ratios (O.R.) and 95% Confidence Intervals (95% C.I.) for HDL (< 40 mg/dL) and Triglycerides (>= 150 mg/dL) by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

	HDL < 40 mg/dL				Triglycerides >= 150 mg/dL			
Decile	O.R.[1]	95% C.I.	O.R.[2]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.
1	1.0	-	1.0	--	1.0	-	1.0	-
2	1.1	0.4-3.0	0.9	0.3-2.7	0.7	0.3-1.6	0.6	0.2-1.5
3	0.4	0.1-1.4	0.4	0.1-1.2	0.8	0.4-1.9	0.8	0.3-1.9
4	2.1	0.9-5.4	1.6	0.6-4.4	1.3	0.6-3.0	1.1	0.5-2.6
5	1.1	0.4-3.0	0.8	0.3-2.3	1.2	0.5-2.7	1.0	0.4-2.4
6	1.8	0.7-4.7	1.3	0.5-3.7	1.6	0.7-3.7	1.4	0.6-3.3
7	0.7	0.2-1.9	0.4	0.1-1.3	0.9	0.4-2.0	0.7	0.3-1.6
8	1.6	0.6-4.0	1.0	0.4-2.7	2.5	1.1-5.6	2.0	0.9-4.6
9	1.3	0.5-3.5	0.6	0.2-1.8	2.7	1.2-6.1	1.7	0.7-4.1
10	3.0	1.2-7.5	1.5	0.6-4.0	2.5	1.1-5.8	1.6	0.7-3.7

[1]Not adjusted

[2]Adjusted for location

Table 13. Non-adjusted and Adjusted Ln PFOA Coefficients
for Ln Lipid Clinical Chemistry Result, 2000 Fluorochemical Medical Surveillance Program

	Ln PFOA Non-adjusted Coefficient	SE	p value	Ln PFOA Adjusted[1] Coefficient	SE	p value
			Ln Cholesterol			
All Locations	0.0059	0.0060	.32	0.0076	0.0059	.20
Antwerp	0.0051	0.0106	.63	0.0130	0.0096	.18
Cottage Grove	0.0034	0.0089	.70	0.0021	0.0100	.83
Decatur	0.0221	0.0139	.11	0.0266	0.0141	.06
			Ln LDL			
All Locations	0.0012	0.0089	.89	0.0021	0.0090	.81
Antwerp	-0.0037	0.0157	.81	0.0106	0.0147	.47
Cottage Grove	-0.0022	0.0139	.87	0.0049	0.0145	.73
Decatur	0.0258	0.0199	.20	0.0302	0.0200	.13
			Ln HDL			
All Locations	-0.0307	0.0079	.0001	-0.0183	0.0069	.01
Antwerp	-0.0057	0.0136	.68	-0.0095	0.0131	.47
Cottage Grove	-0.0153	0.0122	.21	-0.0192	0.0120	.11
Decatur	-0.0256	0.0149	.09	-0.0207	0.0141	.14
			Ln Triglycerides			
All Locations	0.0892	0.0185	.0001	0.0711	0.0169	.0001
Antwerp	0.0840	0.0288	.004	0.0980	0.0270	.0004
Cottage Grove	0.0343	0.0316	.28	0.0280	0.0314	.38
Decatur	0.0715	0.0400	.08	0.0689	0.0376	.07

1. See study methods. Adjusted for Ln Age, Ln BMI, Ln Alcohol

Table 14. Mean and Standard Deviation of Hepatic Clinical Chemistry Results, by PFOA Decile, 2000 Medical Fluorochemical Surveillance Program

PFOA Decile	Alk Pos Mean (SD)	AST Mean (SD)	ALT Mean (SD)	AST/ALT Mean (SD)	GGT Mean (SD)	Total Bilirubin Mean (SD)	Direct Bilirubin Mean (SD)
1	65 (13)	26 (8)[5, 6]	29 (15)[9, 10]	0.99 (0.1)[9, 10]	32 (45)[6]	0.9[9] (0.3)	0.1[9] (0.04)
2	59 (15)[7, 9, 10]	25 (7)	28 (15)[9, 10]	1.00 (0.1)[9, 10]	25 (18)	0.9[9] (0.3)	0.1 (0.04)
3	64 (16)[7, 9]	26 (7)[5, 6]	29 (14)[9, 10]	1.00 (0.1)[9, 10]	26 (20)	1.0[6-10] (0.3)	0.1 (0.06)
4	65 (15)	24 (8)	28 (15)[9, 10]	0.98 (0.1)[10]	28 (20)	0.9[9] (0.3)	0.1 (0.04)
5	64 (21)[7, 9]	22 (6)[1,3, 7, 8, 9]	27 (15)[9, 10]	0.98 (0.1)[10]	24 (13)[9]	0.9[9] (0.3)	0.1[9] (0.06)
6	66 (19)	22 (5)[1,3, 7, 8, 9]	24 (9)[7, 9, 10]	1.01 (0.1)[9, 10]	22 (10)[1, 9]	0.9[3,9] (0.3)	0.1 (0.06)
7	72 (17)[2, 3, 5]	26 (7)[5, 6]	31 (15)[6]	0.98 (0.1)[10]	28 (19)	0.9[3,9] (0.3)	0.1 (0.03)
8	65 (17)	26 (9)[5, 6]	29 (16)[8]	1.00 (0.1)[9, 10]	29 (22)	0.8[3] (0.2)	0.1[9] (0.09)
9	72 (21)[2, 3, 5]	26 (9)[5, 6]	36 (14)[1-6, 8]	0.93 (0.1)[1-3,6,8]	33 (18)[5, 6]	0.7[1-7] (0.3)	0.1[1, 5, 8] (0.04)
10	68 (20)[2]	24 (7)	35 (17)[1-6]	0.93 (0.2)[1-8]	30 (16)	0.8[1,3] (0.3)	0.1 (0.08)

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 15A. Adjusted* Mean and 95% Confidence Intervals
for Hepatic Clinical Chemistry Results by PFOA Decile Adjusted

PFOA Decile	Alk Phos		AST		ALT		GGT		Total Bilirubin		Direct Bilirubin	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
1	66	61-71	26[5,6]	24-28	29	25-33	32	27-38	0.9[9]	0.86-1.02	0.1	0.09-0.12
2	59[7,9,10]	54-64	25	23-27	29	25-33	25	19-31	0.9	0.84-1.00	0.1	0.09-0.12
3	64[7]	59-69	26[5,6]	24-28	30	26-34	27	21-33	1.0[6-10]	0.89-1.06	0.1	0.09-0.12
4	65	61-70	24	22-26	28[9,10]	24-32	28	22-34	0.9[9]	0.82-0.99	0.1	0.08-0.11
5	64[7]	60-69	22[1,3,7-9]	20-25	27[9,10]	23-31	24[9]	18-30	0.9	0.79-0.95	0.1[9]	0.10-0.13
6	66	61-71	22[1,3,7-9]	20-24	25[7,9,10]	21-28	21[1,9]	15-27	0.9[3]	0.78-0.95	0.1	0.08-0.11
7	72[2,3,5,8]	67-77	26[5,6]	24-28	31[6]	27-35	28	22-34	0.9[3]	0.77-0.94	0.1	0.08-0.11
8	65[7]	60-70	26[5,6]	24-28	29	26-33	29	23-35	0.9[3]	0.77-0.93	0.1[9]	0.10-0.13
9	70	66-75	26[5,6]	24-28	34[4-6]	30-38	33[5,6]	27-39	0.8[1,3,4]	0.69-0.85	0.1[5,8]	0.07-0.10
10	68[2]	63-72	24	22-26	34[4-6]	30-38	30	24-36	0.8[3]	0.75-0.92	0.1	0.08-0.12

*Adjusted for Age, BMI and Alcohol using analysis of covariance
[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 15B. Adjusted* Mean and 95% Confidence Intervals (95% CI) for Hepatic Clinical Chemistry Results by PFOA Decile

PFOA Decile	Alk Plus		AST		ALT		GGT		Total Bilirubin		Direct Bilirubin	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
1	66	61-71	26[5,6]	24-28	30	26-34	33[5,6]	27-39	0.9[9]	0.85-1.01	0.1	0.09-0.12
2	60[7,9,10]	55-65	25[6]	23-27	30	26-34	26	20-32	0.9[9]	0.83-0.99	0.1	0.09-0.12
3	64[7]	59-69	26[5,6]	24-28	29	25-33	27	21-33	1.0[6-10]	0.90-1.06	0.1	0.09-0.12
4	66	61-71	24	22-26	29[9]	25-33	28[9]	23-34	0.9[9]	0.82-0.98	0.1	0.08-0.11
5	64[7]	60-69	22[1,3,7,8]	20-24	27[9,10]	23-31	24[1,9]	18-30	0.9	0.80-0.96	0.1[9]	0.10-0.13
6	66	61-71	22[1-3,7-9]	20-24	25[7,9,10]	21-28	21[1,9]	15-27	0.9[3]	0.78-0.95	0.1	0.08-0.11
7	72[2,3,5,8]	67-77	26[5,6]	24-28	31[6]	27-35	28	23-34	0.9[3]	0.78-0.94	0.1	0.08-0.11
8	65[8]	61-69	26[5,6]	24-28	29[9]	25-33	28	23-34	0.9[3]	0.76-0.93	0.1[9]	0.10-0.13
9	70[2]	66-75	26[6]	24-28	36[4,5,6,8]	31-39	33	28-39	0.8[1-4]	0.68-0.85	0.08[5,8]	0.07-0.10
10	67[2]	62-72	24	22-26	33[5,6]	29-37	27	22-33	0.9[3]	0.0.77-0.94	0.1	0.09-0.12

*Adjusted for Age, Triglycerides, and Alcohol using analysis of covariance

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 15C. Adjusted Means and 95% Confidence Intervals (CI) for AST/ALT Ratios by PFOA Decile

PFOA Decile	AST/ALT Mean[a]	95% CI	AST/ALT Mean[b]	95% CI
1	0.99[10]	0.96-1.02	0.99	0.95-1.01
2	0.98[10]	0.96-1.02	0.98	0.95-1.02
3	1.00[10]	0.96-1.03	1.00[9]	0.97-1.03
4	0.98	0.95-1.01	0.98	0.94-1.00
5	0.97	0.94-1.01	0.95	0.94-1.00
6	1.00[9,10]	0.97-1.04	1.01[9,10]	0.97-1.04
7	0.98	0.95-1.01	0.98	0.95-1.01
8	1.00[9,10]	0.97-1.03	1.00[9,10]	0.97-1.04
9	0.95[6,8]	0.92-0.98	0.95[3,6,8]	0.91-0.98
10	0.94[1-3,6,8]	0.91-0.98	0.95[6,8]	0.0.92-0.98

a. Adjusted for Age, BMI and Alcohol using analysis of covariance

b.Adjusted for Age, Triglycerides and Alcohol using analysis of covariance

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 16. Number and Percent of Hepatic Clinical Chemistry Results by Reference Points, by PFOA Decile, 2000 Medical Fluorochemical Surveillance Program

PFOA Decile	Alk Phos >= 120 N (%)	AST >= 50 N (%)	ALT >= 50 N (%)	GGT >= 50 N (%)	Total Bilirubin >1.5	Direct Bilirubin > 0.4
1	0 (0)	2 (4)	6 (12)	6 (12)	2 (4)	0 (0)
2	0 (0)	0 (0)	4 (8)	2 (4)	1 (2)	0 (0)
3	0 (0)	0 (0)	4 (8)	5 (10)	4 (8)	0 (0)
4	0 (0)	0 (0)	4 (8)	5 (10)	2 (4)	0 (0)
5	1 (2)	1 (2)	3 (6)	2 (4)	1 (2)	0 (0)
6	1 (2)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)
7	1 (2)	1 (2)	4 (8)	5 (10)	1 (2)	0 (0)
8	0 (0)	2 (4)	5 (9)	5 (9)	0 (0)	1 (2)
9	1 (2)	1 (2)	7 (14)	8 (16)	1 (2)	0 (0)
10	1 (2)	0 (0)	7 (14)	4 (8)	1 (2)	1 (2)
p value*	.81	.49	.38	.46	.58	.56

*chi square test of significance

Table 17A. Odds Ratios (O.R.) and 95% Confidence Intervals (95% C.I.) for Hepatic Clinical Chemistry Results, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	ALT ≥ 50 IU/L						GGT ≥ 50 IU/L					
	O.R[1].	95% C.I.	O.R[2].	95% C.I.	O.R[3].	95% C.I.	O.R[1].	95% C.I.	O.R[2].	95% C.I.	O.R[3].	95% C.I.
1	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-
2	0.6	0.2-2.4	0.8	0.2-3.0	0.8	0.2-3.2	0.3	0.0-1.4	0.3	0.0-1.4	0.3	0.0-1.6
3	0.6	0.2-2.4	0.7	0.2-2.9	0.6	0.1-2.2	0.8	0.2-2.9	0.9	0.2-3.1	0.7	0.2-2.8
4	0.7	0.2-2.4	0.6	0.1-2.3	0.6	0.1-2.4	0.8	0.2-3.0	0.8	0.2-2.7	0.8	0.2-2.9
5	0.5	0.1-1.9	0.4	0.1-1.9	0.4	0.1-1.7	0.3	0.0-1.4	0.3	0.0-1.3	0.3	0.0-1.3
6	0.2	0.0-1.0	0.1	0.0-0.9	0.1	0.0-0.9	0.3	0.0-1.5	0.3	0.0-1.3	0.3	0.0-1.3
7	0.7	0.2-2.4	0.8	0.2-3.0	0.6	0.1-2.3	0.8	0.2-3.0	0.9	0.2-3.1	0.8	0.2-2.9
8	0.8	0.2-2.7	0.7	0.2-2.8	0.7	0.2-2.5	0.8	0.2-2.7	0.7	0.2-2.6	0.6	0.2-2.4
9	1.3	0.4-4.2	1.0	0.3-3.4	1.0	0.3-3.6	1.5	0.5-4.8	1.7	0.5-5.6	1.7	0.5-5.8
10	1.2	0.4-4.1	1.1	0.3-3.8	0.7	0.2-2.6	0.7	0.2-2.4	0.7	0.2-2.5	0.4	0.1-1.7

1. Not adjusted
2. Adjusted for age, BMI and alcohol
3. Adjusted for age, triglycerides and alcohol

Table 17B. Odds Ratios (O.R.) and 95% Confidence Intervals (95% C.I.) for Hepatic Clinical Chemistry Results, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	ALT ≥ 40 IU/L						GGT ≥ 40 IU/L					
	O.R[1].	95% C.I.	O.R[2].	95% C.I.	O.R[3].	95% C.I.	O.R[1].	95% C.I.	O.R[2].	95% C.I.	O.R[3].	95% C.I.
1	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-
2	0.9	0.3-2.4	1.1	0.4-3.2	1.1	0.4-3.3	0.6	0.2-1.9	0.6	0.2-1.9	0.7	0.2-2.3
3	0.8	0.3-2.1	0.8	0.3-2.5	0.7	0.2-2.0	0.7	0.2-2.2	0.8	0.3-2.4	0.7	0.2-2.2
4	0.9	0.3-2.5	0.8	0.3-2.4	0.9	0.3-2.4	1.0	0.4-2.9	1.0	0.4-2.8	1.0	0.3-3.0
5	0.3	0.1-1.1	0.3	0.1-1.1	0.3	0.1-1.0	0.9	0.3-2.5	0.8	0.3-2.4	0.8	0.1-1.5
6	0.3	0.1-0.9	0.2	0.1-0.9	0.2	0.1-0.9	0.5	0.2-1.7	0.5	0.1-1.6	1.1	0.4-3.3
7	1.3	0.5-3.4	1.5	0.5-4.1	1.2	0.5-3.4	1.2	0.4-3.2	1.2	0.4-3.5	0.6	0.2-1.7
8	1.4	0.6-3.7	1.5	0.6-4.3	1.3	0.5-3.6	0.7	0.2-2.0	0.7	0.2-2.0	1.6	0.6-4.7
9	2.2	0.9-5.6	1.7	0.7-4.8	1.7	0.7-4.6	1.5	0.6-4.1	1.6	0.6-4.5	1.2	0.4-3.4
10	1.4	0.6-3.8	1.2	0.5-3.4	0.9	0.3-2.5	1.6	0.6-4.4	1.7	0.6-4.5	1.3	0.3-4.6

1. Not adjusted
2. Adjusted for age, BMI and alcohol
3. Adjusted for age, triglycerides and alcohol

Table 18. Non-adjusted and Adjusted Ln PFOA Coefficients
for Ln Hepatic Clinical Chemistry, 2000 Fluorochemical Medical Surveillance Program

	Non-adjusted Ln PFOA Coefficient	SE	p value	Adjusted[1,2] Ln PFOA Coefficient	SE	p value
			Ln Alkaline Phosphatase			
All Locations	0.0155	0.0082	.06	0.0093[1]	0.0081	.25
				0.0037[2]	0.0081	.65
Antwerp	-0.0025	0.0137	.85	-0.0060	0.0139	.67
				-0.0170	0.0140	.22
Cottage Grove	-0.0141	0.0113	.21	-0.0127	0.0117	.28
				-0.0140	0.0117	.24
Decatur	0.0394	0.0191	.04	0.0460	0.0192	.02
				0.0394	0.0192	.04
			Ln AST			
All Locations	-0.0018	0.0086	.83	-0.0051	0.0086	.55
				-0.0089	0.0087	.31
Antwerp	-0.0048	0.0137	.73	-0.0029	0.0138	.83
				-0.0066	0.0142	.64
Cottage Grove	-0.0281	0.0141	.05	-0.0258	0.0146	.08
				-0.0271	0.0145	.07
Decatur	0.0205	0.0200	.31	0.0114	0.0203	.57
				0.0062	0.0203	.76
			Ln ALT			
All Locations	0.0402	0.0143	.005	0.0249	0.0132	.06
				0.0115	0.0136	.40
Antwerp	-0.0122	0.0220	.58	-0.0085	0.0222	.70
				-0.0293	0.0222	.19

Table 18. (Continued)

	Non-adjusted Ln PFOA Coefficient	SE	p value	Adjusted[1,2] Ln PFOA Coefficient	SE	p value
			Ln ALT (Cont'd)			
Cottage Grove	- 0.0131	0.0215	.54	-0.0096	0.0209	.65
				-0.0008	0.0208	.69
Decatur	0.0954	0.0300	.002	0.0704	0.0287	.02
				0.0581	0.0287	.04
			Ln GGT			
All Locations	0.0409	0.0174	.02	0.0326	0.0166	.05
				0.0097	0.0163	.55
Antwerp	0.0170	0.0307	.58	0.0269	0.0294	.36
				-0.0047	0.0295	.87
Cottage Grove	-0.0088	0.0292	.76	-0.0198	0.0286	.49
				-0.0233	0.0270	.39
Decatur	0.0754	0.0344	.03	0.0800	0.0344	.02
				0.0599	0.0329	.07
			Ln Total Bilirubin			
All Locations	-0.0406	0.0101	.0001	-0.0325	0.0099	.001
				-0.0267	0.0101	.01
Antwerp	-0.0117	0.0178	.51	-0.0122	0.0182	.50
				-0.0093	0.0188	.62
Cottage Grove	-0.0060	0.0138	.66	-0.0098	0.0142	.49
				-0.0067	0.0141	.64
Decatur	-0.0528	0.0203	.01	-0.0537	0.0209	.01
				-0.0462	0.0206	.03

1. See study methods. Adjusted for Ln Age, Ln BMI, Ln Alcohol
2. See study methods. Adjusted for Ln Age, Ln Triglycerides, Ln Alcohol

Table 19. Mean and Standard Deviation (SD) of Thyroid-Related Clinical Chemistry Results, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	TSH Mean (SD)		T4 Mean (SD)		Free T4 Mean (SD)		T3 Mean SD	
1	2.06	(1.17)[4]	8.28	(1.51)	1.15	(0.15)[5, 7, 10]	124	(28)
2	2.03	(1.09)[4]	8.41	(1.40)	1.11	(0.15)	124	(21)
3	1.84	(0.73)[4]	8.12	(1.31)	1.15	(0.14)[5, 10]	125	(19)
4	3.41	(9.07)[1, 2, 3]	8.04	(1.51)	1.12	(0.19)	127	(19)
5	2.60	(2.63)	7.96	(1.37)	1.07	(0.15)[1, 3]	126	(17)
6	2.10	(1.09)	8.49	(1.33)	1.10	(0.13)	128	(23)
7	2.19	(1.23)	8.08	(1.29)	1.09	(0.13)[1]	129	(21)
8	2.43	(2.92)	8.37	(1.29)	1.09	(0.17)	130	(27)
9	2.84	(3.40)	8.49	(1.30)	1.10	(0.14)	130	(20)
10	2.41	(1.27)	7.97	(1.33)	1.07	(0.14)[1, 3]	130	(31)

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 20. Adjusted* Mean and 95% Confidence Intervals for Thyroid Clinical Chemistry Results by PFOA Decile

PFOA Decile	TSH		T4		Free T4		T3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
1	2.07[4]	1.13-3.01	8.27	7.91-8.66	1.15[7,10]	1.11-1.19	124	118-131
2	2.00[4]	1.04-2.96	8.45	8.07-8.83	1.11	1.07-1.15	125	118-131
3	1.89[4]	0.94-2.85	8.08	7.70-8.46	1.14[5,10]	1.10-1.18	124	118-131
4	3.43[2,3,6]	2.48-4.38	8.04	7.67-8.41	1.12	1.08-1.16	126	120-133
5	2.60	1.65-3.55	7.98	7.60-8.35	1.07[1,3]	1.03-1.11	126	120-133
6	2.07[4]	1.11-3.03	8.53[10]	8.15-8.91	1.10	1.05-1.14	128	121-134
7	2.21	1.26-3.16	8.07[10]	7.70-8.44	1.09[1]	1.05-1.13	129	123-135
8	2.39	1.46-3.32	8.40	8.03-8.76	1.10	1.06-1.14	130	124-136
9	2.84	1.87-3.81	8.42	8.03-8.80	1.11	1.07-1.15	1329	123-136
10	2.41	1.44-3.37	7.94[6]	7.56-8.32	1.07[1,3]	1.03-1.11	129	123-136

*Adjusted for Age, BMI and Alcohol using analysis of covariance

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or 10

Table 21. Number and Percent Subjects Above or Below Reference Points for Thyroid-Related Clinical Chemistry Results, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	TSH (µIU/mL) <0.35 N (%)	TSH (µIU/mL) >5.5 N (%)	T4 (µg/dL) <4.5 N (%)	T4 (µg/dL) >12.0 N (%)	Free T4 (ng/dL) <0.70 N (%)	Free T4 (ng/dL) >1.53 N (%)	T3 (ng/dL) <60 N (%)	T3 (ng/dL) >181 N (%)
1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)
2	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
3	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4	1 (2)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
5	0 (0)	4 (8)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
6	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)
7	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
8	0 (0)	4 (8)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	2 (4)
9	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
10	1(2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
p value*	.63	.10	.44	-	.65	.46	-	.46

*chi square test of significance

Table 22. Thyroid related hormone tests results by subject when TSH ≥ 4.0 μIU/mL (ascending order) and corresponding PFOA (μg/mL) concentration. Results out-of-reference range (see Table 21) are shaded.

