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FYI-0500-1378
AR226-0030
VOL III

(84000000018)

April 21, 2000

3M

Attachments To April 21, 2000 Letter to C. Auer from W. Weppner
(Medical Surveillance and Epidemiology)

Final Reports

1. An Epidemiologic Investigation of Clinical Chemistries, Hematology and Hormones in Relation to Serum Levels of Perfluorooctanesulfonate in Male Fluorochemical Production Employees. [Included is a 3M report of medical surveillance data. Also included is a published paper from this 3M report.]

2. Fluorochemical Exposure (Serum) Assessment of (3M) Decatur Chemical and Film Plant Employees. [Included are a 3M study protocol and report.]

3. Mortality Study of Employees at 3M Plant in Decatur, Alabama [Included is a University of Minnesota final report.]

4. Determination of Serum Fluorochemical Levels in Sumitomo 3M Employees [Included are a 3M study protocol and final report.]

5. Analysis of Selected Decatur Employee Serum for Sulfonic and Carboxylic Fluorochemicals [Included is a 3M technical report.]

6. Fluorochemical Control Study [Included is a 3M report of medical surveillance data.]

7. Working Memorandum on Data Quality Assessment [Included is a Battelle Laboratory memorandum regarding the mean and range of perfluorooctanesulfonate sera sample data collected by 3M from current and historical human populations.)

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An Epidemiologic Investigation of Clinical Chemistries, Hematology and Hormones in Relation to Serum Levels of Perfluorooctane Sulfonate in Male Fluorochemical Production Employees

Following reports of the finding of organic fluorine in sera samples, a fluorochemical medical surveillance program began at 3M's Decatur manufacturing facility in the late 1970's. The surveillance program has generally consisted of annual or biannual tests of clinical chemistries, pulmonary function, blood counts and a biomonitor of fluorochemical exposure. A total organic fluorine measurement was routinely done until 1993. This measures the amount of fluorine that was covalently bound to carbon in the serum sample. When test data were available, a company physician reviewed each employee's results. These physicians did not, and have not, found abnormalities in individuals that they felt were related to fluorochemical exposure. That is, medical conditions, medications and lifestyle factors adequately explained the laboratory abnormalities (which one expects to find in this type of program.)

Beginning in 1994, the 3M Decatur (Alabama) plant medical surveillance program incorporated a serum measurement of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA). Total organic fluorine was not measured. A formal report was written of the aggregate analyses conducted of the medical surveillance clinical program data for the Decatur (Alabama) and Antwerp (Belgium) employees who voluntarily participated in 1994, 1995 and 1997. The findings from this aggregate

analysis suggested that, among these participating Antwerp and Decatur male fluorochemical production employees, significant hematological, clinical chemistry and hormonal abnormalities were not associated with serum PFOS levels up to 6 ppm. It was not possible to derive inferences from the few employees with serum PFOS levels > 6 ppm. Limitations of this study include its cross-sectional design, the voluntary participation rates, the few subjects exposed at the highest levels, and the lower levels of serum PFOS measured among these employees compared to those estimated to cause effects in laboratory animals. Results of the hepatic and lipid clinical chemistry tests were published in *the Journal of Occupational and Environmental Medicine* (1999;41:799-806). In the Spring of 2000, medical surveillance will again be offered to 3M fluorochemical production employees at the Antwerp and Decatur manufacturing sites.

April 22, 1998

An Epidemiologic Investigation of Clinical Chemistries, Hematology and Hormones in Relation to Serum Levels of Perfluorooctane Sulfonate in Male Fluorochemical Production Employees

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ABSTRACT

3M manufactures products which contain chemical compounds, either as intentional components or residual impurities, that have as a parent molecule, perfluorooctane sulfonyl fluoride. These chemicals include: perfluorooctane sulfonate (PFOS), N-ethyl perfluorooctanesulfonamide, N-ethyl perfluorooctanesulfonamido ethanol, N-methyl perfluoroctanesulfonamido ethanol and chemicals derived from it, and the mixture of mono-, di- and tri [N-ethyl perfluorooctane sulfonamidoethyl] phosphates. There may be other precursors in the workplace. These molecules enter a number of product applications (e.g., surfactants, food packaging additives, polymers). These compounds may be expected to transform metabolically, to an undetermined degree, to PFOS as an end-stage metabolite. Potassium perfluorooctane sulfonate ($C_8F_{17}OSO_2K^+$) is, itself, a surfactant used as a wetting and foaming agent in industrial and commercial processes.