Subject	TSH	T4	Free T4	T3	PFOA
1	4.03	6.1	1.13	103	1.615
2	4.06	6.2	1.13	106	60.225
3	4.12	7.9	0.98	117	3.115
4	4.12	8.2	1.17	156	3.554
5	4.15	5.1	0.76	90	0.070
6	4.21	8.9	1.0	127	0.071
7	4.21	6.0	0.87	109	1.606
8	4.23	10.9	1.23	116	0.042
9	4.24	8.8	1.03	164	0.081
10	4.25	6.4	1.25	153	0.604
11	4.26	6.2	1.22	154	0.517
12	4.32	6.7	0.99	125	0.202
13	4.48	7.2	0.91	112	1.070
14	4.60	7.8	1.01	143	2.143
15	4.64	6.6	1.13	114	2.252
16	4.71	6.1	0.94	116	0.126
17	4.90	8.2	1.14	109	1.415
18	4.91	6.3	0.76	118	1.252
19	4.94	7.9	1.16	100	1.727
20	4.96	7.8	1.35	119	0.185
21	5.03	9.0	1.22	128	2.152
22	5.12	6.2	0.88	119	1.388
23	5.20	6.4	0.97	102	0.160
24	5.36	7.6	0.94	157	12.696
25	5.38	9.4	1.17	117	0.126
26	5.46	8.0	1.09	106	4.157
27	5.47	8.8	1.19	132	5.154
28	5.60	8.8	0.83	144	2.579
29	5.68	7.0	1.00	135	1.625
30	5.73	9.4	1.01	124	1.888
31	5.75	9.1	1.09	118	0.731
32	5.87	7.7	0.94	116	1.106
33	6.01	6.7	0.92	140	0.718
34	6.05	8.9	1.10	136	1.525
35	6.09	8.8	1.25	146	0.879
36	6.32	5.6	0.88	114	4.715
37	7.51	6.7	0.94	134	2.060
38	7.99	8.8	1.04	102	3.670
39	8.55	9.7	1.54	109	2.343
40	9.42	9.0	1.23	133	3.637
41	11.83	9.4	1.07	164	0.576
42	18.78	8.4	0.84	123	0.725
43	19.39	4.7	0.95	102	2.434
44	23.24	6.9	0.91	120	2.715
45	65.28	4.6	0.55	121	0.457

Table 23. Non-adjusted and Adjusted[1] Ln PFOA Coefficients for Ln Thyroid-Related Hormone, 2000 Fluorochemical Medical Surveillance Program

	Non-adjusted Ln PFOA Coefficient	SE	p value	Adjusted[1] Ln PFOA Coefficient	SE	p value
			Ln TSH			
All Locations	0.0395	0.0204	.05	0.0360	0.0207	.08
Antwerp	0.0509	0.0329	.12	0.0391	0.0333	.24
Cottage Grove	-0.0016	0.0310	.96	-0.0111	0.0322	.73
Decatur	0.0343	0.0497	.49	0.0365	0.0513	.48
			Ln T4			
All Locations	-0.0037	0.0054	.50	-0.0057	0.0054	.29
Antwerp	-0.0022	0.0099	.83	-0.0041	0.0099	.68
Cottage Grove	-0.0124	0.0072	.09	-0.0093	0.0072	.20
Decatur	-0.0012	0.0126	.92	-0.0083	0.0127	.51
			Ln Free T4			
All Locations	-0.0138	0.0044	.002	-0.0117	0.0043	.01
Antwerp	-0.0108	0.0078	.17	-0.0140	0.0078	.07
Cottage Grove	-0.0093	0.0058	.11	-0.0071	0.0059	.23
Decatur	-0.0138	0.0103	.18	-0.0184	0.0105	.08
			Ln T3			
All Locations	0.0107	0.0052	.04	0.0105	0.0053	.05
Antwerp	0.0222	0.0077	.005	0.0216	0.0077	.006
Cottage Grove	0.0026	0.0096	.79	0.0006	0.0099	.95
Decatur	0.0317	0.0117	.008	0.0271	0.0119	.02

1. See study methods. Adjusted for Ln Age, Ln BMI, Ln Alcohol

Table 24. Predicted Thyroid-Related Clinical Chemistry Results Based on Multiple Regression Models for 40 Year Old Male with BMI = 28 and Drinks 0.5 Alcohol Beverages per Day.

Reference Range	Predicted TSH (μIU/mL) (0.25 – 5.5)	Predicted T4 (μg/dL) (4.5-12.0)	Predicted Free T4 (ng/dL) (0.70-1.53)	Predicted T3 (ng/dL) (60-181)
PFOA Serum Concentration (μg/mL)				
0.005	1.58	8.22	1.15	119
0.01	1.62	8.19	1.15	119
0.10	1.76	8.08	1.11	121
0.50	1.87	8.01	1.09	124
1.00	1.91	7.98	1.09	125
5.00	2.03	7.90	1.06	128
10.00	2.07	7.87	1.06	128
50.00	2.20	7.80	1.04	131
100.00	2.26	7.77	1.03	132

Table 25. Number (percent), Odds Ratios (O.R.) and 95% Confidence Intervals (95% C.I.) with Metabolic Syndrome, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program

PFOA Decile	N (%)	Non-adjusted O.R.	95% C.I.	Adjusted[1] O.R.	95% C.I.
1	6 (12)	1.0	-	1.0	-
2	4 (8)	0.6	0.2-2.4	0.6	0.1-2.2
3	1 (2)	0.2	0.0-0.9	0.2	0.0-1.0
4	8 (16)	1.4	0.5-4.7	1.5	0.5-4.9
5	5 (10)	0.8	0.2-2.9	0.8	0.2-2.9
6	6 (12)	1.0	0.3-3.6	1.0	0.3-3.5
7	3 (6)	0.5	0.1-1.9	0.5	0.1-2.0
8	6 (12)	0.9	0.3-3.2	0.9	0.3-3.0
9	6 (12)	1.0	0.3-3.6	1.1	0.3-3.6
10	6 (12)	1.0	0.3-3.5	1.0	0.3-3.6

1. Adjusted for age

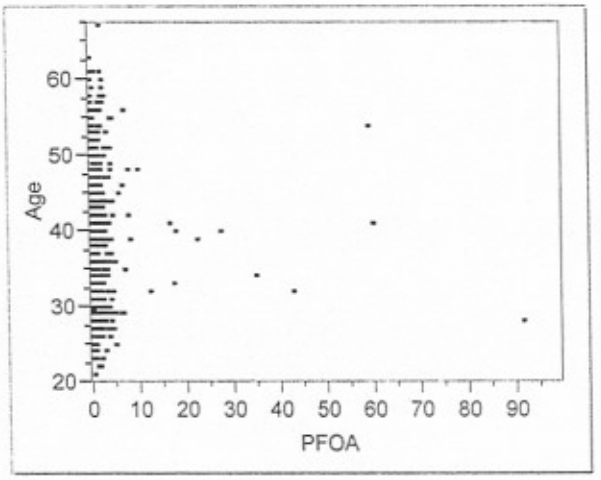
Appendix A

Table A1. Correlation Coefficients (same as Table D1)

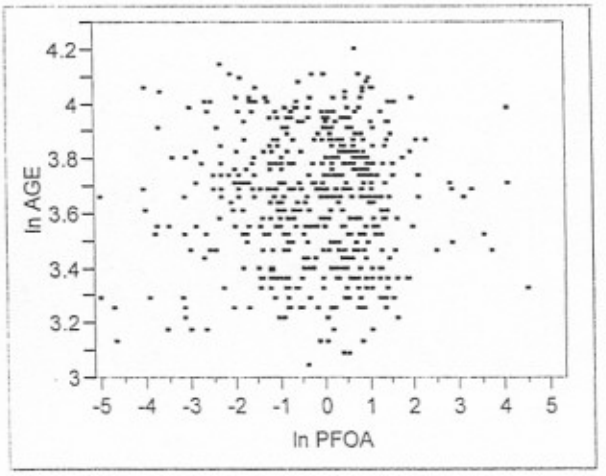
Ln (Variable)	Ln (PFOA)	Ln(PFOS)	Ln(Age)	Ln(BMI)	Ln(Alcohol)
PFOA	1.0				
PFOS	0.55****	1.0			
Age	0.03	0.06	1.0		
BMI	0.11*	0.00	0.20****	1.0	
Alcohol	-0.12**	-0.10*	-0.15***	-0.26****	1.0
Cholesterol	0.04	0.08	0.15***	0.00	0.10*
LDL	0.00	0.06	0.13**	-0.02	0.01
HDL	-0.17****	-0.07	-0.13**	-0.43****	0.37****
Triglycerides	0.210****	0.13**	0.18****	0.44****	-0.12**
Glucose	-0.01	-0.13**	0.26****	0.28****	-0.19****
Alk Phos	0.08	0.08	0.08	0.12**	-0.25****
AST	-0.01	0.00	0.00	0.15***	-0.04
ALT	0.12**	0.08	0.03	0.41****	-0.16***
AST/ALT	-0.15***	-0.09*	-0.05	-0.39****	0.17***
GGT	0.10*	0.10*	0.15***	0.31****	0.20****
Total Bilirubin	-0.18****	-0.13**	-0.08	-0.18****	-0.02
Direct Bilirubin	-0.06	-0.03	-0.03	-0.03	-0.02
TSH	0.09	0.04	-0.01	0.08	-0.02
T4	-0.03	0.002	-0.09	-0.05	-0.17***
Free T4	-0.15**	-0.06	-0.18***	-0.17***	0.08
T3	0.09	0.03	-0.10*	0.02	-0.01

*$p < .05$
** $p < .01$
*** $p < .001$
**** $p < .0001$

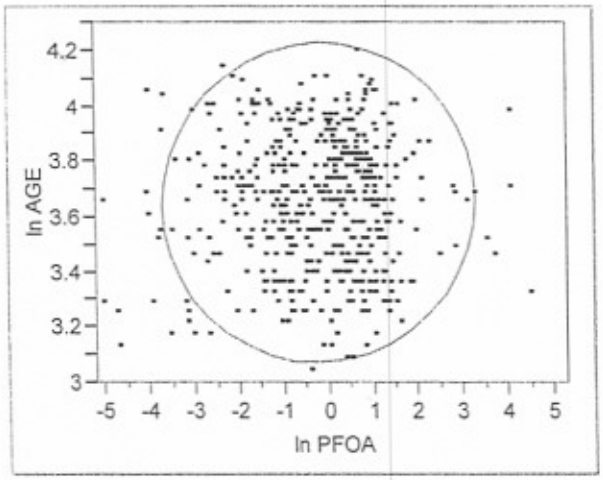
Age by PFOA (µg/mL)



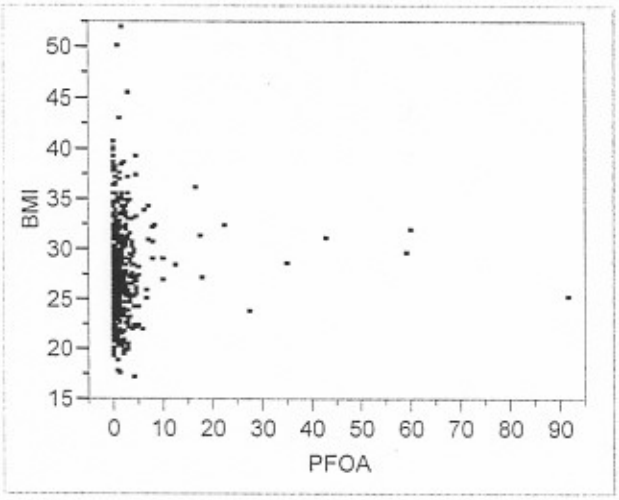
LN Age by LN PFOA (µg/mL)



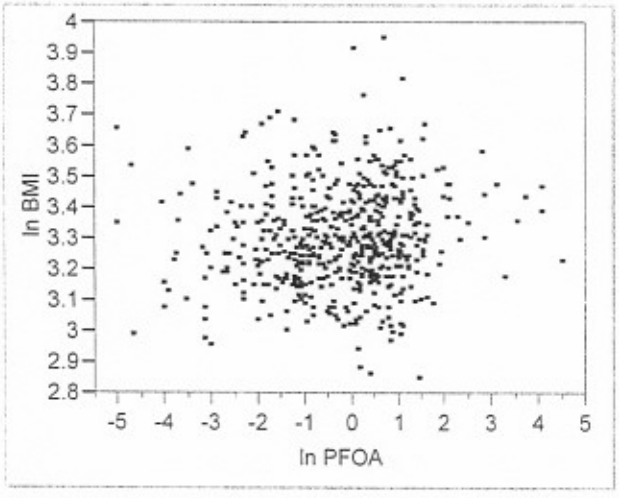
LN Age by LN PFOA (µg/mL)



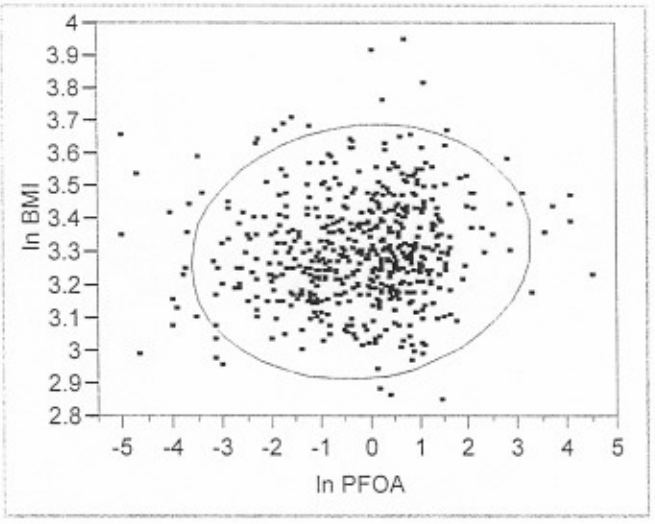
BMI by PFOA (µg/mL)



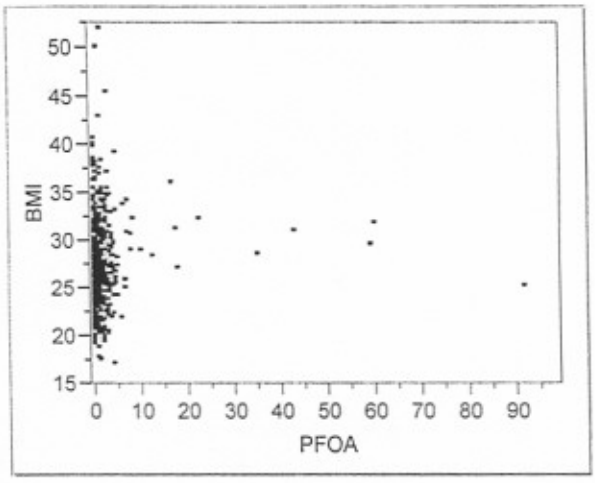
LN BMI by LN PFOA (µg/mL)



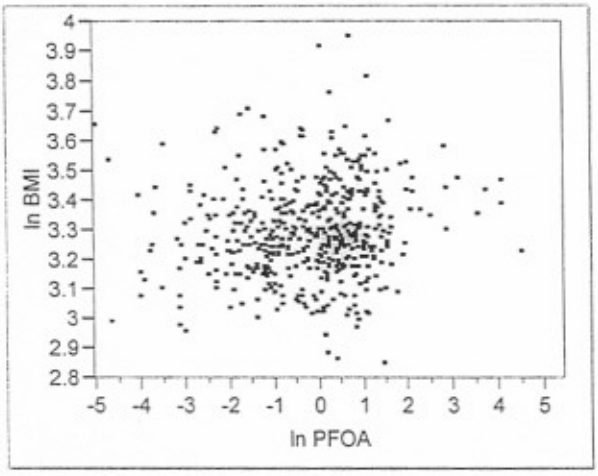
LN BMI by LN PFOA (µg/mL)



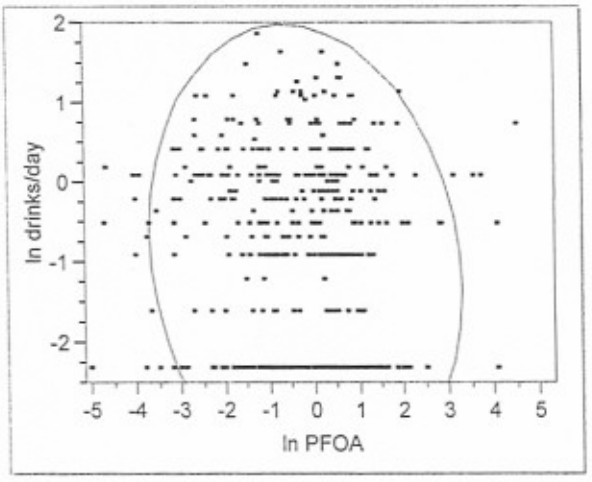
Alcohol (Drinks/Day) by PFOA(µg/mL)



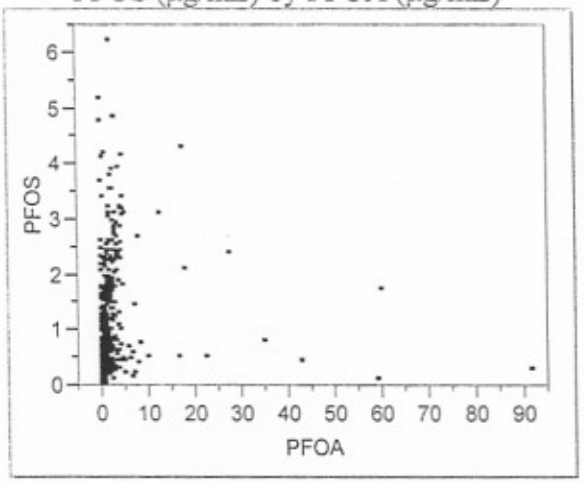
LN Alcohol (Drinks/Day) by Ln PFOA(µg/mL)



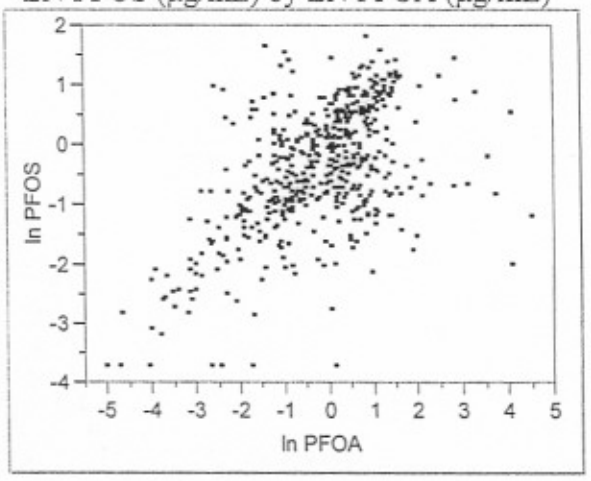
LN Drinks/day by PFOA (µg/mL)



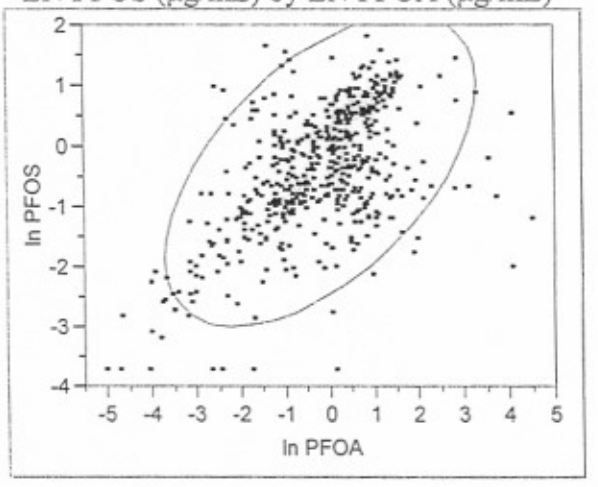
PFOS (µg/mL) by PFOA (µg/mL)