Subchronic studies in rats and primates suggest there may be a potential for cumulative toxicity with PFOS over time with the primary effect related to metabolic wasting. Although the mechanism of toxicity is not fully understood, toxicity may be due to an effect on peroxisome proliferation, fatty acid metabolism, membrane function, protein synthesis and/or mitochondrial bioenergetics.

Medical surveillance has been routinely performed on 3M fluorochemical production workers (in Decatur, Alabama and Antwerp, Belgium) with potential exposure to PFOS and/or to perfluorinated precursors that may metabolically degrade to PFOS. The purpose of this study was to provide an analysis of the hematology (hematocrit, hemoglobin, red blood cells, white blood cells and platelet count), clinical chemistries

(alkaline phosphatase, gamma glutamyl transferase, aspartate aminotransferase, alanine aminotransferase, total and direct bilirubin, blood urea nitrogen, creatinine, glucose, cholesterol, low density lipoproteins, high density lipoproteins and triglycerides) and hormonal parameters (cortisol, dehydroepiandrosterone sulfate, estradiol, follicle stimulating hormone, 17-alpha hydroxyprogesterone, luteinizing hormone, prolactin, sex hormone binding globulin, free testosterone, bound testosterone, and thyroid stimulating hormone) in relation to serum PFOS as determined by high performance liquid chromatography mass spectrometry methods. These relationships were assessed in fluorochemical production employees from two time periods, 1995 (N = 178) and 1997 (N = 149).

Descriptive simple and stratified analyses, Pearson correlation coefficients, analysis of variance and multivariable regression were used to evaluate for possible associations between PFOS and each hematological and clinical chemistry test and hormonal assay. Age, body mass index, current alcohol consumption (drinks per day) and cigarette use (cigarettes smoked per day) were potential confounding factors that were considered in the analyses. Multivariable regression models were fitted with PFOS analyzed as a continuous variable using linear as well as non-linear transformations in order to maximize the possibility of finding associations between PFOS and the parameters of interest.

Four categorizations of serum PFOS levels were assessed in relation to the response variables: 0 - < 1 ppm; 1 - < 3 ppm; 3 - < 6 ppm; and $\geq$ 6 ppm. In 1995, mean serum PFOS levels by category were 0.49 ppm, 1.82 ppm, 4.12 ppm and 8.17 ppm, respectively. In 1997, mean serum PFOS levels by category were 0.52 ppm, 1.78 ppm,

3.87 ppm and 7.20 ppm, respectively. For both years, 95 percent of the employees' serum PFOS levels were below 6 ppm. Although the two plant populations differed by age, body mass index and alcohol consumption, no consistent associations, by both plant locations and year, were observed between the clinical chemistries, hematology and hormone parameters and the employees' serum PFOS levels.

The findings from this study suggest that, among these Antwerp and Decatur male fluorochemical production employees, significant hematological, clinical chemistry and hormonal abnormalities are not associated with serum PFOS levels up to 6 ppm. It is not possible to derive inferences from the few employees with serum PFOS levels $\geq$ 6 ppm. Limitations of this study include its cross-sectional design, the voluntary participation rates, the few subjects exposed at the highest levels, and the lower levels of serum PFOS measured among these employees compared to those that caused effects in laboratory animals.

INTRODUCTION

3M manufactures products which contain chemical compounds, either as intentional components or residual impurities, that have as a parent molecule, perfluorooctane sulfonyl fluoride. These chemicals include: perfluorooctane sulfonate (PFOS), N-ethyl perfluorooctanesulfonamide, N-ethyl perfluorooctanesulfonamido ethanol, N-methyl perfluoroctanesulfonamido ethanol and chemicals derived from it, and the mixture of mono-, di- and tri [N-ethyl perfluorooctane sulfonamidoethyl] phosphates. There may be other precursors in the workplace. These molecules enter a number of product applications (e.g., surfactants, food packaging additives, polymers). These compounds can be expected to be transformed metabolically, to an undetermined degree, to PFOS as an end-stage metabolite [Gibson et al., 1983]. Potassium perfluorooctane sulfonate ($C_8F_{17}OSO_2K^+$) is, itself, a surfactant used as a wetting and foaming agent in industrial and commercial processes.

Potassium perfluorooctane sulfonate is readily absorbed by ingestion [Johnson and Ober, 1979; O'Malley and Ebbens, 1980]. Ninety five percent of a single oral dose of [^{14}C] PFOS administered to male rats was absorbed within 24 hours [Johnson and Ober, 1979].