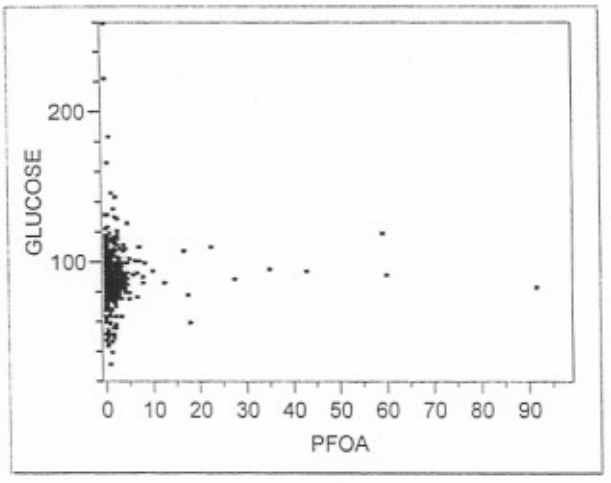
LN PFOS (µg/mL) by LN PFOA (µg/mL)



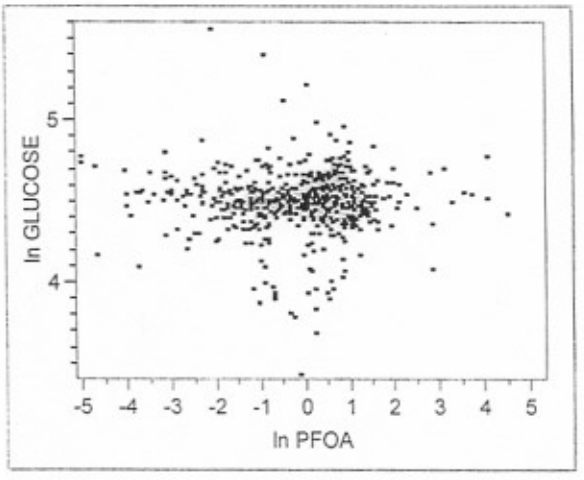
LN PFOS (µg/mL) by LN PFOA (µg/mL)



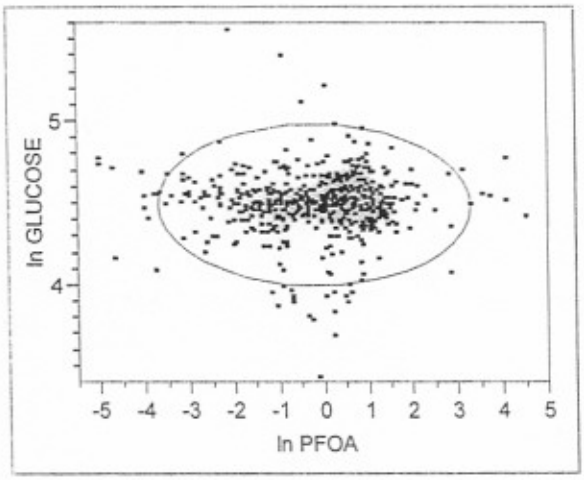
Glucose (mg/dL) by PFOA (µg/mL)



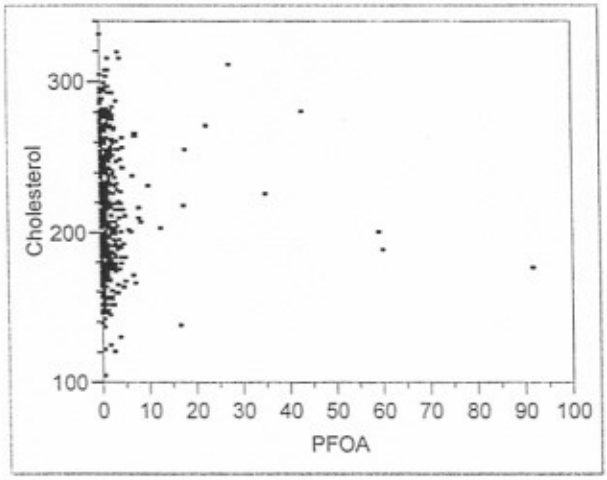
LN Glucose (mg/dL) by LN PFOA (µg/mL)



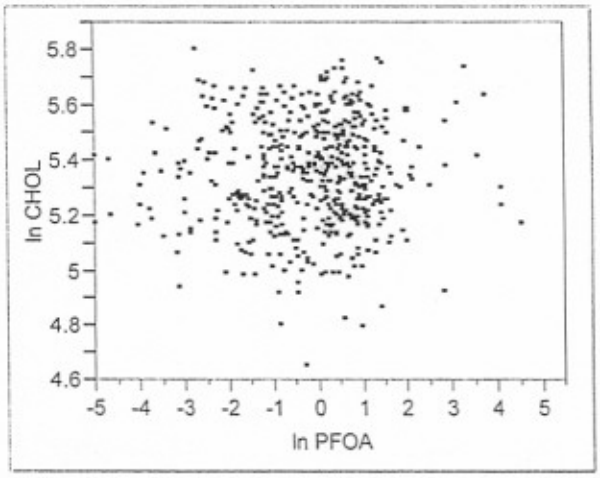
LN Glucose (mg/dL) by LN PFOA (µg/mL)



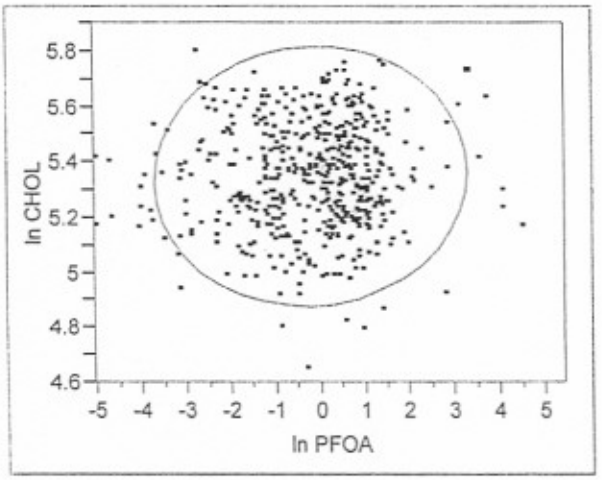
Cholesterol (mg/dL) by PFOA (µg/mL)



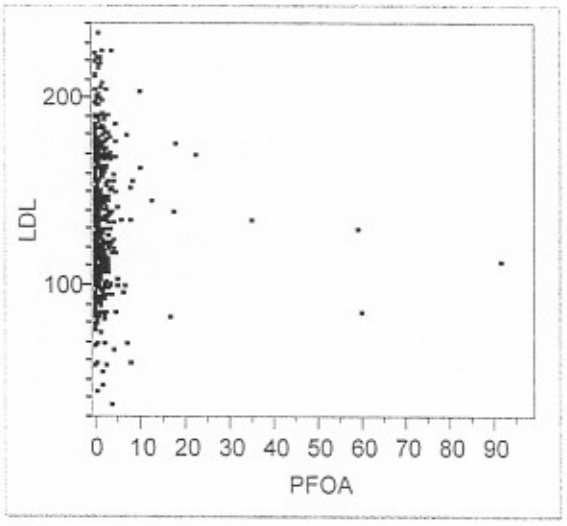
LN Cholesterol (mg/dL) by LN PFOA (µg/mL)



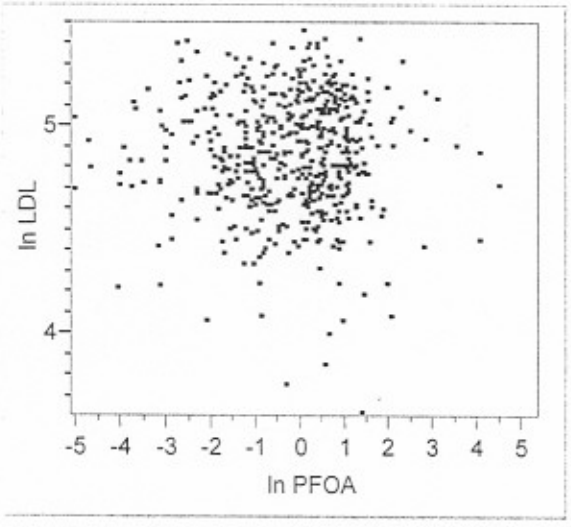
LN Cholesterol (mg/dL) by LN PFOA (µg/mL)



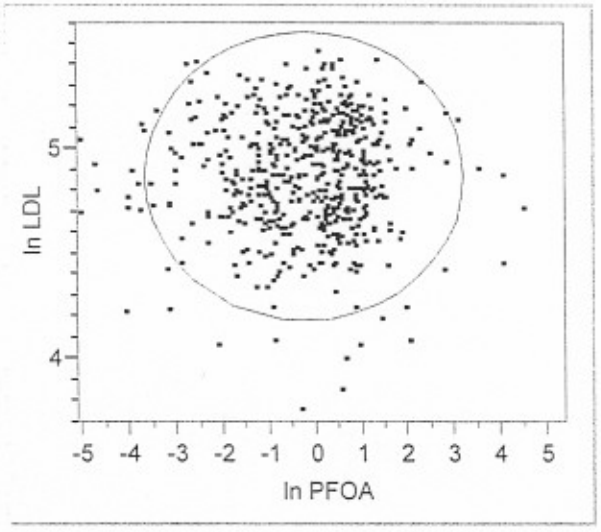
LDL (mg/dL) by PFOA (µg/mL)



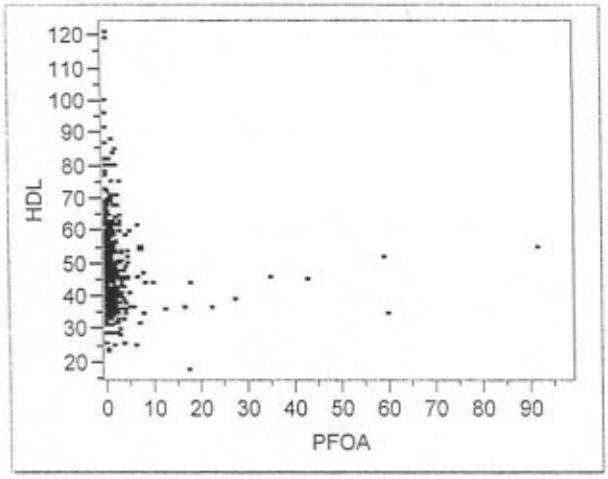
LN LDL (mg/dL) by LN PFOA (µg/mL)



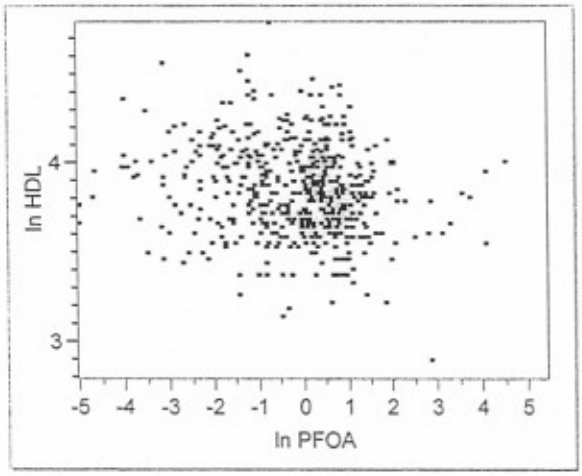
LN LDL (mg/dL) by LN PFOA (µg/mL)



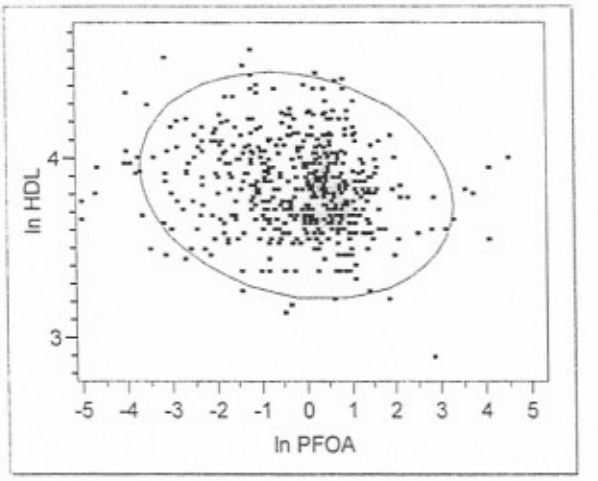
HDL (mg/dL) by PFOA (µg/mL)



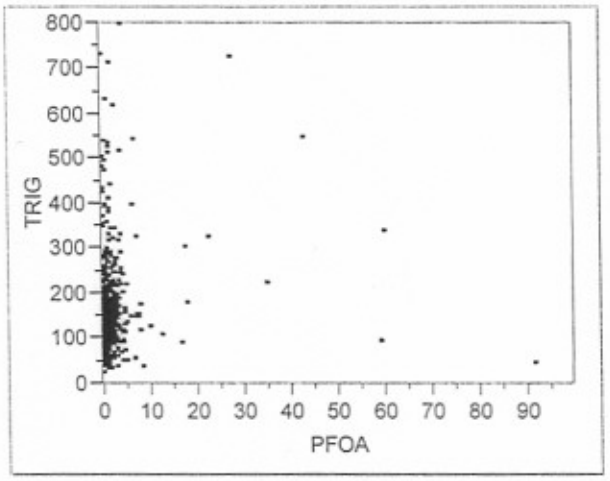
LN HDL (mg/dL) by LN PFOA (µg/mL)



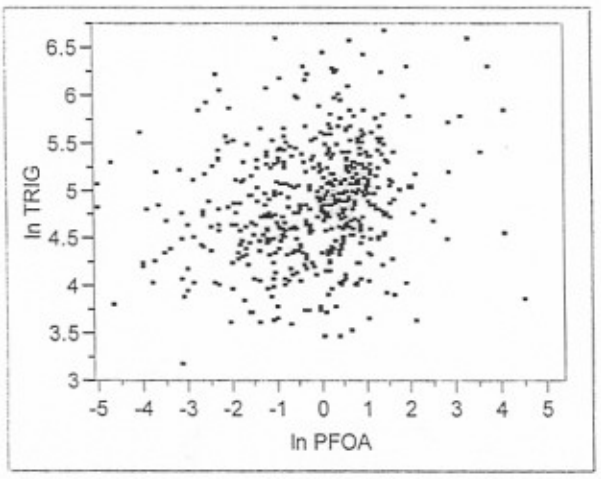
LN HDL (mg/dL) by LN PFOA (µg/mL)



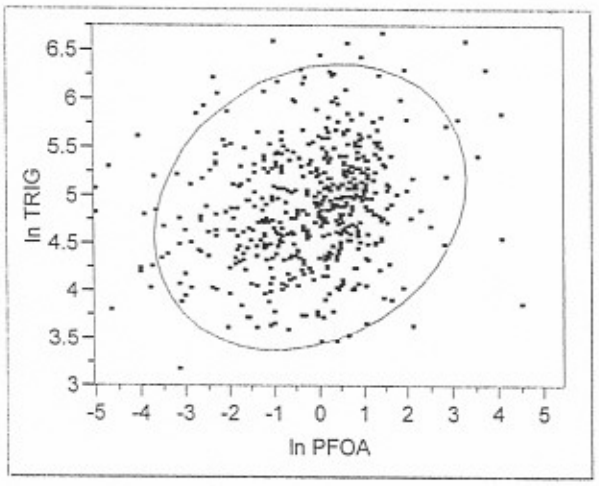
Triglycerides(mg/dL) by PFOA (µg/mL)



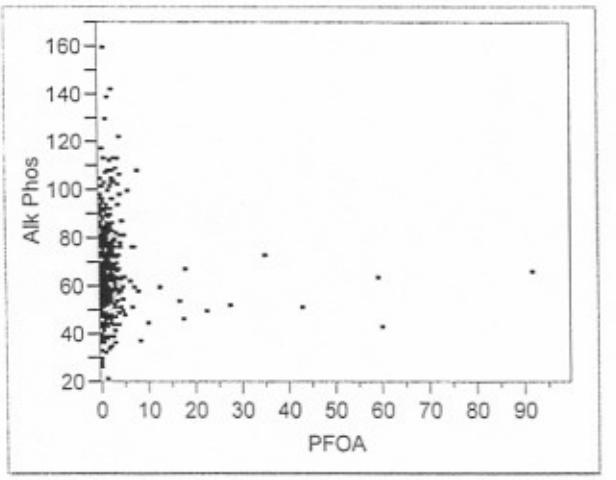
LN Triglycerides (mg/dL) by LN PFOA (µg/mL)



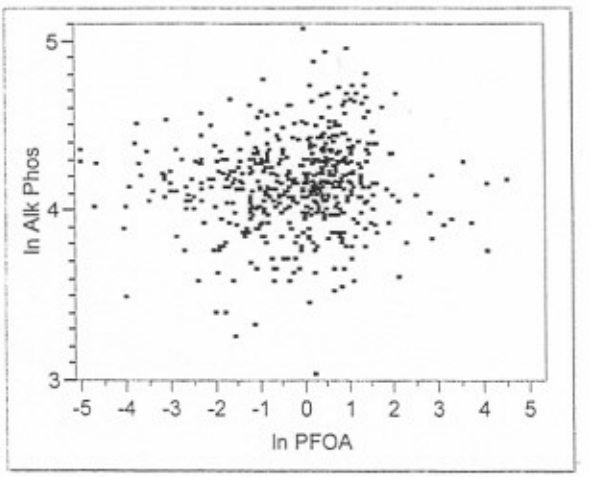
LN Triglycerides (mg/dL) by LN PFOA (µg/mL)



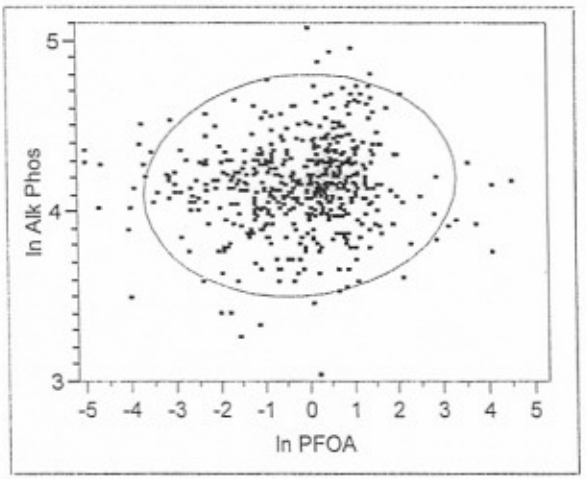
Alkaline Phosphatase (IU/L) by PFOA (µg/mL)



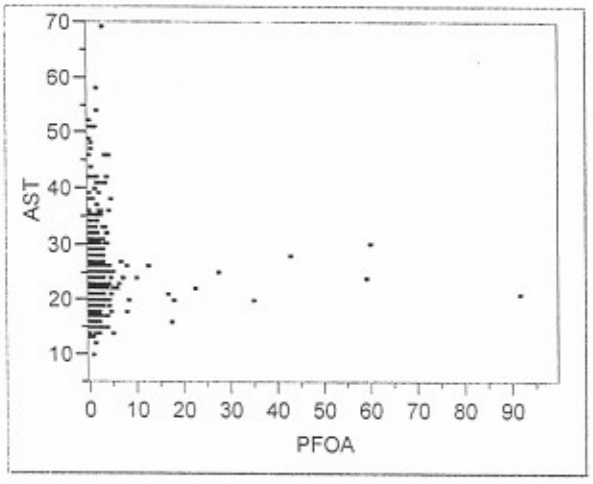
LN Alkaline Phophatase (IU/L) by LN PFOA (µg/mL)



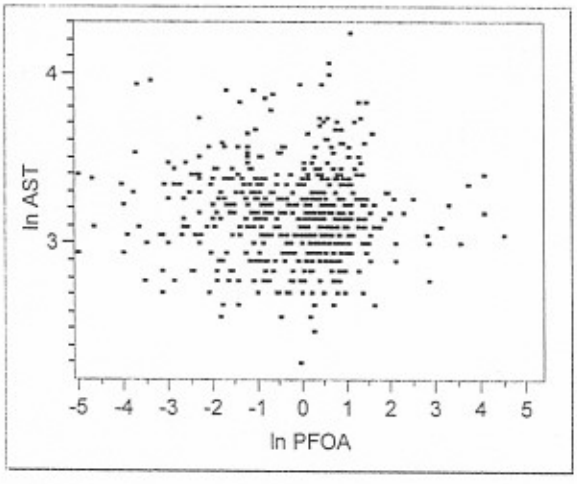
LN Alkaline Phosphatase (IU/L) by LN PFOA (µg/mL)