After a single, 24-hour occluded dermal exposure to PFOS at a dose of 5000 mg/kg, total serum organic fluorine concentrations were 10.3 and 0.9 ppm for male and female albino rabbits, respectively [O'Malley and Ebbens, 1980]. Twenty eight days after dosing, total serum organic fluorine concentrations had risen to 130.2 and 128.0 ppm for male and female albino rabbits, respectively. On the other hand, no quantifiable

organic fluorine could be detected 28 days after a single, 24 hour occluded dermal exposure to a 0.06% solution of PFOS in water at doses of 0, 0.003, 0.06, and 0.3 mg PFOS solution/kg, respectively, to 3 male and 3 female albino rabbits per dose group [Glaza, 1995].

Once in the body, PFOS concentrates primarily in the liver of rats [Johnson et al., 1979]. Eighty-nine days after a single intravenous dose (mean 4.2 mg/kg) of radiolabeled PFOS, mean tissue concentrations (μg PFOS equivalent/g tissue) were: liver, 20.56; plasma, 2.21; kidney, 1.09; lung, 1.06; spleen, 0.51; bone marrow, 0.46; red blood cells, 0.45; adrenals, 0.41; testes, 0.36; skin, 0.35; muscle, 0.29; subcutaneous fat, 0.20; eye, 0.16; abdominal fat, $\leq$ 0.08; and brain, $<$ 0.05. Johnson et al. [1979] observed that 30.2 percent of the dose 89 days after administration had been excreted in the urine and 12.6 percent in the feces. Analyses of the urine, feces and tissues have suggested that PFOS is not metabolized [Johnson et al., 1984]. The plasma half-life was calculated to be 7.5 days after a single oral dose of radiolabeled PFOS (mean dose, 4.2 mg/kg) in solution to three male rats [Johnson and Ober, 1979].

There appears to be significant enterohepatic circulation of PFOS with both urinary and fecal excretion [Johnson et al., 1979; 1980; 1984]. In male rats, cholestyramine administered in the feed decreased the retention of radiolabeled PFOS in liver, plasma, and red blood cells, 3.8, 7.7 and 6.0 fold, respectively, and increased its elimination via feces 9.5 fold after the rats were given intravenous radiolabeled PFOS (mean dose, 3.4 mg/kg) [Johnson et al., 1980; 1984]. There was a lower clearance rate of ^{14}C in the urine compared to control animals because of the increased rate of fecal elimination. Cholestyramine is a bile acid sequestrant that acts by binding bile acids in

the intestinal tract. This reduces bile acid resorption and its return to the liver. Decreased flow of bile acids in the enterohepatic circulation results in increased conversion of hepatic cholesterol into bile acids. This results in a decline in hepatic cholesterol concentration and the stimulation of low density lipoprotein (LDL) receptor synthesis, which subsequently produces a decline in serum LDL cholesterol levels.

Upon acute exposure, PFOS was moderately toxic by oral administration [Gabriel, 1976; Dean et al., 1978; Rusch and Rinehart, 1979], but not dermal [O'Malley and Ebbens, 1980]. There have been two acute oral toxicity studies reported [Gabriel, 1976; Dean et al., 1978]. In the more recent study PFOS was suspended in a 20% acetone/80% corn oil mixture and administered orally by gavage levels to 5 male and 5 female rats per group at the following dosages: 100, 215, 464 and 1000 mg/kg [Dean et al., 1978]. Animals were observed for 14 days. The acute oral LD50 values (95% confidence limits in parentheses) were male rats, 233 (160 - 339) mg/kg; female rats 271 (200 -369) mg/kg; combined male and female rats; 251 (199 - 318) mg/kg. Clinical signs included diarrhea, hypoactivity, decreased limb tone, ataxia, corneal opacity, ptosis, piloerection, prostration and tremors. In the previous study, PFOS was administered in water and the LD50 in the rat was determined to be 1.25 - 2.50 g/kg [Gabriel, 1976]. Gabriel's results appear to be inconsistent with subsequent toxicity studies.

In an acute inhalation toxicity study [Rusch and Rinehart, 1979], a series of one-hour inhalation exposures in rats at exposure concentrations of PFOS at 24.09, 7.05, 6.49, 4.88, 2.86, 1.89 and 0.0 mg/L produced 100 percent mortality at the highest level and partial mortality (10 - 80%) at all other PFOS levels. Observations included dyspnea, tremors, convulsions, hypersensitivity, hypoactivity, excessive salivation and lacrimation

and general poor condition. The LC50 was determined to be 5.2 mg/L (95% CI = 4.4 - 6.4 mg/L).