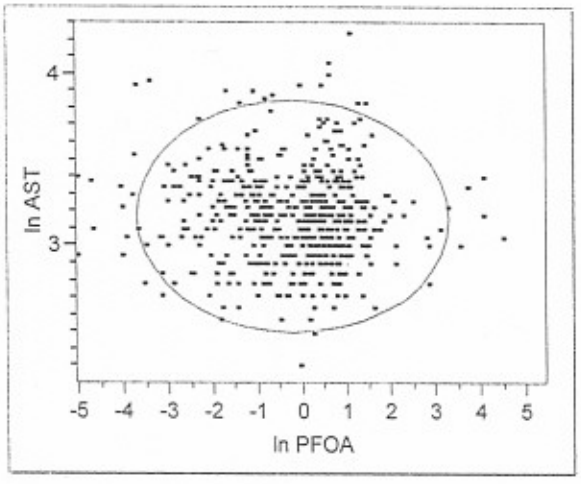
AST (IU/L) by PFOA (µg/mL)



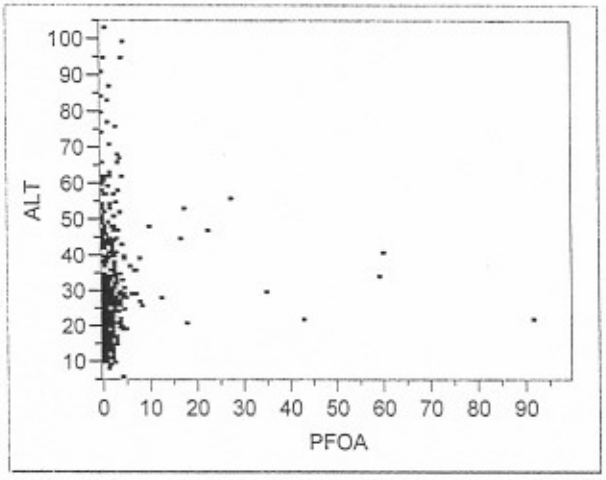
LN AST (IU/L) by LN PFOA (µg/mL)



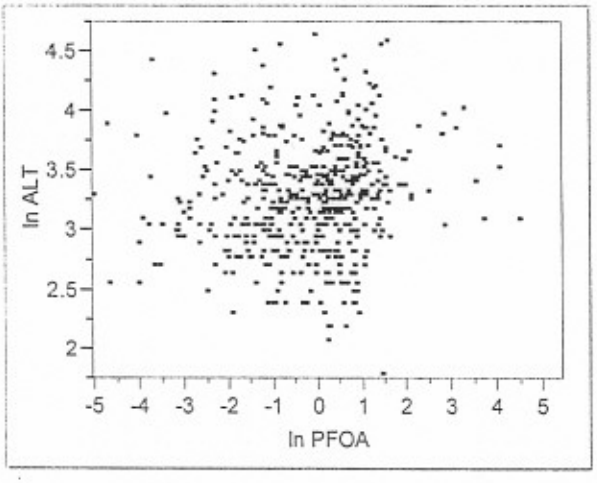
LN AST (IU/L) by LN PFOA (µg/mL)



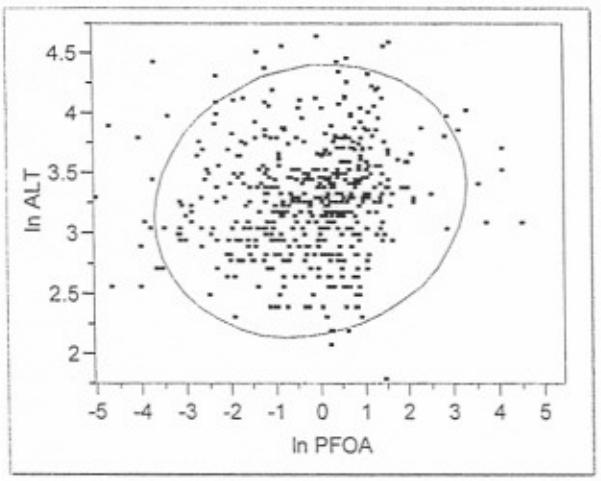
ALT (IU/L) by PFOA (µg/mL)



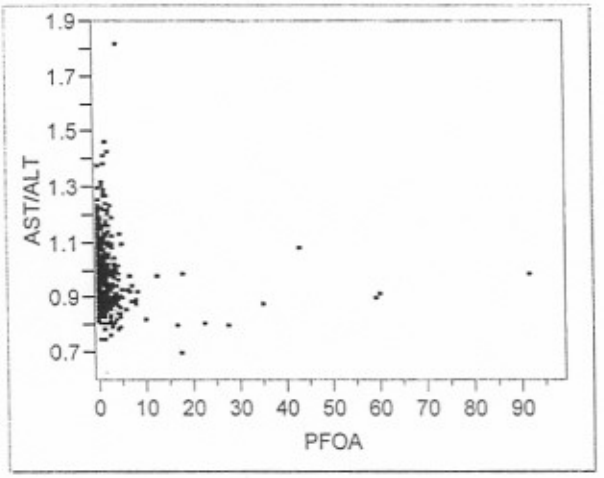
LN ALT(IU/L) by LN PFOA (µg/mL)



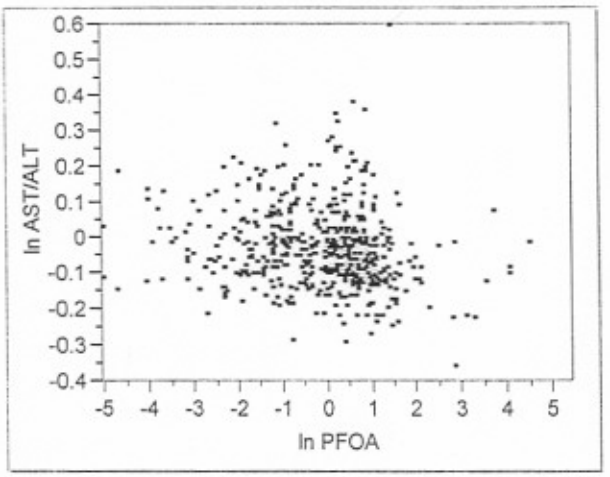
LN ALT (IU/L) by LN PFOA (µg/mL)



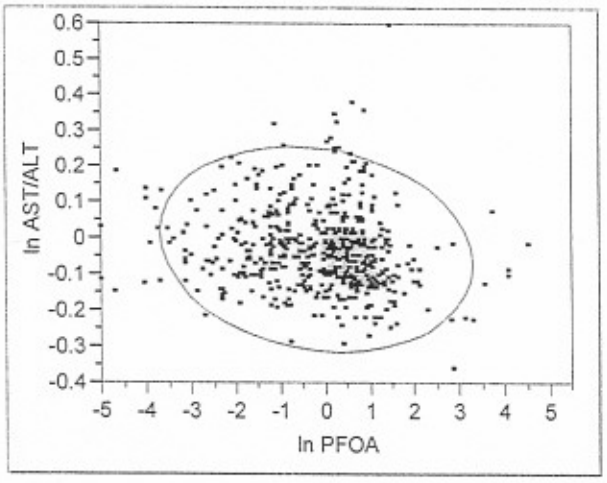
AST/ALT by PFOA (µg/mL)



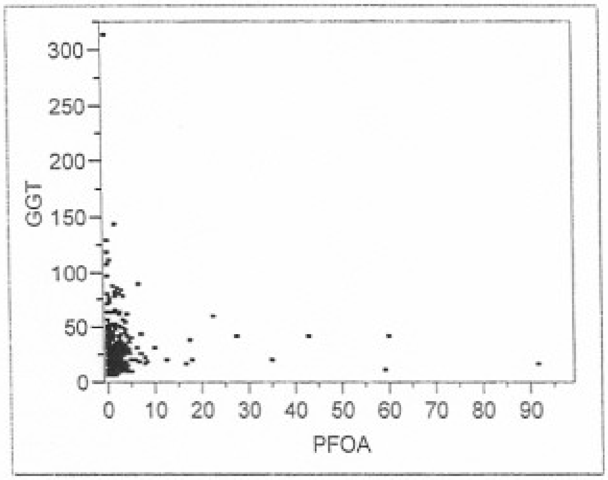
AST/ALT by LN PFOA (µg/mL)



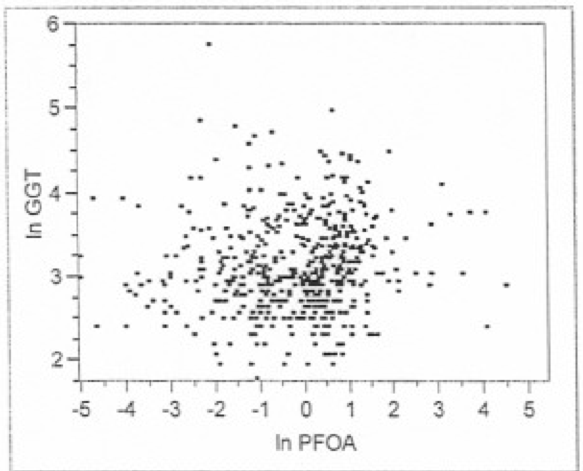
LN AST/ALT by LN PFOA (µg/mL)



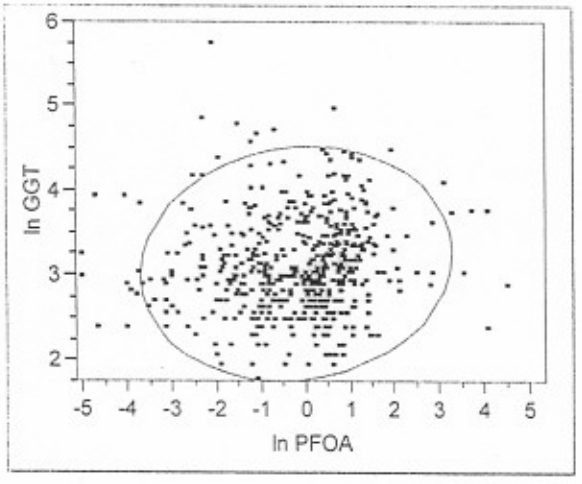
GGT (IU/L) by PFOA (µg/mL)



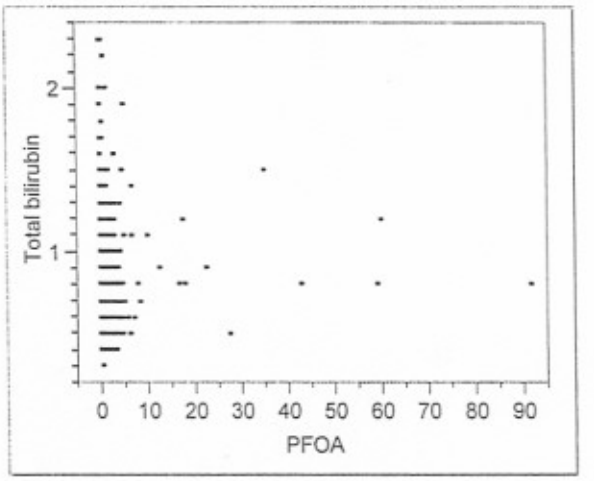
LN GGT (IU/L) by LN PFOA (µg/mL)



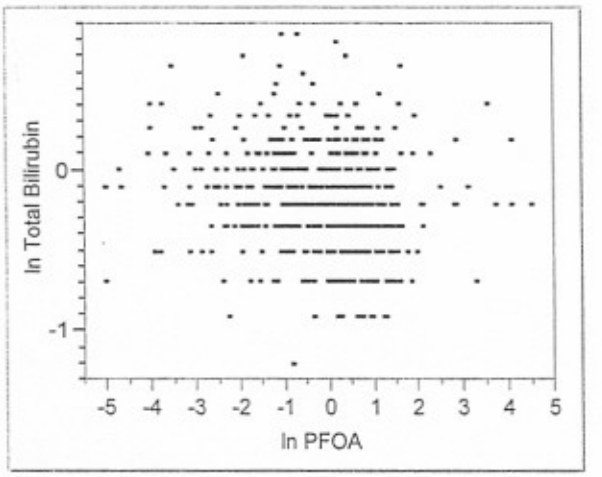
LN GGT (IU/L) by LN PFOA (µg/mL)



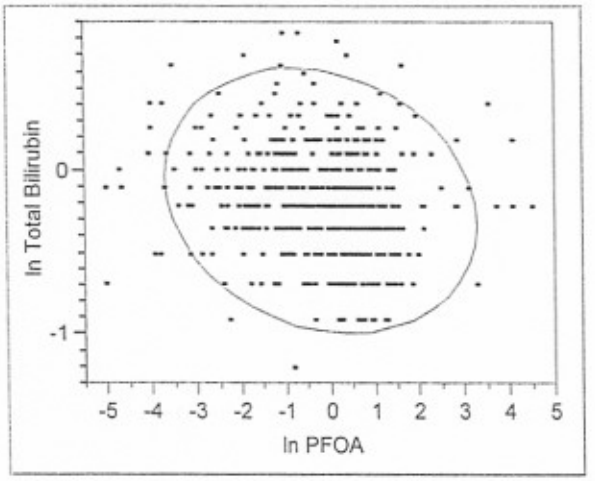
Total Bilirubin (mg/dL) by PFOA (µg/mL)



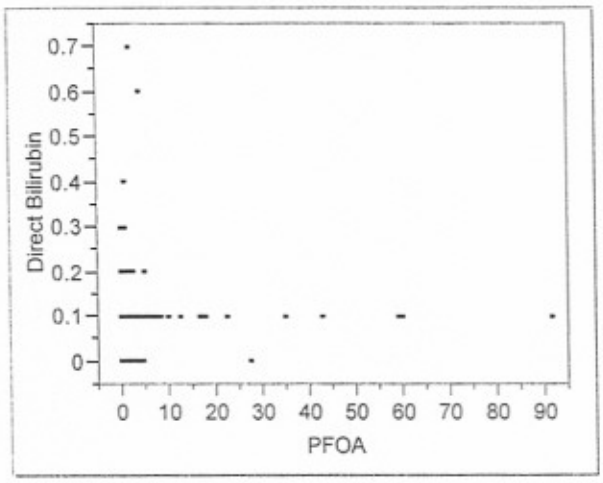
LN Total Bilirubin (mg/dL) by LN PFOA (µg/mL)



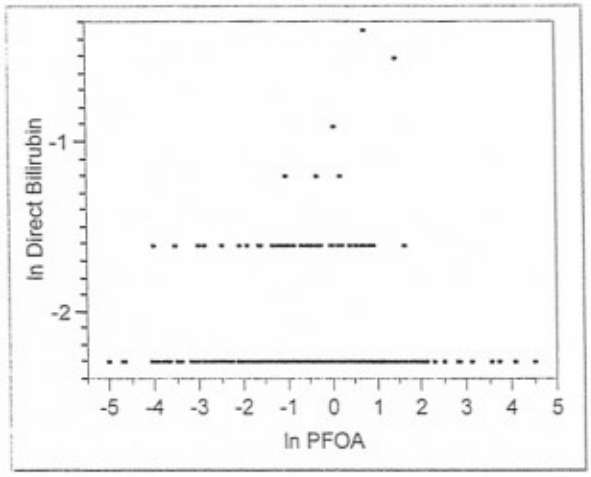
LN Total Bilirubin (mg/dL) by LN PFOA (µg/mL)



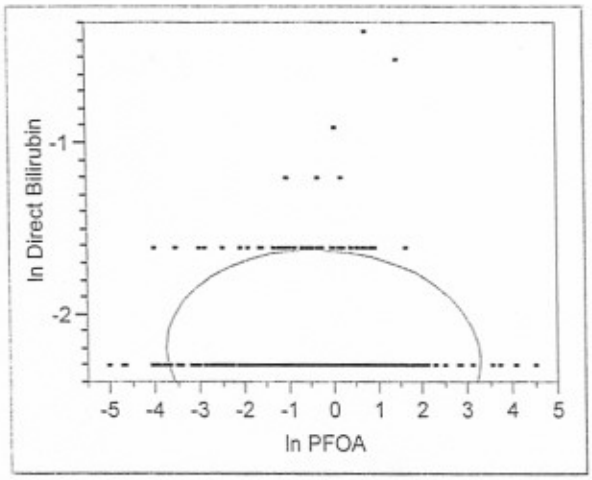
Direct Bilirubin (mg/dL) by PFOA (µg/mL)



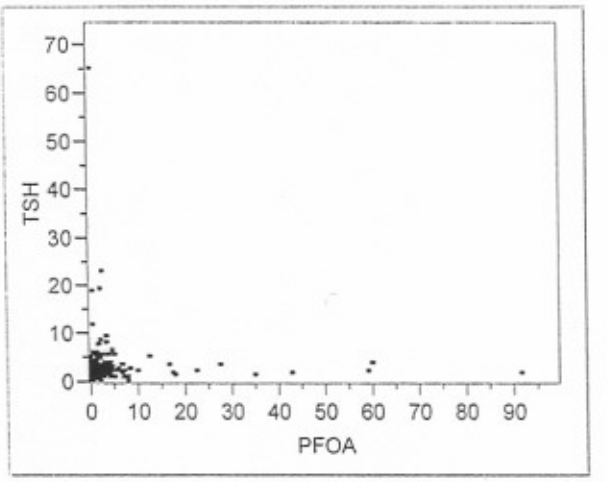
LN Direct Bilirubin (mg/dL) by LN PFOA (µg/mL)



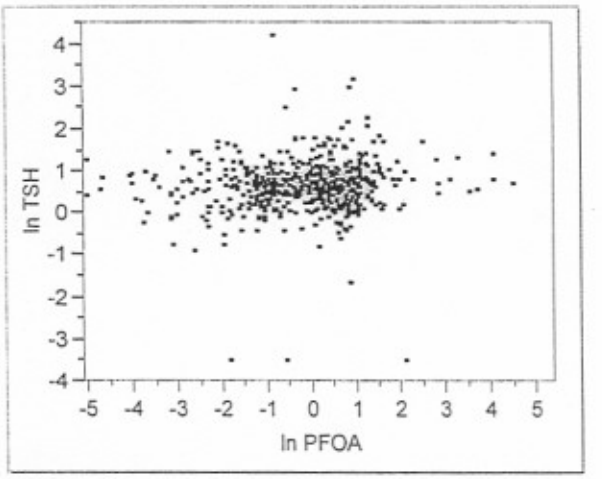
LN Direct Bilirubin (mg/dL) by LN PFOA (µg/mL)



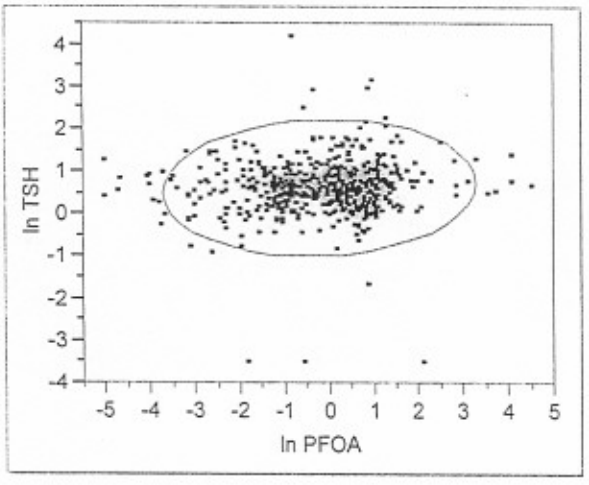
TSH (µIU/mL) by PFOA (µg/mL)



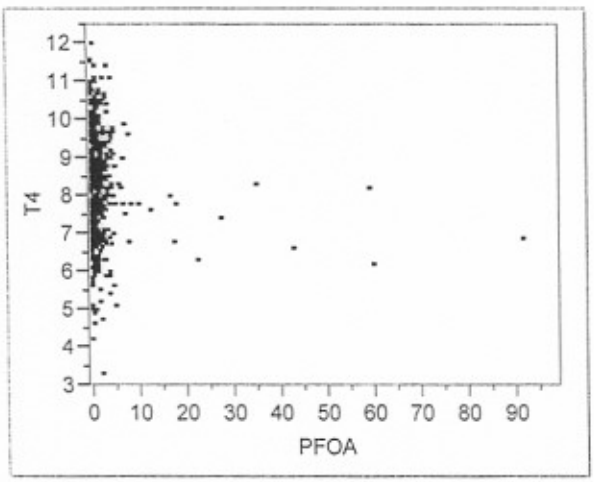
LN TSH (µIU/mL) by LN PFOA (µg/mL)



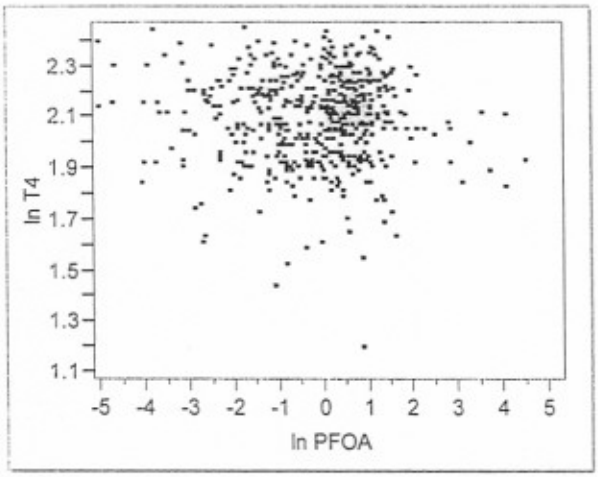
LN TSH (µg/mL) by LN PFOA (µg/mL)



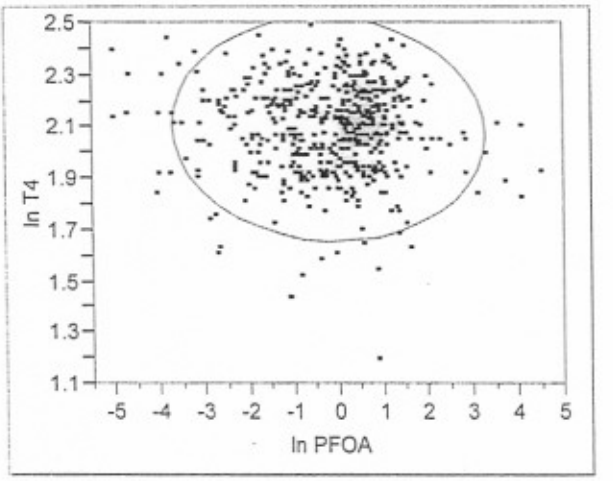
T4 (µg/dL) by PFOA (µg/mL)



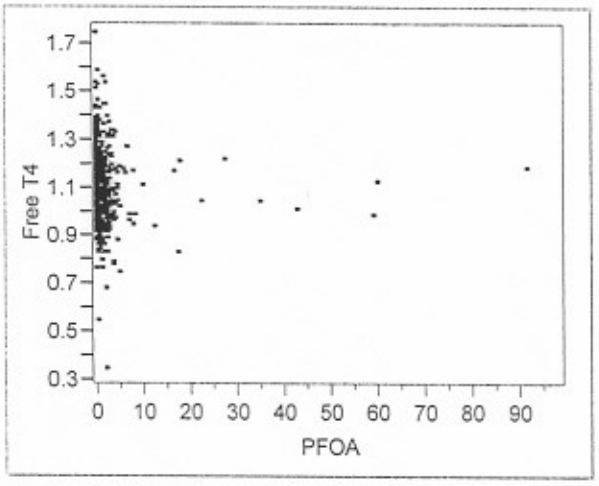
LN T4 (µ g/dL) by PFOA (µg/mL)



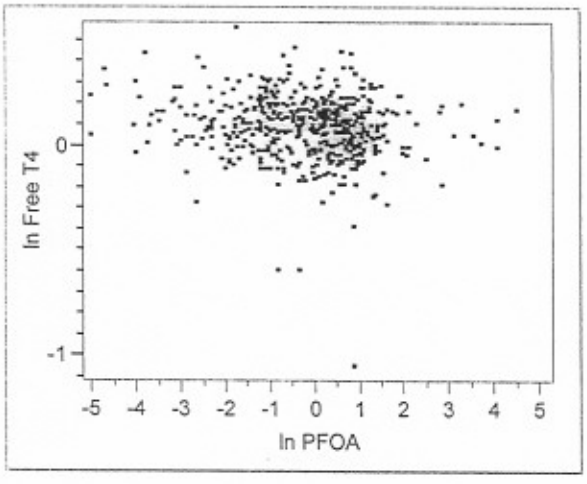
LN T4 (µg/dL) by LN PFOA (µg/mL)



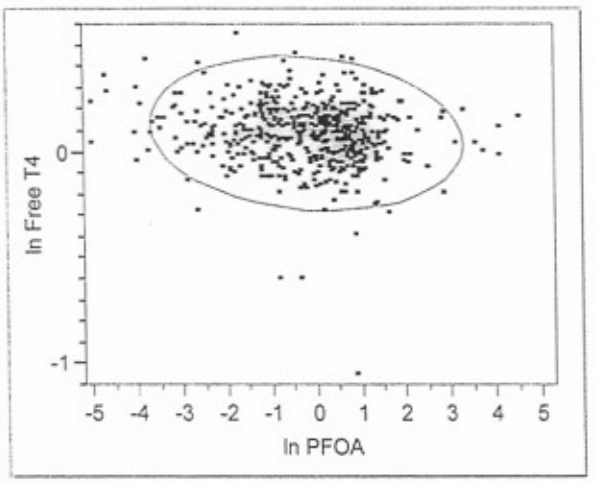
Free T4 (ng/dL) by PFOA (µg/mL)



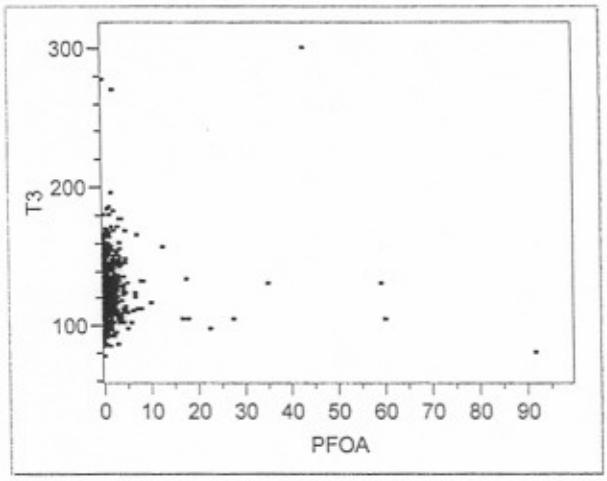
LN Free T4 (ng/dL) by LN PFOA (µg/mL)



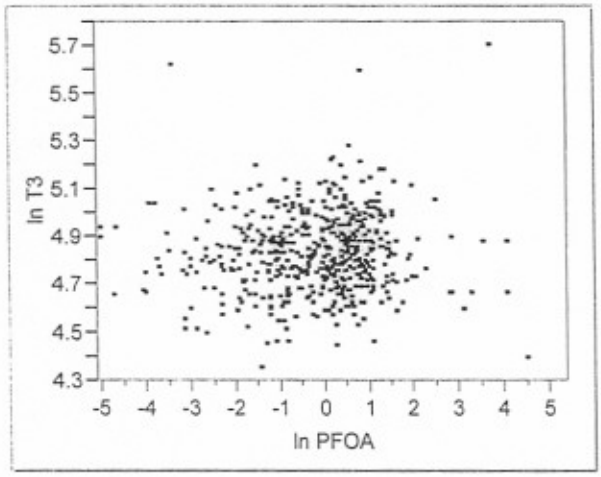
LN Free T4 (ng/dL) by LN PFOA (µg/mL)



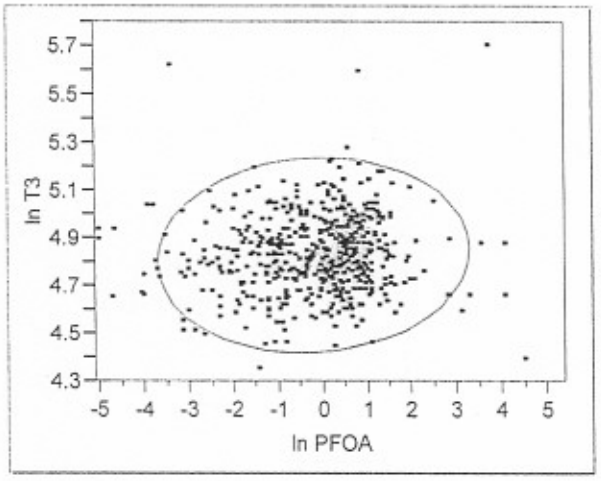
T3 (ng/dL) by PFOA (µg/mL)



LN T3 (ng/dL) by LN PFOA (µg/mL)



LN T3 (ng/dL) by LN PFOA (µg/mL)



Appendix B

Table B1. Demographic and Clinic Chemistry Comparisons (Mean, Standard Deviation (SD), Median and Range) of Employees Who Self-Reported Prescribed Cholesterol-Lowering Medications (N = 46) Versus Those Who Did Not (N = 506), 2000 Fluorochemical Medical Surveillance Program

	Prescribed Medication (N=46)				Not Prescribed (N=506)			
	Mean	(SD)	Median	Range	Mean	(SD)	Median	Range
PFOA	1.98	2.12	1.21	0.14-10.30	2.21	6.40	1.10	0.01-92.03
PFOS	1.69*	1.72	1.27	0.11-10.06	1.05	0.97	0.72	0.02-6.24
Age	49*	7	50	31-60	40	9	39	21-67
BMI	28.8*	4.5	28.4	19.9-39.3	27.4	4.6	26.6	17.2-52.1
Alcohol	0.4	0.6	0.0	0.0-2.0	0.6	0.9	0.3	0.0-6.4
% Antwerp	21*	-	-	-	39	-	-	-
% Cottage Grove	20*	-	-	-	24	-	-	-
% Decatur	59*	-	-	-	37	-	-	-
Glucose	103*	38	99	54-331	91	19	91	31-251
Cholesterol	221	45	217	144-384	214	41	211	105-331
LDL	134	40	130	59-222	136	36	133	37-235
HDL	47	14	43	31-91	49	13	46	18-121
Triglycerides	226*	160	194	35-792	159	112	128	24-796
Alk Phos	73*	21	73	30-126	66	18	64	21-160
AST	27*	8	25	7-48	25	7	24	10-69
ALT	36*	20	32	9-96	30	15	26	6-103
GGT	36*	24	28	10-144	28	22	22	6-314
Total Bilirubin	0.8	0.2	0.8	0.4-1.5	0.9	0.3	0.8	0.3-2.3

Table B1. (continued)

	Prescribed Lipid-Lowering Medication (N=46)				Not Prescribed (N=506)			
	Mean	(SD)	Median	Range	Mean	(SD)	Median	Range
Direct Bilirubin	0.1	0.06	0.1	0.0-0.3	0.1	0.06	0.1	0.0-0.7
AST/ALT	0.89	0.42	0.82	0.22-2.22	0.98	0.12	0.97	0.70-1.82
TSH	2.8	3.1	2.1	0.4-21.5	2.4	3.4	1.9	0.03-65.3
T4	8.1	1.4	7.9	5.8-12.9	8.2	1.4	8.2	4.2-12.0
Free T4	1.1	0.2	1.1	0.8-1.5	1.1	0.2	1.1	0.6-1.8
T3	125	19	123	93-190	127	23	125	78-300

* $p < .05$ (prescribed vs. non-prescribed)

Table B2. Mean and Standard Deviation (SD) of PFOA, PFOS, Demographics and Clinical Chemistry Results by Location by Cholesterol-Lowering Medication Status

	Antwerp				Cottage Grove				Decatur			
	Cholesterol-Lowering Med				Cholesterol-Lowering Med				Cholesterol-Lowering Med			
	Yes		No		Yes		No		Yes		No	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
PFOA	1.16	(1.53)	1.02	(1.06)	2.94	(3.66)	4.63	(12.53)	1.97	(1.52)	1.89	(1.61)
PFOS	1.25	(0.91)	0.95	(0.97)	0.76	(0.74)	0.86	(0.98)	2.18*	(2.01)	1.29	(0.92)
Age	50*	(5)	37	(8)	50*	(7)	41	(9)	48*	(7)	42	(9)
BMI	25.9	(3.4)	24.7	(3.0)	29.5	(4.2)	29.9	(4.8)	29.7	(4.6)	28.6	(4.6)
Alcohol	0.7	(0.8)	1.1	(1.1)	0.7	(0.7)	0.7	(0.7)	0.2	(0.4)	0.1	(0.3)
Glucose	96	(30)	84	(17)	103	(13)	100	(23)	106*	(46)	93	(14)
Cholesterol	232	(38)	218	(41)	214	(38)	210	(39)	220	(50)	214	(41)
LDL	152	(43)	139	(37)	126	(47)	130	(32)	130	(35)	136	(36)
HDL	52	(18)	55	(15)	52	(17)	46	(11)	44	(10)	44	(10)
Triglycerides	195*	(125)	120	(83)	180	(83)	187	(139)	253*	(187)	182	(110)
Alk Phos	58	(20)	60	(14)	77*	(23)	65	(15)	77	(19)	73	(20)

Table B2 (continued)

	Antwerp				Cottage Grove				Decatur			
	Cholesterol-Lowering Med				Cholesterol-Lowering Med				Cholesterol-Lowering Med			
	Yes		No		Yes		No		Yes		No	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
AST	25	(6)	23	(6)	30	(8)	25	(8)	27	(9)	26	(8)
ALT	22	(9)	23	(10)	43	(25)	34	(17)	39	(19)	34	(16)
AST/ALT	1.3	(0.6)	1.2	(0.4)	0.8	(0.3)	0.8	(03)	0.8	(0.3)	0.9	(0.4)
GGT	25	(13)	23	(17)	53	(40)	31	(32)	35	(18)	30	(17)
Tot Bilirubin	1.0	(0.3)	1.0	(0.3)	0.9	(0.2)	0.9	(0.3)	0.7	(0.2)	0.7	(0.2)
Dir Billirubin	0.1	(0.03)	0.1	(0.05)	0.1	(0.03)	0.1	(0.02)	0.1	(0.07)	0.1	(0.08)
TSH	1.9	(0.7)	2.0	(1.6)	2.5	(0.6)	2.4	(1.4)	3.2	(4.0)	2.8	(5.2)
T4	8.6	(1.7)	8.2	(1.4)	7.2	(1.2)	7.9	(1.1)	8.2	(1.3)	8.4	(1.4)
Free T4	1.2	(0.2)	1.1	(0.2)	1.1	(0.1)	1.1	(0.1)	1.1	(0.2)	1.1	(0.1)
T3	128	(18)	131	(19)	117	(16)	125	(30)	127	(20)	125	(22)

* $p < .05$ cholesterol lowering medication (yes vs. no within each location)

Table B3. Mean, Standard Deviation, Median and Range of PFOA, PFOS, Demographic Factors and Clinical Chemistry Results, By Location, 2000 Fluorochemical Medical Surveillance Program, For Employees Prescribed Cholesterol-Lowering Medications

	Antwerp (N=10)				Cottage Grove (N=9)				Decatur (N=27)			
	Mean	(SD)	Median	Range	Mean	(SD)	Median	Range	Mean	(SD)	Median	Range
PFOA	1.16	1.53	0.62	0.14-5.31	2.95	3.67	1.55	0.29-10.30	1.97	1.52	1.76	0.15-4.97
PFOS	1.25	0.91	0.98	0.23-2.77	0.76[3]	0.74	0.36	0.11-2.10	2.18[2]	2.01	1.58	0.15-10.06
Age	50	5	51	41-56	50	7	52	39-60	48	7	47	31-60
BMI	25.9[3]	3.4	24.7	22.4-34.2	29.5	4.2	30.9	23.4-35.5	29.7[1]	4.6	29.4	19.9-39.3
Alcohol	0.7[3]	0.8	0.5	0.0-2.0	0.7[3]	0.7	1.0	0.0-2.0	0.2[2,3]	0.4	0.0	0.0-1.6
Glucose	96	30	89	54-168	103	13	104	82-122	106	46	99	70-331
Cholesterol	232	38	243	179-280	214	38	216	154-280	220	50	216	144-384
LDL	152	44	160	85-222	126	47	124	59-203	130	35	129	66-216
HDL	52	18	45	31-87	52	17	49	37-91	44	10	42	31-73
Triglycerides	195	124	179	35-463	180	83	193	67-294	253	187	230	52-792
Alk Phos	58[2,3]	20	58	30-84	77[1]	23	81	40-105	77[1]	19	74	44-126
AST	25	6	24	17-37	30	8	27	20-41	27	9	25	7-48
ALT	22[2,3]	9	22	9-38	43[1]	25	33	16-96	39[1]	19	34	17-94
AST/ALT	1.3	0.6	1.2	0.6-2.2	0.8	0.3	0.8	0.4-1.3	0.8	0.3	0.7	0.2-1.2

Table B3
(Continued)

	Antwerp (N=9)				Cottage Grove (N=9)				Decatur (N=27)			
	Mean	(SD)	Med	Range	Mean	(SD)	Med	Range	Mean	(SD)	Med	Range
GGT	25[2]	13	21	10-49	53[1,3]	40	41	14-144	35[2]	18	28	13-89
Total Bil	1.0[3]	0.3	0.9	0.7-1.5	0.9	0.2	0.9	0.6-1.2	0.7[1]	0.2	0.7	0.4-1.1
Direct Bil	0.1	0.03	0.1	0.1-0.2	0.9	0.03	0.1	0.0-0.1	0.1	0.07	0.1	0.0-0.3
TSH	1.9	0.7	1.8	0.7-3.1	2.5	0.6	2.1	1.7-3.5	3.2	4.0	2.5	0.4-21.5
T4	8.6[2]	1.7	8.3	5.9-11.5	7.2[1]	1.2	7.4	5.8-9.1	8.2	1.3	8.0	6.2-12.9
Free T4	1.2	0.2	1.2	0.9-1.5	1.1	0.1	1.0	0.8-1.3	1.1	0.2	1.1	0.8-1.4
T3	128	18	128	98-162	117	16	117	96-141	127	20	123	93-190

1. Statistically significantly ($p < .05$) different than Antwerp
2. Statistically significantly ($p < .05$) different than Cottage Grove
3. Statistically significantly ($p < .05$) different than Decatur

Table B4. Non-adjusted and Adjusted* Regression PFOA Coefficients for Lipid Clinical Chemistry Results, 2000 Fluorochemical Results Restricted to Employee Taking Cholesterol-Lowering Medications (N = 46)

Ln of Response Variable	Non-adjusted Ln PFOA Coefficient	SE	p value	Adjusted* Ln PFOA Coefficient	SE	p value
Cholesterol	0.0453	0.0263	.09	0.0501	0.0292	.09
LDL	0.0253	0.0494	.61	0.0303	0.0536	.58
HDL	0.0003	0.0364	.99	0.0140	0.0346	.69
Triglycerides	0.0681	0.0968	.49	0.1015	0.0972	.30
Alk Phosphatase	0.0612	0.0420	.15	0.0533	0.0420	.21
				0.0347**	0.0428	.42
AST	0.0305	0.0437	.49	0.0434	0.0475	.37
				0.0340**	0.0469	.47
ALT	0.1040	0.0672	.13	0.0862	0.0674	.21
				0.0544**	0.0669	.42
GGT	0.0591	0.0734	.43	0.0653	0.0812	.43
				0.0404**	0.0746	.59
Total Bilirubin	-0.0818	0.0356	.03	-0.0649	0.0369	.09
				-0.0623**	0.0361	.09
TSH	0.0928	0.0904	.31	0.1803	0.0918	.06
T4	-0.0223	0.0226	.33	-0.0415	0.0236	.09
Free T4	-0.0219	0.0197	.27	-0.0307	0.0213	.16
T3	0.0007	0.0199	.72	0.0041	0.0207	.84

* Ln of PFOA coefficient adjusted for Ln Age, Ln BMI and Ln Alcohol unless otherwise (**) noted

** Ln PFOA coefficient adjusted for Ln Age, Ln Triglycerides and Ln Alcohol

Appendix C

Table C1 Number of Employees, Mean, 95% Confidence Interval, Median and Range by PFOA Decile Distribution , 2000 Fluorochemical Medical Surveillance Program for Antwerp, Cottage Grove and Decatur (N = 552)

PFOA Decile	N	PFOA Mean	95% C.I.	Median	Range
1	51	0.06[8-10]	0.05-0.07	0.06	0.007-0.13
2	58	0.20[8-10]	0.19-0.21	0.19	0.13-0.29
3	54	0.36[9,10]	0.35-0.37	0.36	0.30-0.44
4	55	0.55[9,10]	0.53-0.55	0.55	0.44-0.71
5	59	0.90[9,10]	0.87-0.94	0.88	0.71-1.10
6	50	1.26[10]	1.23-1.28	1.26	1.11-1.40
7	54	1.64[10]	1.60-1.67	1.63	1.42-1.85
8	60	2.17[1,2,10]	2.12-2.23	2.16	1.86-2.50
9	53	3.0[1-4510]	2.90-3.10	2.96	2.51-3.69
10	58	11.27[1-9]	6.98-15.56	4.94	3.71-92.03

[1-10] Statistically significantly ($p < .05$) different than PFOA decile(s) 1, 2, 3 . . . and/or10

Table C2. Adjusted Odds Ratios (O.R.) and 95% Confidence Interval (95% C.I.) for Lipid Clinical Chemistry Reference Points, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program (N = 552)

PFOA Decile	Chol >= 200 mg/dl		Chol >= 240 mg/dl		LDL >= 130 mg/dl		HDL<= 40 mg/dl		Triglycerides >= 150 mg/dl	
	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.	O.R.[1]	95% C.I.
1	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-
2	0.4	0.2-0.9	1.1	0.4 -2.4	0.6	0.3-1.3	1.4	0.5-3.6	0.8	0.4-2.0
3	0.8	0.4-1.8	0.9	0.3-2.2	0.7	0.3-1.5	0.4	0.1-1.3	1.0	0.4-2.5
4	1.0	0.4-2.2	1.2	0.5-3.0	0.8	0.4-1.7	1.9	0.7-4.9	1.4	0.6-3.3
5	1.7	0.8-3.9	1.6	0.7-3.8	1.1	0.5-2.3	1.1	0.4-3.0	1.1	0.5-2.5
6	1.0	0.4-2.3	1.2	0.5-3.0	0.8	0.4-1.7	1.7	0.6-4.6	1.7	0.7-4.2
7	0.9	0.4-1.9	1.0	0.4-2.5	0.7	0.3-1.5	0.6	0.2-1.8	1.0	0.4-2.5
8	1.1	0.5-2.4	1.5	0.6-3.4	1.0	0.5-2.2	1.2	0.5-3.2	2.7	1.2-6.4
9	1.5	0.7-3.5	1.4	0.6-3.5	1.2	0.5-2.6	0.9	0.3-2.3	2.4	1.0-5.7
10	1.1	0.5-2.5	1.0	0.4-2.4	0.9	0.4-1.8	2.9	1.2-7.5	2.7	1.2-6.3