PFOS has been shown to be a potent inducer of hepatic peroxisomes and fatty acid beta-oxidation in the rat [Ikeda et al., 1987] and mouse [Sohlenius et al., 1993]. After feeding male rats for two weeks with a powdered chow containing 0.02% PFOS, hepatic catalase, fatty acyl-CoA, carnitine acetyl transferase and carnitine palmitoyl transferase increased by 1.74, 4.90, 6.84 and 1.69 fold, respectively, compared to control animals [Ikeda et al., 1987]. PFOS also induced cytochrome P-450 activity. Male mice administered perfluorooctane sulfonic acid at a concentration of 0.05% weight/weight in the diet for 5 days resulted in weight loss and increased peroxisomal fatty acid beta-oxidation, peroxisomal catalase activity, Ω-hydroxylation of lauric acid, cytosolic epoxide hydrolase activity and cytosolic DT-diaphorase activity [Sohlenius et al., 1993].

Haughom and Spydevold [1992] fed 0.02% perfluorooctane sulfonic acid in the diet for 7 - 14 days to male Wistar rats which resulted in increased liver weight, liver triacylglycerol, liver free cholesterol and decreased liver cholesterol ester as well as decreased serum cholesterol and triacylglycerol levels. There was reduced cholesterol synthesis from acetate, pyruvate and hydroxymethyl glutarate but no reduction in synthesis from mevalonic acid in the hepatocytes from the treated rats. The activity of liver hydroxymethyl glutaric acid-Co-A reductase (HMG-CoA) and acyl-CoA cholesterol acyltransferase (ACAT) was reduced. Haughom and Spydevold [1992] suggested that the hypolipidemic effect of perfluorooctane sulfonic acid may be due to downregulation of HMG-CoA reductase and ACAT with enhanced fatty acid oxidation in the liver. This would subsequently reduce very low density lipoprotein (VLDL) production by the liver.

Recently, Nabbefeld et al. [1998] tested the hypothesis that PFOS and other fluorocompounds may act as peroxisome proliferators by displacing fatty acids from liver fatty acid binding protein (L-FABP). 10 μM PFOS caused a 66 percent reduction of the fluorescently labeled fatty acid analog 11-(5-dimethylaminonapthalenesulfphonyl)-undecanoic acid from L-FABP *in vitro*. Comparable results were observed for bovine serum albumin. These findings demonstrated that PFOS has a high affinity for fatty acid carrier proteins and can displace the endogenous ligand.

Results from three subchronic studies have been reported [Goldenthal et al., 1978a; 1978b; 1979]. PFOS was fed in the diet of Charles River CD rats at 0 (control), 30, 100, 300, 1,000 and 3,000 ppm for 90 days [Goldenthal et al., 1978a]. At the 300, 1,000 and 3,000 ppm dosage level, all rats died prior to scheduled termination. Toxicity signs included emaciation, convulsions, ocular and anogenital discharges, increased sensitivity to external stimuli and reduced motor activity. Histopathology showed compound-related lesions which included hepatic hypertrophy and necrosis, thymic and splenic follicular atrophy, bone marrow hypocellularity and atrophy of mesenteric lymph nodes, small intestinal villi and skeletal muscle. Among the 100 ppm dose group there was weight loss, elevated plasma creatinine phosphokinase, alkaline phosphatase, blood glucose and blood urea nitrogen, decreased hemoglobin, hematocrit, erythrocyte and leukocyte counts, hepatic enlargement and necrosis, and stomach discoloration and hemorrhage. Among the 30 ppm dose group there was weight loss, elevated plasma glutamate-pyruvate transaminase and plasma glutamate oxalacetate transaminase, and liver discoloration.

In a subchronic (90 day) study [Goldenthal et al., 1979], two male and two female rhesus monkeys per group received 0 (control), 10, 30, 100 and 300 mg/kg/day of PFOS by oral gavage. All animals (except controls) died within 20 days and timing was related to dosage. Monkeys treated with 300 mg/kg/day died between the second and fourth day. Monkeys treated with 100 mg/kg/day died between the 3rd and 5th day. Monkeys treated at 30 mg/kg/day died between the 7th and 10th day and those treated at 10 mg/kg/day died between the 11th and 20th day of the study. Signs of toxicity at each dosage level were comparable and included anorexia, diarrhea, decreased activity, emesis, weight loss, marked weakness, prostration, and general body tremors. There were no consistent histopathologic changes with exposure. Adrenal changes, including congestion, hemorrhage and lipid depletion of the adrenal cortex, were observed in all dose groups.