[1] Adjusted for age, BMI and alcohol

Table C3. Nonadjusted and Adjusted Odds Ratios (O.R.) and 95% Confidence Intervals (95% C.I.) for HDL (< 40 mg/dL) and Triglycerides (>= 150 mg/dL) by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program (N = 552)

PFOA Decile	HDL < 40 mg/dL				Triglycerides >= 150 mg/dL			
	O.R.[1]	95% C.I.	O.R.[2]	95% C.I.	O.R.[1]	95% C.I.	O.R.[2]	95% C.I.
1	1.0	-	1.0	-	1.0	-	1.0	-
2	1.4	0.6-3.6	1.1	0.4-2.`	0.9	0.3-2.0	0.8	0.3-1.8
3	0.4	0.1-1.3	0.3	0.1-1.1	0.8	0.4-1.9	0.8	0.3-1.9
4	2.0	0.8-5.0	1.6	0.6-4.2	1.4	0.7-3.2	1.2	0.5-2.8
5	1.3	0.5-3.3	0.9	0.3-2.4	1.1	0.5-2.5	0.9	0.4-2.0
6	1.8	0.7-4.5	1.3	0.5-3.6	1.7	0.8-3.9	1.5	0.6-3.5
7	0.7	0.3-2.0	0.5	0.2-1.3	1.0	0.4-2.3	0.8	0.3-1.9
8	1.5	0.6-3.8	0.9	0.3-2.4	2.6	1.2-5.8	2.0	0.9-4.5
9	0.6	0.5-3.5	0.6	0.2-1.8	2.6	1.2-5.9	1.7	0.7-4.0
10	3.4	1.5-8.5	1.8	0.7-4.6	2.8	1.3-6.3	1.8	0.8-4.1

[1]Not adjusted

[2]Adjusted for location

Table C4. Odds Ratios (O.R.) and 95% Confidence Intervals (95% C.I.) for Hepatic Clinical Chemistry Results, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program (N = 552)

PFOA Decile	ALT ≥ 50 IU/L						GGT ≥ 50 IU/L					
	O.R[1].	95% C.I.	O.R[2].	95% C.I.	O.R[3].	95% C.I.	O.R[1].	95% C.I.	O.R[2].	95% C.I.	O.R[3].	95% C.I.
1	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-	1.0	-
2	0.7	0.2-2.5	0.8	0.2-3.1	0.9	0.2-3.4	0.3	0.0-1.2	0.2	0.0-1.1	0.3	0.0-1.2
3	0.6	0.1-2.2	0.7	0.2-2.9	0.6	0.1-2.2	0.8	0.2-2.7	0.8	0.2-3.0	0.7	0.2-2.7
4	0.8	0.2-2.7	0.7	0.2-2.7	0.8	0.2-2.7	1.1	0.3-3.6	1.0	0.3-3.5	1.1	0.3-3-6
5	0.4	0.1-1.6	0.3	0.1-1.6	0.4	0.1-1.7	0.4	0.1-1.6	0.4	0.1-1.6	0.4	0.1-1.5
6	0.2	0.0-0.9	0.1	0.1-0.9	0.1	0.0-0.9	0.3	0.4-1.4	0.3	0.0-1.3	0.3	0.0-1.3
7	0.8	0.2-2.7	0.9	0.2-3.5	0.7	0.2-2.7	0.9	0.3-3.2	1.0	0.3-3.4	0.9	0.2-3.1
8	0.7	0.2-2.4	0.6	0.1-2.4	0.5	0.1-2.0	0.7	0.2-2.4	0.6	0.2-2.3	0.5	0.1-1.9
9	1.1	0.4-3.8	0.9	0.3-3.3	1.0	0.3-3.4	1.7	0.6-5.5	2.0	0.7-6.4	2.0	0.7-6.6
10	1.8	0.6-5.5	1.7	0.5-5.5	1.1	0.4-3.7	0.7	0.2-2.5	0.7	0.2-2.6	0.4	0.1-1.7

1. Not adjusted
2. Adjusted for age, BMI and alcohol
3. Adjusted for age, triglycerides and alcohol

Table C5. Non-adjusted and Adjusted Regression PFOA Coefficients for Lipid Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program for Participants Who Did Not Self-Report Taking Cholesterol Lowering Medications (N = 506) and All Participants (N = 552)

	Ln PFOA Non-adjusted Coefficient	SE	p value	Ln PFOA Adjusted[1] Coefficient	SE	p value
			Ln Cholesterol			
All Locations						
Not Prescribed	0.0059	0.0060	.32	0.0076	0.0059	.20
All Participants	0.0083	0.0058	.15	0.0099	0.0058	.09
Antwerp						
Not Prescribed	0.0051	0.0106	.63	0.0130	0.0096	.18
All Participants	0.0050	0.0104	.63	0.0121	0.0094	.20
Cottage Grove						
Not Prescribed	0.0034	0.0089	.70	0.0021	0.0100	.83
All Participants	0.0045	0.0087	.61	0.0051	0.0091	.58
Decatur						
Not Prescribed	0.0221	0.0139	.11	0.0266	0.0141	.06
All Participants	0.0310	0.0131	.02	0.0348	0.0133	.01
			Ln LDL			
All Locations						
Not Prescribed	0.0005	0.0089	.96	0.0021	0.0091	.81
All Participants	0.0018	0.0088	.84	0.0029	0.0089	.75
Antwerp						
Not Prescribed	-0.0037	0.0157	.81	0.0106	0.0147	.47
All Participants	-0.0041	0.0156	.79	0.0092	0.0146	.53
Cottage Grove						
Not Prescribed	-0.0036	0.0138	.79	0.0049	0.0145	.73
All Participants	-0.0001	0.0140	.99	0.0071	0.0146	.63
Decatur						
Not Prescribed	0.0258	0.0199	.20	0.0302	0.0200	.13
All Participants	0.0276	0.0189	.15	0.0294	0.0191	.12

Table C5
(continued)

			Ln HDL			
All Locations						
Not Prescribed	-0.0307	0.0079	.0001	-0.0183	0.0069	.01
All Participants	-0.0295	0.0077	.0001	-0.0167	0.0067	.01
Antwerp						
Not Prescribed	-0.0057	0.0136	.68	-0.0095	0.0131	.47
All Participants	-0.0030	0.0137	.83	-0.0078	0.0130	.55
Cottage Grove						
Not Prescribed	-0.0153	0.0122	.21	-0.0192	0.0120	.11
All Participants	-0.0154	0.0121	.20	-0.0199	0.01170	.09
Decatur						
Not Prescribed	-0.0256	0.0149	.09	-0.0207	0.0141	.14
All Participants	-0.0200	0.0140	.16	-0.0159	0.0133	.23
			Ln Triglycerides			
All Locations						
Not Prescribed	0.0892	0.0185	.0001	0.0711	0.0169	.0001
All Participants	0.0917	0.0185	.0001	0.0738	0.0168	.0001
Antwerp						
Not Prescribed	0.0840	0.0288	.004	0.0980	0.0270	.0004
All Participants	0.0734	0.0294	.01	0.0920	0.0274	.0001
Cottage Grove						
Not Prescribed	0.0343	0.0316	.28	0.0280	0.0314	.28
All Participants	0.0317	0.0306	.30	0.0269	0.0300	.37
Decatur						
Not Prescribed	0.0715	0.0400	.08	0.0689	0.0376	.07
All Participants	0.0983	0.0394	.01	0.0106	0.0373	.01

1. Multiple Regression Model: LN (lipid clinical chemistry) = Intercept + LN (age) + LN (BMI) + LN (alcohol) + LN (PFOA)

Table C6. Non-adjusted and Adjusted[1,2] Regression PFOA Coefficients for Hepatic Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program (N = 552)

	Non-adjusted Ln PFOA Coefficient	SE	p value	Adjusted[1,2] Ln PFOA Coefficient	SE	p value
			Ln Alkaline Phosphatase			
			Not Prescribed (N = 506)			
All Locations	0.0155	0.0082	.06	0.0093[1]	0.0081	.25
				0.0037[2]	0.0081	.65
Antwerp	-0.0025	0.0137	.85	-0.0060	0.0139	.67
				-0.0170	0.0140	.22
Cottage Grove	-0.0141	0.0113	.21	-0.0127	0.0117	.28
				-0.0140	0.0117	.24
Decatur	0.0394	0.0191	.04	0.0460	0.0192	.02
				0.0394	0.0192	.04
			All Participants (N = 552)			
All Locations	0.0189	0.0082	.02	0.0117	0.0080	.14
				0.0006	0.0080	.45
Antwerp	-0.0082	0.0139	.56	-0.0109	0.0140	.44
				-0.0218	0.0139	.12
Cottage Grove	-0.0091	0.0115	.43	-0.0098	0.0119	.41
				-0.0100	0.0120	.40
Decatur	0.0445	0.0176	.01	0.0492	0.0179	.01
				0.0429	0.0181	.02

Ln AST

Not Prescribed (N = 506)

All Locations	-0.0018	0.0086	.83	-0.0051	0.0086	.55
				-0.0089	0.0087	.31
Antwerp	-0.0048	0.0137	.73	-0.0029	0.0138	.83
				-0.0066	0.0142	.64
Cottage Grove	-0.0281	0.0141	.05	-0.0258	0.0146	.08
				-0.0271	0.0145	.07
Decatur	0.0205	0.0200	.31	0.0114	0.0203	.57
				0.0062	0.0203	.76

All Participants (N = 552)

All Locations	0.0001	0.0085	.92	-0.0019	0.0085	.82
				-0.0059	0.0087	.50
Antwerp	-0.0050	0.0135	.71	-0.0034	0.0135	.80
				-0.0069	0.0137	.62
Cottage Grove	-0.0254	0.0139	.07	-0.0240	0.0144	.10
				-0.0250	0.0145	.09
Decatur	0.0239	0.0194	.22	0.0179	0.0198	.37
				0.0104	0.0200	.60

Ln ALT

Not Prescribed (N = 506)

All Locations	0.0402	0.0143	.005	0.0249	0.0132	.06
				0.0115	0.0136	.40
Antwerp	-0.0122	0.0220	.58	-0.0085	0.0222	.70
				-0.0293	0.0222	.19
Cottage Grove	- 0.0131	0.0215	.54	-0.0096	0.0209	.65
				-0.0008	0.0208	.69
Decatur	0.0954	0.0300	.002	0.0704	0.0287	.02
				0.0581	0.0287	.04

All Participants (N = 552)

All Locations	0.0457	0.0141	.001	0.0316	0.0131	.02
				0.0170	0.0135	.21
Antwerp	-0.0151	0.0218	.49	-0.0118	0.0219	.59
				-0.0311	0.0218	.15
Cottage Grove	-0.0143	0.0215	.50	-0.0089	0.0207	.67
				-0.0134	0.0215	.53
Decatur	0.1081	0.0278	.0001	0.0898	0.0270	.001
				0.0691	0.0274	.01

Table C6
(continued)

Ln GGT

Not Prescribed (N = 506)

All Locations	0.0409	0.0174	.02	0.0326	0.0166	.05
				0.0097	0.0163	.55
Antwerp	0.0170	0.0307	.58	0.0269	0.0294	.36
				-0.0047	0.0295	.87
Cottage Grove	-0.0088	0.0292	.76	-0.0198	0.0286	.49
				-0.0233	0.0270	.39
Decatur	0.0754	0.0344	.03	0.0800	0.0344	.02
				0.0599	0.0329	.07

Not Prescribed (N = 552)

All Locations	0.0454	0.0170	.01	0.0380	0.0163	.02
				0.0135	0.0158	.39
Antwerp	0.0114	0.0302	.71	0.0214	0.0290	.46
				-0.0097	0.0286	.73
Cottage Grove	-0.0062	0.0295	.83	-0.0183	0.0289	.53
				-0.0290	0.0278	.30
Decatur	0.0851	0.0319	.01	0.0974	0.0320	.003
				0.0673	0.0308	.03

1. Adjusted for Ln Age, Ln BMI, Ln Alcohol
2. Adjusted for Ln Age, Ln BMI, Ln Alcohol

Table C7. Non-adjusted and Adjusted[1] Regression PFOA Coefficients for Thyroid-Related Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program (N = 552)

	Non-adjusted Ln PFOA Coefficient	SE	p value	Adjusted[1] Ln PFOA Coefficient	SE	p value
			Ln TSH			
All Locations						
Not Prescribed	0.0395	0.0204	.05	0.0360	0.0207	.08
All Participants	0.0439	0.0199	.03	0.0400	0.0201	.05
Antwerp						
Not Prescribed	0.0509	0.0329	.12	0.0391	0.0333	.24
All Participants	0.0568	0.0319	.08	0.0463	0.0322	.15
Cottage Grove						
Not Prescribed	-0.0016	0.0310	.96	-0.0111	0.0322	.73
All Participants	0.0031	0.0295	.92	-0.0066	0.0306	.83
Decatur						
Not Prescribed	0.0343	0.0497	.49	0.0365	0.0513	.48
All Participants	0.0319	0.0477	.50	0.0328	0.0490	.44
			Ln T4			
All Locations						
Not Prescribed	-0.0037	0.0054	.50	-0.0057	0.0054	.29
All Participants	-0.0049	0.0053	.35	-0.0072	0.0052	.17
Antwerp						
Not Prescribed	-0.0022	0.0099	.83	-0.0041	0.0099	.68
All Participants	-0.0035	0.0098	.72	-0.0047	0.0098	.63
Cottage Grove						
Not Prescribed	-0.0124	0.0072	.09	-0.0093	0.0072	.20
All Participants	-0.0149	0.0072	.04	-0.0121	0.0072	.12
Decatur						
Not Prescribed	-0.0012	0.0126	.92	-0.0083	0.0127	.51
All Participants	-0.0015	0.0150	.90	-0.0057	0.0116	.63

Table C7
(continued)

			Ln Free T4			
All Locations						
Not Prescribed	-0.0138	0.0044	.002	-0.0117	0.0043	.01
All Participants	-0.0144	0.0042	.001	-0.0124	0.0042	.003
Antwerp						
Not Prescribed	-0.0108	0.0078	.17	-0.0140	0.0078	.07
All Participants	-0.0113	0.0077	.15	-0.0139	0.0078	.07
Cottage Grove						
Not Prescribed	-0.0093	0.0058	.11	-0.0071	0.0059	.23
All Participants	-0.0012	0.0057	.04	-0.0091	0.0057	.12
Decatur						
Not Prescribed	-0.0138	0.0103	.18	-0.0184	0.0105	.08
All Participants	-0.0100	0.0096	.30	-0.0146	0.0098	.14
			Ln T3			
All Locations						
Not Prescribed	0.0107	0.0052	.04	0.0105	0.0053	.05
All Participants	0.0103	0.0050	.04	0.0099	0.0051	.05
Antwerp						
Not Prescribed	0.0222	0.0077	.005	0.0216	0.0077	.01
All Participants	0.0207	0.0076	.007	0.0204	0.0076	.01
Cottage Grove						
Not Prescribed	0.0026	0.0096	.79	0.0006	0.0099	.95
All Participants	-0.0012	0.0092	.90	-0.0001	0.0095	.99
Decatur						
Not Prescribed	0.0317	0.0117	.008	0.0271	0.0119	.02
All Participants	0.0331	0.0108	.003	0.0293	0.0109	.01

1. Adjusted for Ln Age, Ln BMI, Ln Alcohol

Table C8. Number and Percent Subjects Above or Below Reference Points for Thyroid-Related Clinical Chemistry Results, by PFOA Decile, 2000 Fluorochemical Medical Surveillance Program (N = 552)

PFOA Decile	TSH (µIU/mL) ≤0.25 N (%)	TSH (µIU/mL) >5.5 N (%)	T4 (µg/dL) ≤4.5 N (%)	T4 (µg/dL) >12.0 N (%)	Free T4 (ng/dL) ≤0.70 N (%)	Free T4 (ng/dL) >1.53 N (%)	T3 (ng/dL) ≤60 N (%)	T3 (ng/dL) >181 N (%)
1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)
2	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
3	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4	1 (2)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
5	0 (0)	4 (7)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)
6	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)
7	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
8	0 (0)	6 (10)	0 (0)	0 (0)	1 (2)	2 (3)	0 (0)	2 (3)
9	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
10	1(2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (3)
p value	.67	.03	.41	.49	.68	.47	-	.38

Table C9 . Predicted Thyroid-Related Clinical Chemistry Results Based on Multiple Regression Models for 40 Year Old Male with BMI = 28 and Drinks 0.5 Alcohol Beverages per Day (N = 552)

Reference Range	Predicted TSH (μIU/mL) (0.25 – 5.5)	Predicted T4 (μg/dL) (4.5-12.0)	Predicted Free T4 (ng/dL) (0.70-1.53)	Predicted T3 (ng/dL) (60-181)
PFOA Serum Concentration (μg/mL)				
0.005	1.57	8.28	1.16	119
0.01	1.61	8.24	1.15	120
0.10	1.77	8.10	1.12	123
0.50	1.89	8.00	1.09	125
1.00	1.94	7.97	1.08	125
5.00	2.07	7.88	1.06	127
10.00	2.13	7.84	1.05	128
50.00	2.27	7.74	1.03	130
100.00	2.33	7.71	1.02	131

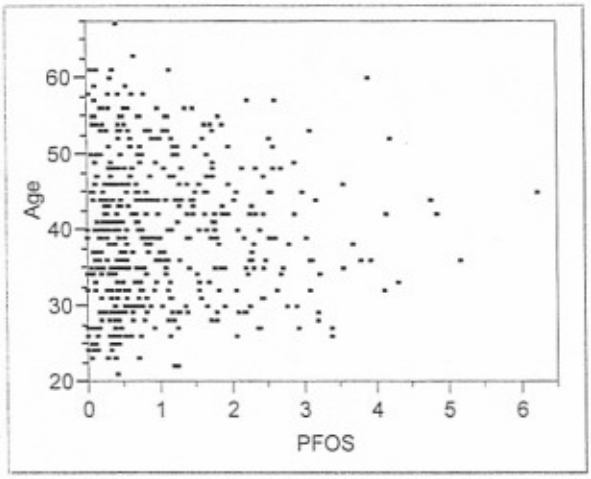
Appendix D

Table D1. Correlation Coefficients (same as Table A1)

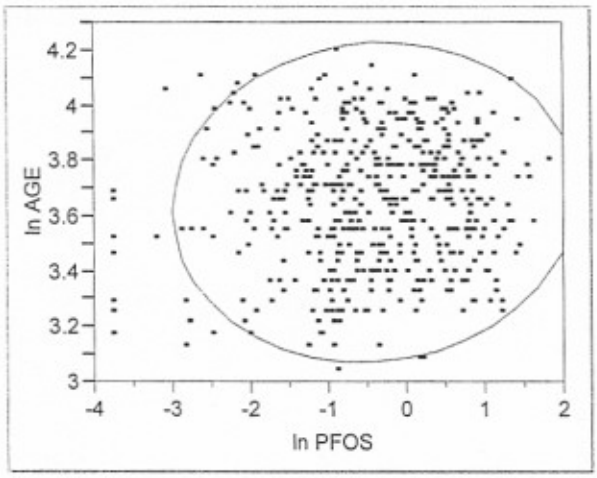
Ln (Variable)	Ln (PFOA)	Ln(PFOS)	Ln(Age)	Ln(BMI)	Ln(Alcohol)
PFOA	1.0				
PFOS	0.55****	1.0			
Age	0.03	0.06	1.0		
BMI	0.11*	0.00	0.20****	1.0	
Alcohol	-0.12**	-0.10*	-0.15***	-0.26****	1.0
Cholesterol	0.04	0.08	0.15***	0.00	0.10*
LDL	0.00	0.06	0.13**	-0.02	0.01
HDL	-0.17****	-0.07	-0.13**	-0.43****	0.37****
Triglycerides	0.210****	0.13**	0.18****	0.44****	-0.12**
Glucose	-0.01	-0.13**	0.26****	0.28****	-0.19****
Alk Phos	0.08	0.08	0.08	0.12**	-0.25****
AST	-0.01	0.00	0.00	0.15***	-0.04
ALT	0.12**	0.08	0.03	0.41****	-0.16***
AST/ALT	-0.15***	-0.09*	-0.05	-0.39****	0.17***
GGT	0.10*	0.10*	0.15***	0.31****	0.20****
Total Bilirubin	-0.18****	-0.13**	-0.08	-0.18****	-0.02
Direct Bilirubin	-0.06	-0.03	-0.03	-0.03	-0.02
TSH	0.09	0.04	-0.01	0.08	-0.02
T4	-0.03	0.002	-0.09	-0.05	-0.17***
Free T4	-0.15**	-0.06	-0.17***	-0.17***	0.08
T3	0.09*	0.03	-0.10*	0.02	-0.01

*p < .05
** p < .01
*** p < . 001
**** p < .0001

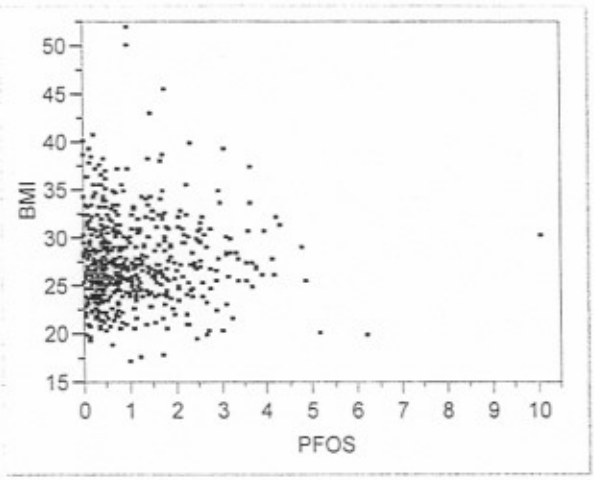
Age (years) by PFOS (µg/mL)



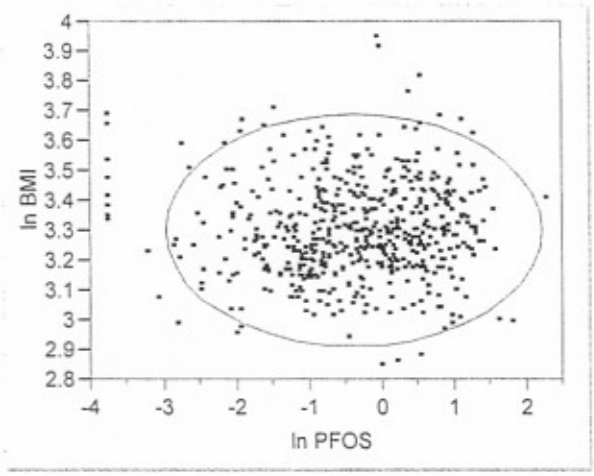
LN Age (years) by LN PFOS (µg/mL)



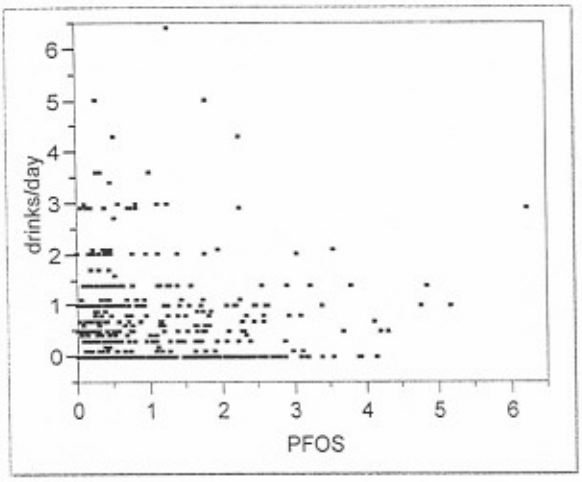
BMI by PFOS (µg/mL)



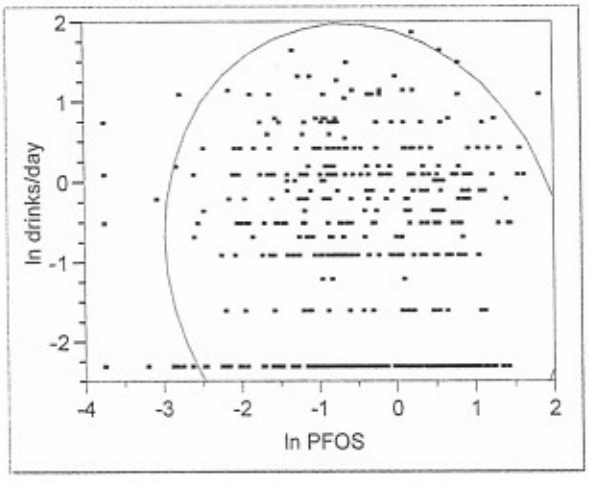
LN BMI by LN PFOS (µg/mL)



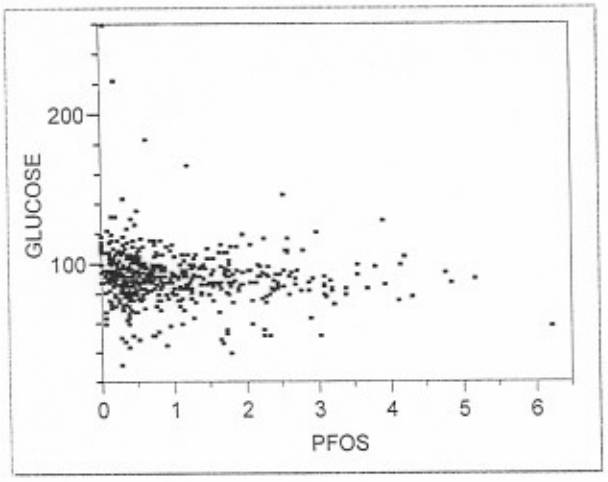
Alcohol (drinks/day) by PFOS (µg/mL)



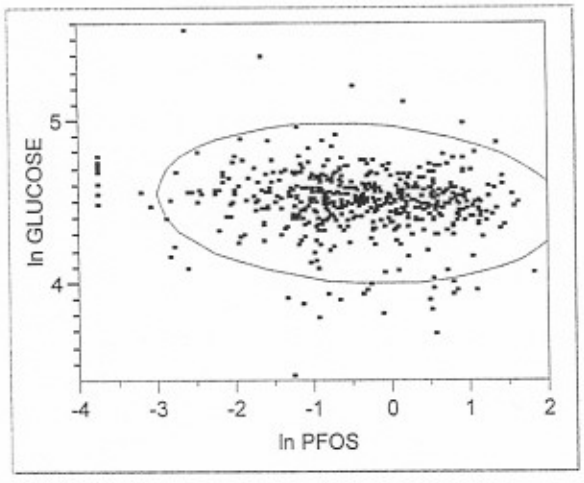
LN Alcohol (drinks/day) by LN PFOS (µg/mL)



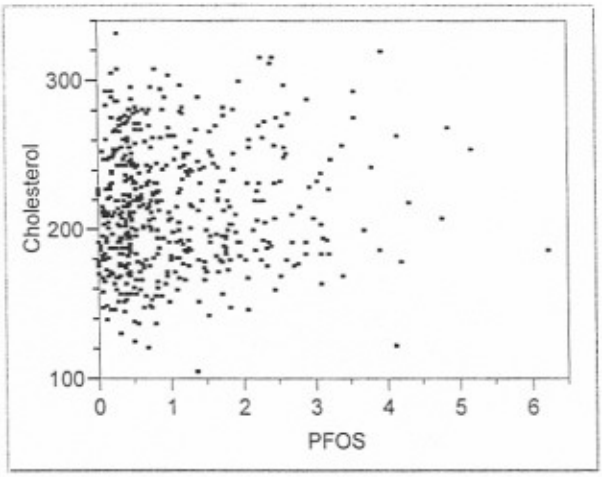
Glucose (mg/dL) by PFOS (µg/mL)



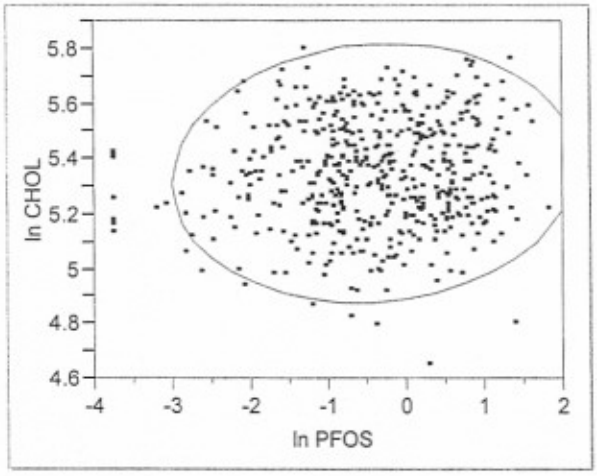
LN Glucose (mg/dL) by LN PFOS (µg/mL)



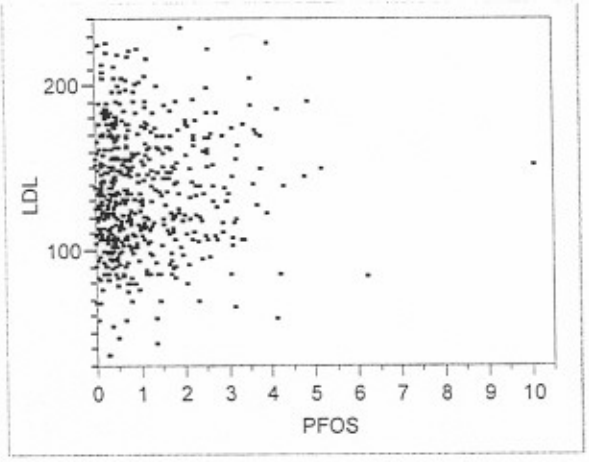
Cholesterol (mg/dL) by PFOS (µg/mL)



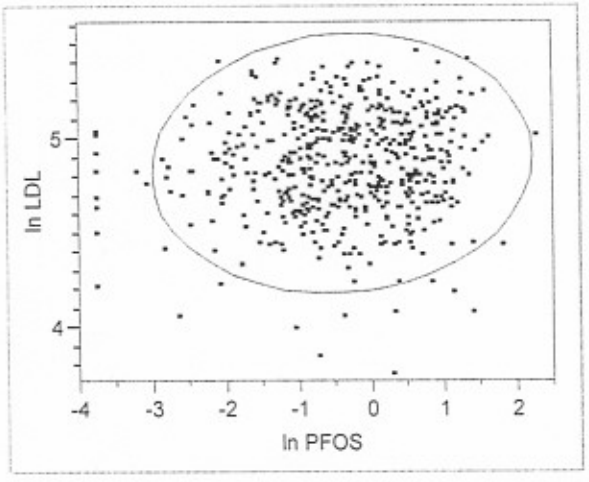
LN Cholesterol (mg/dL) by LN PFOS (µg/mL)



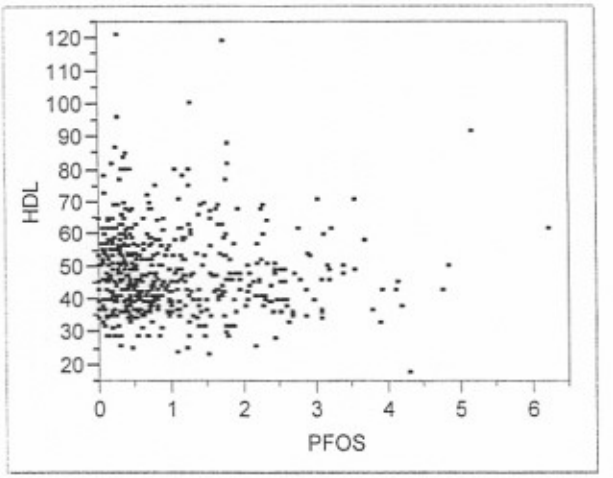
LDL (mg/dL) by PFOS (µg/mL)



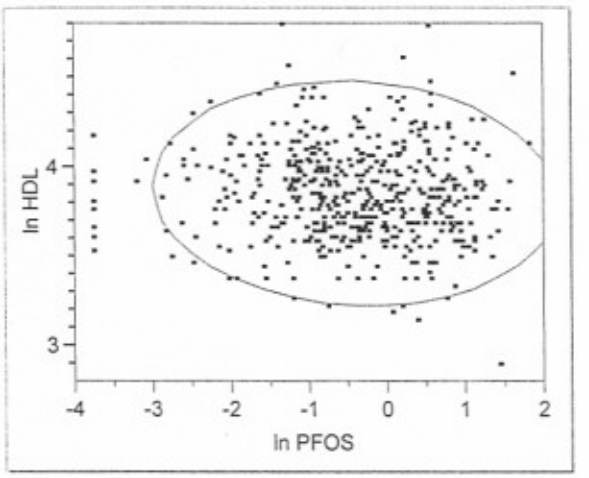
LN LDL (mg/dL) by LN PFOS (µg/mL)



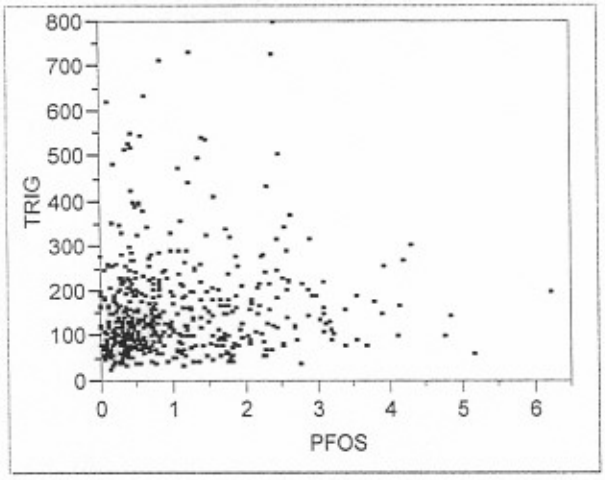
HDL (mg/dL) by PFOS (µg/mL)



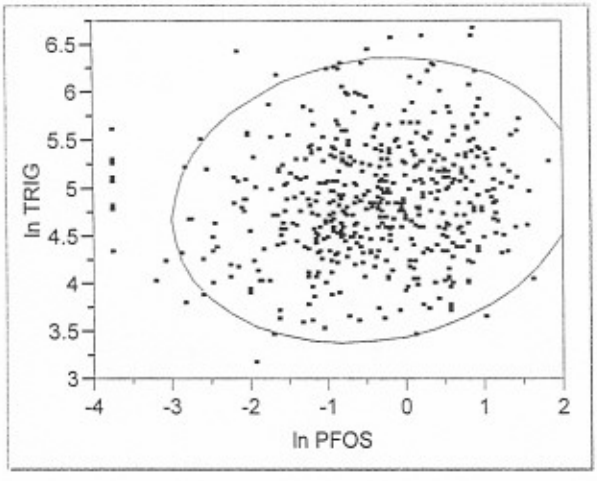
LN HDL (mg/dL) by LN PFOS (µg/mL)



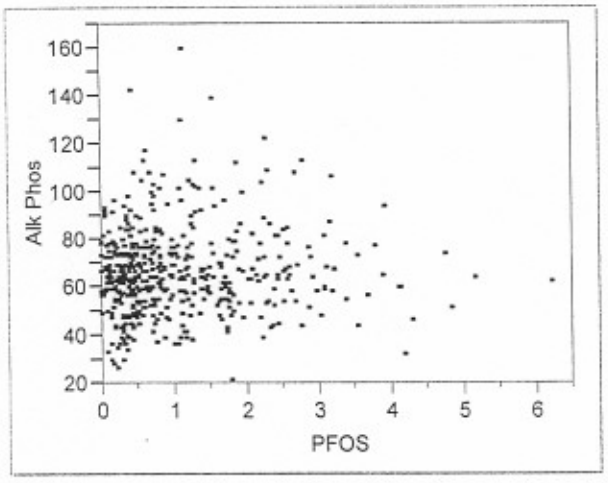
Triglycerides (mg/dL) by PFOS (µg/mL)



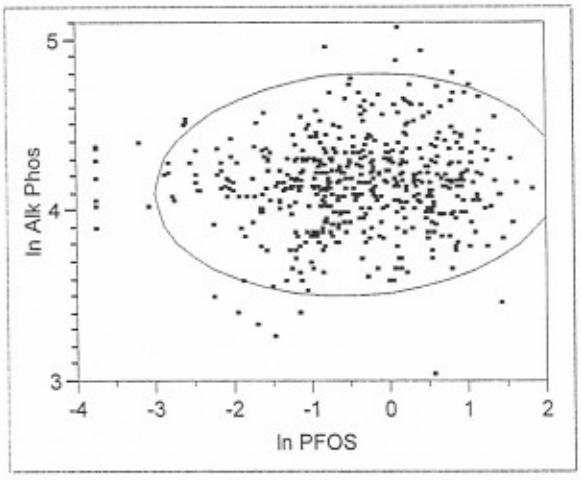
LN Triglycerides (mg/dL) by LN PFOS (µg/mL)



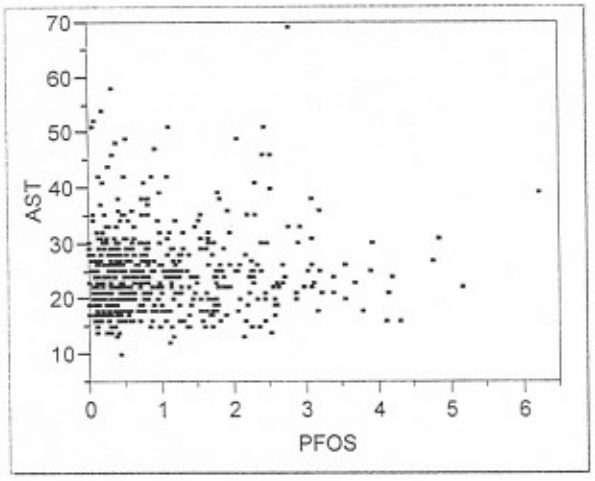
Alkaline Phosphatase (IU/L) by PFOS (µg/mL)



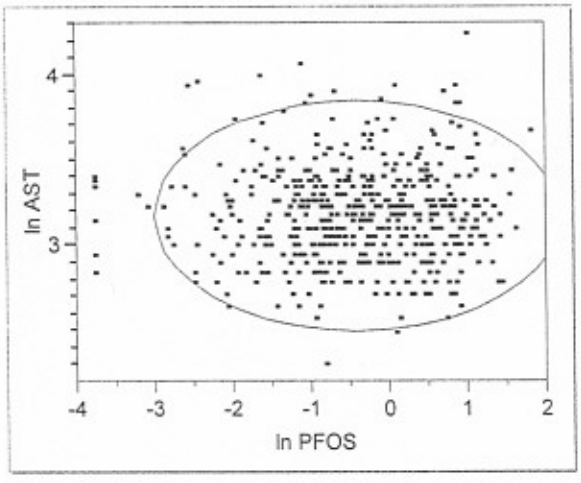
LN Alkaline Phosphatase (IU/L) by LN PFOS (µg/mL)



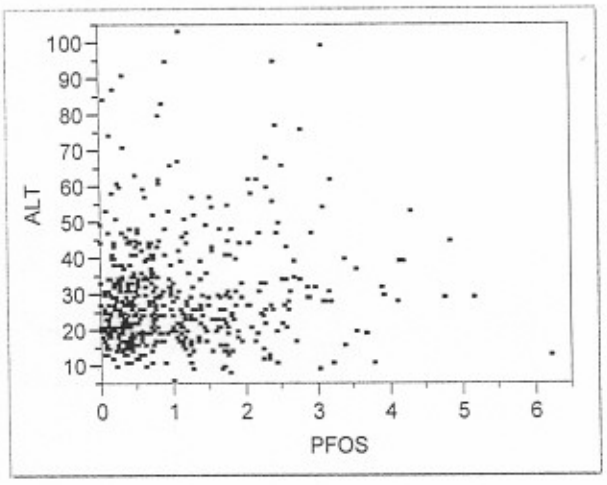
AST (IU/L) by PFOS (µg/mL)



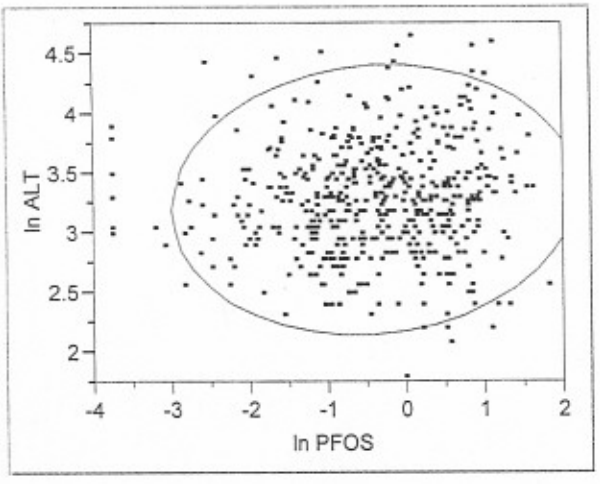
LN AST (IU/L) by LN PFOS (µg/mL)



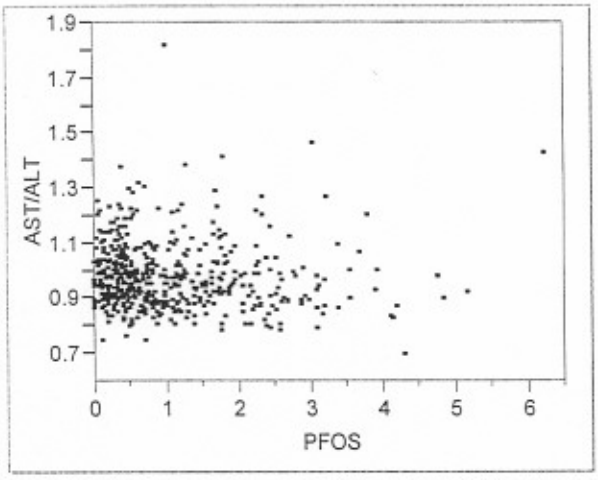
ALT (IU/L) by PFOS (µg/mL)



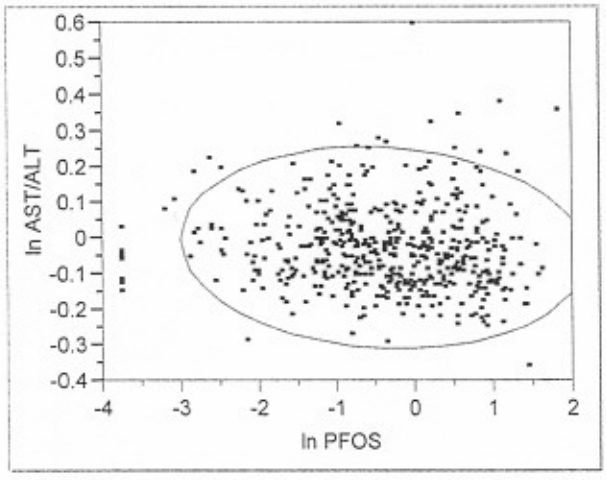
LN ALT (IU/L) by LN PFOS (µg/mL)