An additional subchronic rhesus monkey study was subsequently initiated at much lower dosages [Goldenthal, 1978b]. PFOS was administered by oral gavage to two male and two female monkeys at dosages of 0, 0.5,1.5 or 4.5 mg/kg/day for 90 days. Animals treated at the 4.5 mg/kg/day dosage level died or were sacrificed *in extremis* by the seventh week with signs of gastrointestinal toxicity comparable to those observed in the previous rhesus monkey study by Goldenthal et al. [1978a]. Also, in the 4.5 mg/kg/day dose group, mean serum cholesterol levels declined from 183 mg/100 ml to 99 within 30 days. SGOT increased from 36 to 95 u/l and alkaline phosphatase decreased from 1088 to 590 u/l. SGPT remained unchanged. Histopathology showed compound-related marked diffuse lipid depletion of the adrenals as well as diffuse atrophy of the pancreatic exocrine cells. Animals in the 0.5 mg/kg/day and 1.5 mg/kg/day dosage groups survived to the end of the study. Occasional diarrhea, anorexia and emesis were observed. There

was a decrease in serum alkaline phosphatase and inorganic phosphate in the 1.5 mg/kg/day group and a slight decrease in alkaline phosphatase in the 0.5 mg/kg/day group at the end of 90 days. Histopathology was unremarkable in both dosage groups.

A no observable adverse effect level (NOAEL) was not identified from any of the above three subchronic (90 day) studies. The results from these three subchronic studies suggest there may be a potential for cumulative toxicity over time with the primary toxic effect related to metabolic wasting. This may be due to an effect on peroxisome proliferation, fatty acid metabolism, membrane function, protein synthesis and/or mitochondrial bioenergetics.

To date, there are no data regarding the chronic toxicity and carcinogenicity of PFOS. PFOS was not observed to be mutagenic in several *Salmonella typhimurium* strains with or without metabolic activation [Jagannath and Brusic, 1978]. PFOS was negative in an *in vivo* mouse bone marrow micronucleus assay [Murli, 1996].

There have been two teratology studies conducted with PFOS. Oral administration, via corn oil, of PFOS at doses of 0, 1, 5 and 10 mg/kg/day to pregnant rats during days 6 - 15 of gestation resulted in fetuses with what was initially reported as teratogenic changes in the eye. [Gortner et al., 1980]. These fetal lens abnormalities were subsequently interpreted to be artifacts of the tissue sectioning process. Maternal body weights in the high dose group were significantly reduced but no significant treatment-related teratogenic or embryotoxic effects were reported. In the second teratology study, PFOS was administered in corn oil by oral gavage to groups of 25 pregnant rats on days 6 - 15 of gestation at doses of 0, 1, 5 and 10 mg/kg/day [Wetzel et al., 1983]. Maternal body weights and food consumption at 5 and 10 mg/kg/day were

significantly reduced compared to the control animals. Two female rats in the high dose group died before day 20. Clinical signs in surviving dams included hunching, thinness, alopecia, rough haircoat and anorexia. Treatment-related effects, primarily occurring in the high dose group, included increase resorptions and fetal death, decreased fetal body weight, delayed skeletal ossification, cleft palate, subcutaneous edema and cryptorchidism.

During the past 15 to 20 years there have been several endeavors designed to ascertain the health and exposure status of workers involved with fluorochemical production at the company's Decatur, Alabama and Antwerp, Belgium plants. Medical surveillance has been routinely conducted of fluorochemical production workers at both plants. Medical surveillance activities analyzed for total serum organic fluorine levels until the mid-1990's when serum PFOS determination, quantifiable by liquid chromatography mass spectrometry, became incorporated in the biennial medical surveillance examinations. However, we are aware of one occasion in 1979 where the serum of 5 Decatur employees was measured for PFOS by electron capture gas chromatograph and microwave plasma detection methods [Central Analytical Laboratory, 1979]. Total serum organic fluorine levels for these five employees were 10.1, 5.7, 9.4, 11.8 and 4.1 ppm. The percent of PFOS found was 60%, 70%, 80%, 55% and 65% of the total serum organic fluorine levels, respectively. In 1981, selected clinical chemistries and hematology values of Decatur employees in the chemical plant were compared to those results of employees in the adjacent 3M film plant [Roach, 1982; Schuman, 1982]. There were no significant correlation coefficients between total serum organic fluorine and gamma glutamyl transferase, serum glutamic oxaloacetic

transaminase, serum glutamic pyruvic transaminase, alkaline phosphatase, cholesterol, hemoglobin or red blood counts. However, this analysis was limited in scope (no dose response analysis), did not analyze specifically for PFOS, and did not account for several potential confounding factors. Another research initiative into the health status of Decatur employees was a retrospective cohort mortality study (1961 - 1991) conducted of former and current employees who had worked at least one year at the Decatur plant [Mandel and Johnson, 1995]. Vital status was determined for 99.7% of the 1,957 cohort members who had worked in the chemical and film plants. A total of 74 deaths were identified compared to 117.7 expected (U.S. rates). Among male employees who had worked only in the Decatur chemical plant, there were 32 deaths compared to 44.1 expected. There were no specific causes of death that had significantly elevated standardized mortality ratios. Because of its more recent construction in the 1970's, there has not been a retrospective cohort mortality study conducted of employees at the Antwerp plant.

The purpose of this report is to provide an aggregate analysis of the hematological, clinical chemistry and hormonal parameters, as measured in the medical surveillance examinations of Antwerp and Decatur employees in two separate time periods, in relation to the workers' serum PFOS levels. Although female employees also participated in these medical surveillance examinations, their actual numbers were too few to provide meaningful statistical analysis.

METHODS

PFOS Production

PFOS production began in Antwerp in 1976 and in Decatur in 1961. In general, perfluorinated chemicals are produced via an electrochemical process: a solution of organic substrate is electrolyzed in anhydrous hydrogen fluoride at a low voltage (Simons and Bryce, 1954). Basically, the products of this electrolysis cell reaction are highly fluorinated compounds with the end-product defined by the starting material. Products manufactured at these two plants include: Scotchgard™ brand fiber, leather and carpet protector; Light Water™ brand aqueous film forming foam (AFFF); Scotchban™ paper treatment; Kel-F™ brand plastic and Fluorel™ brand elastomers.

Subject Selection

General medical surveillance occurs biennially for employees at both of these plants. Participation is voluntary with approximately 100 Antwerp and 250 Decatur employees eligible for surveillance. A total of 88 Antwerp employees participated in the medical surveillance examinations in the Spring, 1995 and 90 Decatur employees participated in the Fall, 1994. In the Fall of 1997, a total of 149 employees (Antwerp = 65; Decatur = 84) participated in medical surveillance examinations. For purposes of brevity, these time periods will be referred to as 1995 and 1997. Altogether, 61 employees participated in both examination years (1995 and 1997). This lower number was due to a large turnover of employees at both plant locations during 1996-1997. For each time period the surveillance consisted of a medical questionnaire, measurement of height, weight and blood pressure, standard clinical chemistry and hematology tests, and determination of serum PFOS levels.

In 1995, several hormones were also analyzed for male employees who were judged *a priori* to have had likely PFOS exposure (i.e., those working in or in the immediate vicinity of the PFOS production area). Of the 88 Antwerp employees, 50 had hormone measurements. Of the 90 Decatur employees, 38 underwent hormone measurements.

PFOS Analysis

In 1995 the analysis for serum PFOS was conducted by 3M'S Environmental Technology Services in St. Paul, Minnesota. The method used tetrabutylammonium to ion-pair with PFOS in serum. The ion-pairs were then extracted with ethyl acetate. The abstraction product was then analyzed using high performance liquid chromatography-thermospray mass spectrometry [Johnson et al., 1996]. In 1997 the serum samples were analyzed by TurboIonSpray liquid chromatography/mass spectrometry using selected ion monitoring in the negative ion mode by Advanced Bioanalytical Services, Inc. [Anderson et al., 1997a; 1997b]. The lower limit of quantitation was 0.1 μg/mL for PFOS.

Laboratory Analyses

For both time periods, the United Laboratory Services (St. Paul, Minnesota) performed the standard hematological and clinical chemistry tests. These included the following hematological tests: hematocrit (percent), hemoglobin (gm/dl), red blood cells (RBC, 1000/mm^3), white blood cells (WBC, 1000/ mm^3) and platelet count (1000/ mm^3); and the following clinical chemistry tests: alkaline phosphatase (IU/L), gamma glutamyl transferase (GGT, IU/L), aspartate aminotransferase (AST, IU/L) formerly

known as serum glutamic oxaloacetic acid (SGOT), alanine aminotransferase (ALT, IU/L) formerly known as serum glutamic oxaloacetic transaminase (SGPT), total and direct bilirubin (mg/dl), blood urea nitrogen (BUN, mg/dl), serum creatinine (mg/dl), glucose (mg/dl), cholesterol (mg/dl), high density cholesterol (HDL, mg/dl) and triglycerides (mg/dl). Low density lipoprotein (mg/dl) was calculated as the following: LDL = [cholesterol - HDL - (tryglycerides/5)].

Eleven hormones were assayed in 1995: cortisol, dihydroepiandrosterone sulfate (DHEAS), estradiol, follicle stimulating hormone (FSH), 17 alpha hydroxyprogesterone (17-HP), free testosterone, total testosterone, luteinizing hormone (LH), prolactin, thyroid stimulating hormone (TSH) and sex hormone binding globulin (SHBG). All but SHBG (Endocrine Science Reference Laboratory, Tarzana, CA) were analyzed at the University of Minnesota's Endocrinology Laboratory.