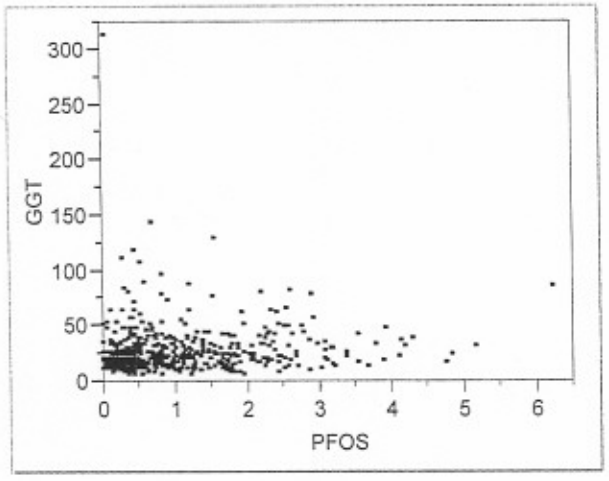
AST/ALT by PFOS (µg/mL)



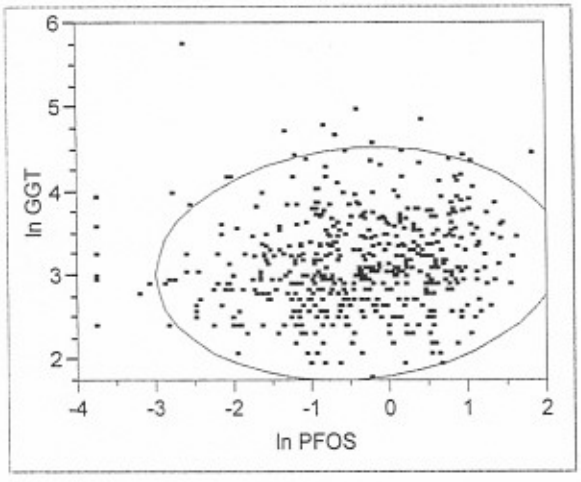
LN AST/ALT by LN PFOS (µg/mL)



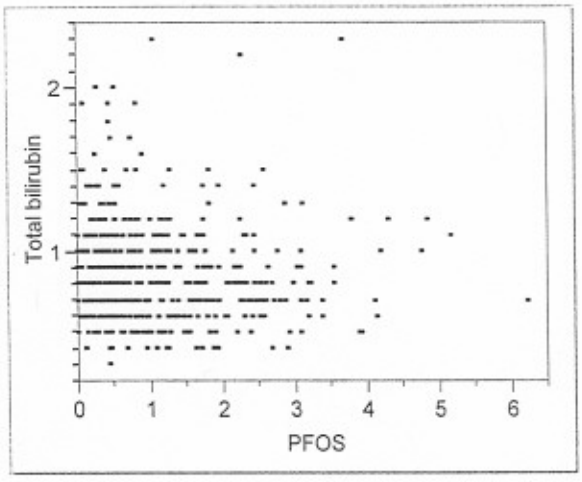
GGT (IU/L) by PFOS (µg/mL)



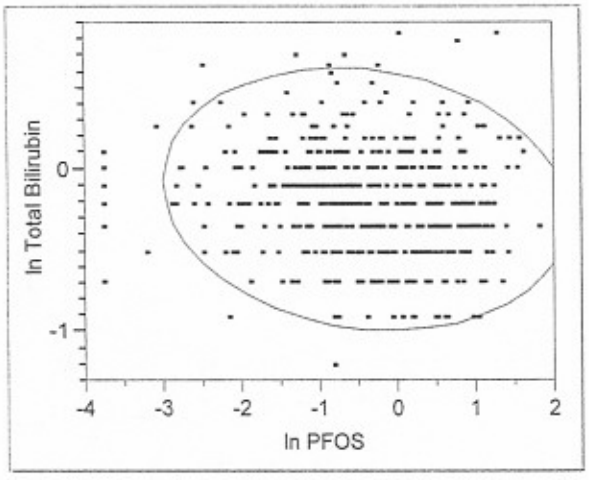
LN GGT (IU/L) by LN PFOS (µg/mL)



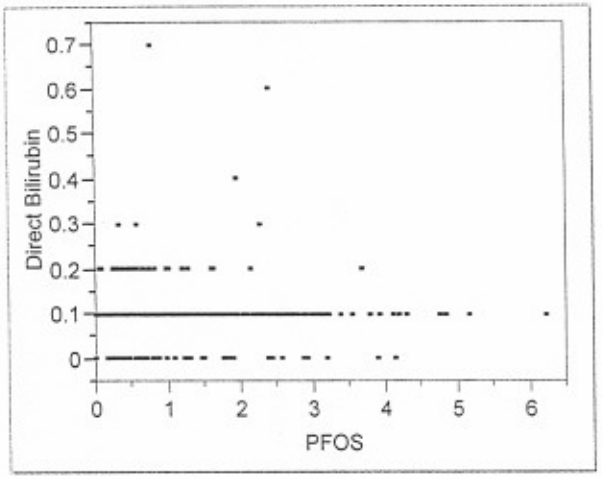
Total Bilirubin (mg/dL) by PFOS (µg/mL)



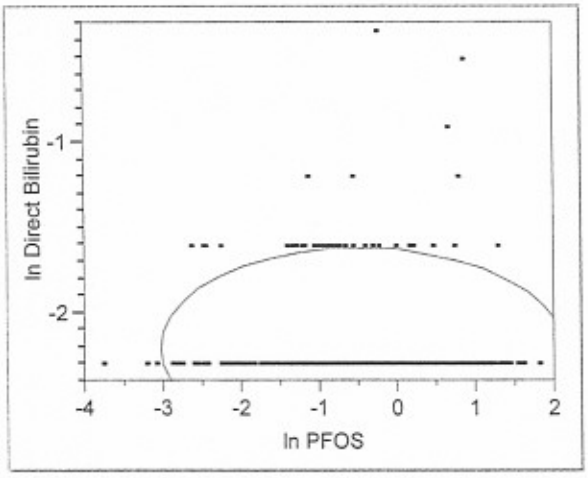
LN Total Bilirubin (mg/dL) by LN PFOS (µg/mL)



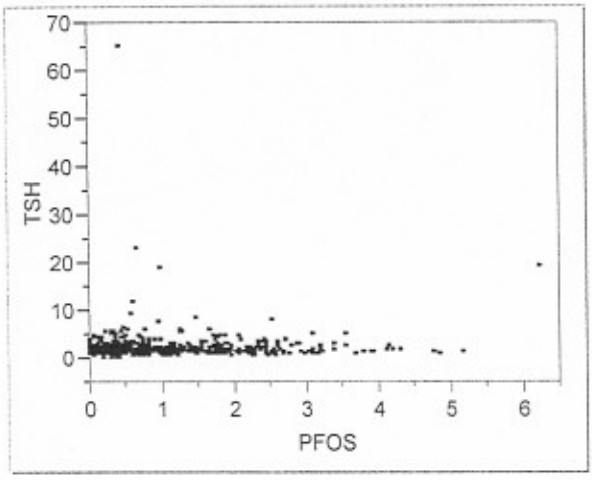
Direct Bilirubin (mg/dL) by PFOS (µg/mL)



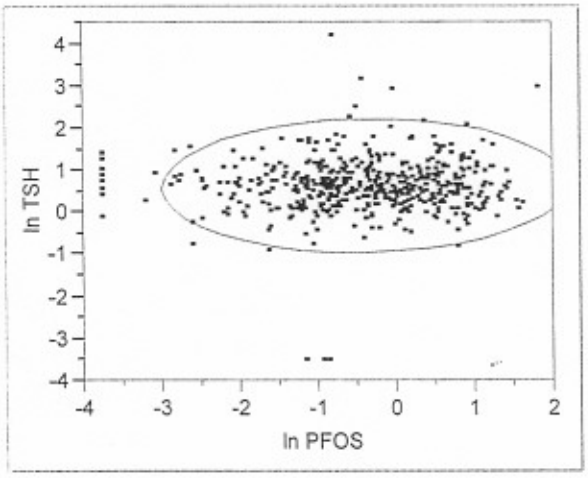
LN Direct Bilirubin (mg/dL) by LN PFOS (µg/mL)



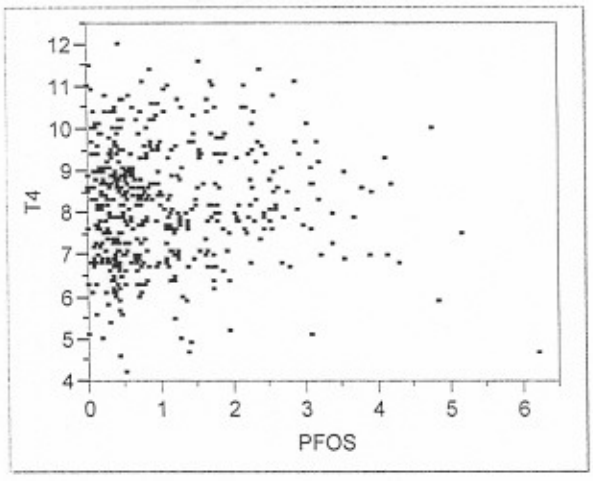
TSH (µIU/mL) by PFOS (µg/mL)



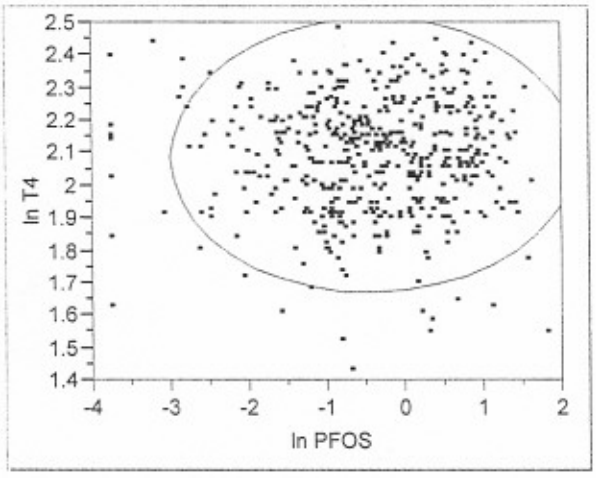
LN TSH (µIU/mL) by LN PFOS (µg/mL)



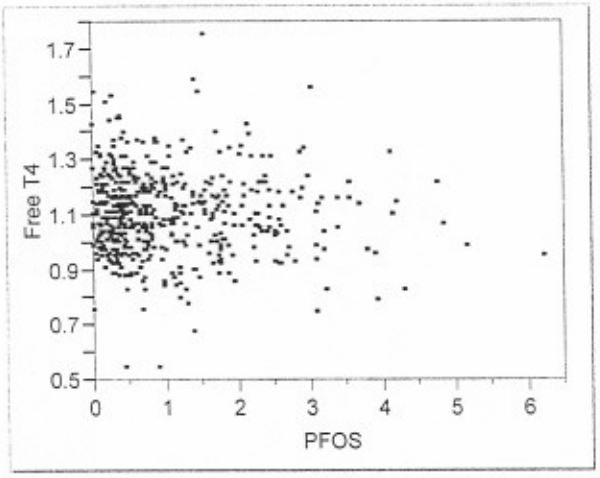
T4 (µg/dL) by PFOS (µg/mL)



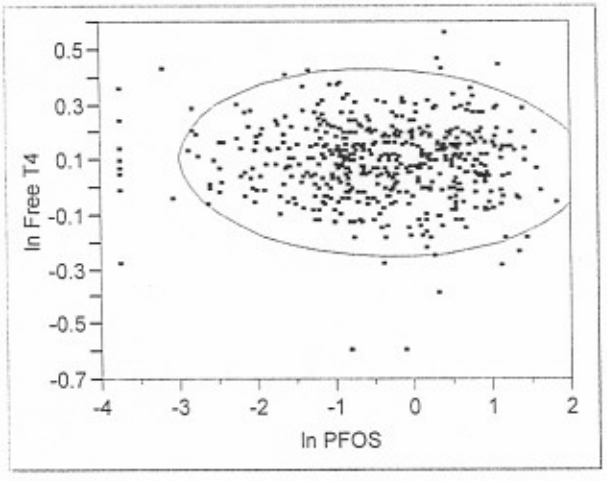
LN T4 (µg/dL) by LN PFOS (µg/mL)



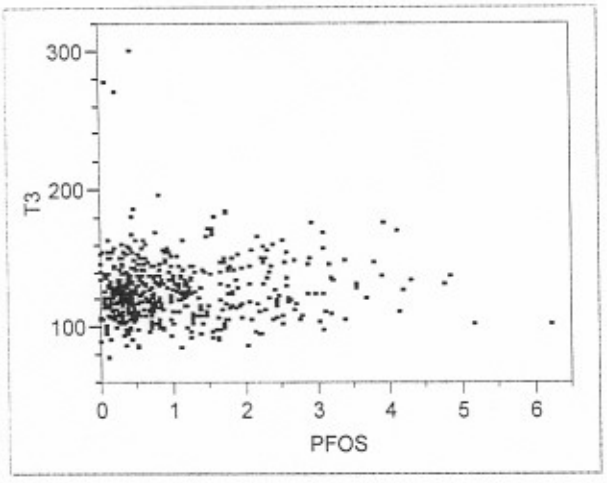
Free T4 (ng/dL) by PFOS (µg/mL)



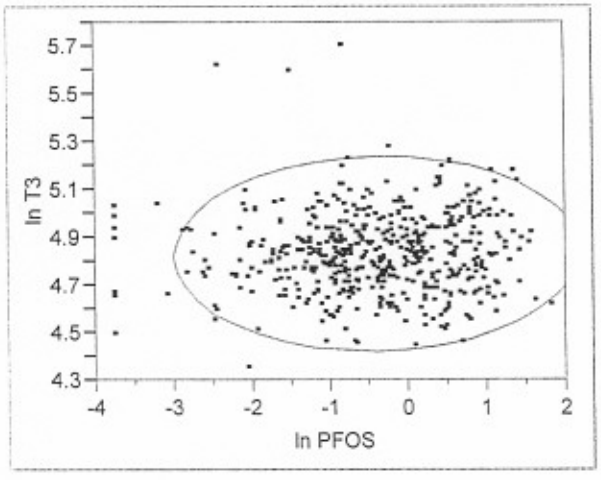
LN Free T4 (ng/dL) by LN PFOS (µg/mL)



T3 (ng/dL) by PFOS (µg/mL)



LN T3 (ng/dL) by LN PFOS (µg/mL)



Appendix E

Table E1. Non-adjusted and Adjusted Regression PFOS Coefficients for Lipid Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program (N = 506)

	Non-adjusted Ln PFOS Coefficient	SE	p value	Adjusted Ln PFOS Coefficient[1]	SE	p value
			Ln Cholesterol			
All Locations	0.0151	0.0081	.06	0.0157	0.0081	.05
Antwerp	0.0091	0.0144	.53	0.0049	0.0128	.70
Cottage Grove	0.0151	0.0130	.25	0.0141	0.0134	.30
Decatur	0.0247	0.0173	.15	0.0235	0.0173	.18
			Ln LDL			
All Locations	0.0153	0.0120	.20	0.0135	0.0120	.26
Antwerp	-0.0068	0.0211	.75	-0.0137	0.0194	.48
Cottage Grove	0.0115	0.0198	.56	0.0187	0.0203	.36
Decatur	0.0457	0.0249	.07	0.0421	0.0245	.09
			Ln HDL			
All Locations	-0.0161	0.0108	.14	-0.0093	0.0094	.33
Antwerp	-0.0014	0.0185	.94	-0.0020	0.0175	.91
Cottage Grove	-0.0018	0.0179	.92	-0.0114	0.0174	.52
Decatur	-0.0242	0.0186	.20	-0.0166	0.0172	.34

Table E1. (continued)

			Ln Triglycerides			
All Locations	0.0778	0.0255	.002	0.0752	0.0230	.001
Antwerp	0.1066	0.0381	.006	0.1063	0.0357	.003
Cottage Grove	0.0453	0.0463	.33	0.0393	0.0455	.39
Decatur	0.0416	0.0501	.41	0.0304	0.0463	.51

1. Adjusted for Ln Age, Ln BMI, Ln Alcohol

Table E2. Non-adjusted and Adjusted[1,2] Regression PFOS Coefficients for Hepatic Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program (N = 506)

	Non-adjusted Ln PFOS Coefficient	SE	p value	Adjusted Ln PFOS Coefficient[1,2]	SE	p value
			Ln Alkaline Phosphatase			
All Locations	0.0189	0.0112	.09	0.0130[1]	0.0110	.24
				0.0074[2]	0.0109	.50
Antwerp	-0.0051	0.0185	.78	-00028[1]	0.0186	.88
				-0.0140[2]	0.0185	.45
Cottage Grove	-0.0137	0.0165	.41	-0.0009[1]	0.0170	.59
				0.0091[2]	0.0171	.59
Decatur	0.0405	0.0238	.09	0.0381[1]	0.0237	.11
				0.0346[2]	0.0234	.14
			Ln AST			
All Locations	-0.0006	0.0117	.96	0.0005[1]	0.0116	.97
				-0.0063[2]	0.0117	.59
Antwerp	-0.0356	0.0183	.05	-0.0370[1]	0.0182	.04
				-0.0420[2]	0.0184	.02
Cottage Grove	0.0081	0.0210	.70	0.0140[1]	0.0214	.51
				0.0123[2]	0.0216	.57
Decatur	0.0111	0.0250	.66	0.0103[1]	0.0247	.68
				0.0082[2]	0.0245	.74

Table E2. (continued)

Ln ALT						
All Locations	0.0354	0.0195	.07	0.0343[1]	0.0179	.06
				0.0106[2]	0.0183	.58
Antwerp	-0.0490	0.0295	.10	-0.0499[1]	0.0293	.09
				-0.0734[2]	0.0289	.01
Cottage Grove	0.0510	0.0311	.10	0.0490[1]	0.0299	.10
				0.0409[2]	0.0310	.19
Decatur	0.0927	0.0376	.01	0.0826[1]	0.0351	.02
				0.0780[2]	0.0347	.03
Ln GGT						
All Locations	0.0534	0.0237	.02	0.0558[1]	0.0225	.01
				0.0251[2]	0.0217	.25
Antwerp	0.0287	0.0416	.49	0.0260[1]	0.0291	.51
				-0.0088[2]	0.0389	.82
Cottage Grove	0.0417	0.0425	.33	0.0321[1]	0.0414	.44
				0.0152[2]	0.0401	.71
Decatur	0.0583	0.0433	.18	0.0612[1]	0.0424	.15
				0.0524[2]	0.0401	.19

Table E2. (continued)

	Ln Total Bilirubin					
All Locations	-0.0415	0.0138	.003	-0.0356[1]	0.0136	.01
				-0.0275[2]	0.0135	.04
Antwerp	-0.0344	0.0240	.15	-0.0354[1]	0.0241	.14
				-0.0324[2]	0.0247	.19
Cottage Grove	-0.0142	0.0201	.48	0.0107[1]	0.0206	.61
				0.0142[2]	0.0205	.49
Decatur	-0.0531	0.0254	.04	-0.0565[1]	0.0255	.03
				-0.0525[2]	0.0250	.04

1. Adjusted for Ln Age, Ln BMI, Ln Alcohol
2. Adjusted for Ln Age, Ln Triglyerides, Ln Alcohol

Table E3. Non-adjusted and Adjusted[1] Regression Coefficients for Thyroid Clinical Chemistry Results, 2000 Fluorochemical Medical Surveillance Program (N = 506)

	Non-adjusted Ln PFOS Coefficient	SE	p value	Adjusted[1] Ln PFOS Coefficient	SE	p value
			Ln TSH			
All Locations	0.0227	0.0275	.41	0.0232	0.0228	.40
Antwerp	0.0306	0.0447	.49	0.0369	0.0446	.41
Cottage Grove	0.0224	0.0442	.51	0.0094	0.0451	.83
Decatur	-0.0132	0.0620	.83	-0.0125	0.0626	.84
			Ln T4			
All Locations	0.0029	0.0073	.69	0.0004	0.0072	.95
Antwerp	-0.0183	0.0133	.17	-0.0179	0.0131	.18
Cottage Grove	0.0010	0.0104	.92	0.0067	0.0105	.51
Decatur	0.0101	0.0156	.52	0.0062	0.0155	.69
			Ln Free T4			
All Locations	-0.0080	0.0059	.18	-0.0064	0.0058	.27
Antwerp	-0.0217	0.0105	.04	-0.0208	0.0104	.05
Cottage Grove	0.0108	0.0083	.20	0.0126	0.0082	.13
Decatur	-0.0015	0.0129	.91	-0.0019	0.0129	.88

Table E3. (continued)

	Ln T3					
All Locations	0.0053	0.0071	.46	0.0061	0.0071	.39
Antwerp	0.0173	0.0106	.10	0.0186	0.0104	.08
Cottage Grove	-0.0200	0.0135	.14	-0.0190	0.0138	.17
Decatur	0.0325	0.0147	.03	0.0304	0.0146	.04

1. Adjusted for Ln Age, Ln BMI, Ln Alcohol