Cortisol was assayed using a fluorescence polarization immunoassay (Abbott TDx). Radioimmunoassays (RIA) were used for DHEAS (Pantex), estradiol (modified Pantex), 17-HP (modified CIS) and total testosterone (Diagnostic Product Corp. Coat-A Count). Free testosterone was determined using equilibrium dialysis. LH, FSH and prolactin were assayed using a microparticle enzyme immunoassay (Abbott Imx). TSH was determined using a chemiluminescence immunometric assay (Nichols). SHBG was assessed via a radioimmunoassay after chromatographic sample purification (Endocrine Science Reference Laboratory). Bound testosterone was calculated as total testosterone less free testosterone.

Data Analysis

Descriptive simple and stratified analyses, Pearson correlation coefficients, ANOVA and ordinary multivariable regression were used to evaluate associations between PFOS and each hematological and clinical chemistry test and hormonal assay. Age, body mass index, current alcohol consumption (drinks per day) and cigarette use (cigarettes smoked per day) were potential confounding factors that were considered in the analyses. For stratified analyses, employees were divided into four PFOS categories: 0-1 ppm, 1 - < 3 ppm, 3 - < 6 ppm and $\geq$ 6 ppm in order to determine if an effect existed at the highest serum PFOS levels. Other categorical cutoff points were also used which provided similar results. For multivariable regression analyses, PFOS and the potential confounders of age, body mass index (BMI), alcohol use and cigarette use were examined as continuous explanatory variables in the models. Multivariable regression models were fitted with PFOS analyzed as a continuous variable using linear as well as non-linear transformations (quadratic, square, square root and inverse) in order to maximize the possibility of finding associations between PFOS and the dependent variable of interest. Linear and nonlinear relationships were examined by residual diagnostics using studentized and Cook's distance values. Natural log transformations of the dependent variables were performed, when necessary, to normalize variables and to enhance model fit. Traditional stepwise selection procedures were also employed (selection in and out of model was set at $p = 0.1$) as well as taking into account other covariants that may be on the biologic pathway of effect [Greenland, 1989]. We did not examine changes in measured PFOS between the two time periods because the estimated half-life of PFOS is at least two years. Study results were analyzed using the SAS System [1990].

Analyses are presented by plant, year and the three major groups of participants: all employees who participated in each year (1995: N = 178; 1997: N = 149); only those employees (N = 61) who participated in both years; and only those employees (N = 88) who participated in the hormone measurements in 1995.

RESULTS

The distribution of employees, by serum PFOS exposure categorization, is presented in Table 1. Whereas 20 percent of the Decatur employees had exposures at ≥ 3 ppm for both years, this proportion in Antwerp went from 25 percent in 1995 to 13 percent in 1997. For both years 95 percent of the measured serum PFOS levels were below 6 ppm. There were no PFOS measurements ≥ 6 ppm in Antwerp in 1997.

The overall mean values of PFOS, demographic, serum chemistry and hematological parameters for both locations, as well as each location separately, are presented in Tables 2 and 3, respectively. In particular, the Antwerp male employee population was significantly younger than Decatur, had lower body mass indices and higher self-reported daily consumption of alcohol. In addition, their clinical profiles were also different for several tests. The Antwerp employees had lower mean alkaline phosphatase, creatinine, glucose and triglyceride values and higher total bilirubin, HDL and hematocrit values.

Presented in Table 4 are the Pearson correlation coefficients between PFOS and the selected parameters of interest by both locations combined, each location separately, and by year of examination. In 1995, variables that were significantly ($p < .05$) correlated with PFOS for both locations combined included total bilirubin, white blood

cells and platelets. Although creatinine was not significantly correlated when both locations were examined, it was negatively correlated with PFOS in Antwerp but positively correlated in Decatur. In 1997, variables that were significantly correlated with PFOS for both locations combined were BMI, ALT, direct bilirubin, cholesterol, LDL and hematocrit. In addition, GGT and triglycerides were significantly positively correlated with PFOS among only Antwerp employees.

Provided in Table 5 are the mean, median, standard deviation and range of the covariates and the clinical chemistries and hematological parameters by four levels of PFOS categorization (0 - < 1, 1 - < 3, 3 < 6 and $\geq$ 6 ppm) for both years. Several observations are noteworthy. First, the mean for the $\geq$ 6 ppm PFOS category was one order of magnitude higher than the lowest PFOS category (0 - < 1 ppm) for both years. Also, the means of the four PFOS categories were significantly different from each other. Second, the youngest employees had the lowest serum levels of PFOS. Third, there was only one variable, total bilirubin, which had significant ($p < .05$) F tests for differences in means in both years of analysis. Besides total bilirubin, the only other variable in which the mean of the higher levels of PFOS exposure (3 - < 6 ppm or $\geq$ 6 ppm) was significantly different from the lowest category level of PFOS exposure (0 - < 1 ppm) was for WBC's in 1995. This was not observed in 1997. The lowest mean platelet count was observed at the highest PFOS exposure category in both years although the mean platelet counts by PFOS categories were not significantly different from each other.

Provided in the next two tables are the mean, median, standard deviation and range of the covariates and the clinical chemistries and hematological parameters by the four levels of PFOS categorization for each plant for 1995 (Table 6) and 1997 (Table 7).

In 1995 (Table 6) in Antwerp only, alcohol consumption was associated with higher PFOS levels. Mean serum creatinine levels declined in Antwerp but increased in Decatur employees. Antwerp employees in the 3 - < 6 ppm PFOS category smoked more cigarettes and had higher WBC levels. In 1997, Antwerp employees in the lowest PFOS exposure category were significantly younger than their counterparts. Antwerp employees in the higher PFOS category levels had higher mean alcohol consumption levels. Mean cholesterol, LDL and triglyceride levels trended upwards by PFOS exposure categories for Antwerp employees.

Linear and nonlinear relationships between PFOS and the dependent variables of interest, taking into account the potential confounding affects of age, BMI, alcohol and cigarettes, resulted in numerous analyses. For purposes of brevity, linear regression models are presented in Table 8 which show the effect that the parameter of interest, PFOS, has on the various dependent variables, adjusted for age, body mass index, alcohol and cigarette use. These covariates were analyzed as continuous variables. In the case of serum creatinine and total bilirubin, a quadratic ($PFOS + PFOS^2$) analysis provided the best statistical model of the data adjusted for the four potential confounders. The natural log transformation of total bilirubin, GGT and glucose provided the best fit for these response variables. PFOS was significantly associated ($p < .10$) in both years for only one clinical parameter: total bilirubin. PFOS was associated in one of the two years for the following variables: direct bilirubin, creatinine, cholesterol, LDL, HDL, hematocrit, hemoglobin and platelet count.

Those variables that were observed to be associated in at least one year in the regression models in Table 8 are separated by plant location and year in Table 9. After

separate analyses by employee population, only two variables, total bilirubin and HDL, remained significantly (negatively) associated with PFOS for at least one plant location for both time periods. Total bilirubin showed a significant negative association with PFOS (quadratic relation) for employees at the Decatur plant in both years. There were no significant associations among the Antwerp population between PFOS and total bilirubin. HDL was significantly negatively associated with PFOS in Antwerp in both 1995 and 1997 but was not significantly associated with PFOS in Decatur in either year. As for inconsistent associations observed in Table 8, direct bilirubin was not significantly associated with PFOS in either plant location (Table 9). The quadratic association for PFOS with creatinine was observed in Antwerp in 1995 and Decatur in 1997 but not in Antwerp in 1997 or Decatur in 1995. Cholesterol (and LDL) was observed to be positively associated with PFOS only in Decatur in 1997. Hematocrit and hemoglobin were associated with PFOS only in Decatur in 1997. Platelet counts were observed to be significantly negatively associated with PFOS only in Decatur in 1995.

Traditional stepwise regression modeling techniques were also used as well as testing models with variables that would be considered on the biological pathway of effect for any dependent variable. The associations (or lack thereof) from these analyses were similar to what has been presented in Tables 8 and 9. For purposes of brevity these analyses are not shown.

To further understand the association between total bilirubin and PFOS, scatter plots are presented for both time periods and by location in Appendix A. In addition, unconjugated bilirubin was also calculated (total bilirubin - direct) and these scatter plots are presented in Appendix B. Table 10 is a summary of these scatter plots from both

Appendices. The strongest associations appeared to be quadratic in nature primarily for the Decatur location and the percent of variability explained ranged between 3 (1995 data) and 7 percent (1997 data). The linear component of the quadratic was negative in direction. The upward trend appeared to occur around 6 ppm PFOS where the data are sparse. These simple linear and quadratic models were not influenced by any one employee according to residual diagnostics.

To further understand the possible association between HDL and PFOS, scatter plots are presented for both times and by location in Appendix C. Both locations combined resulted in significant negative linear and nonlinear (quadratic) associations in 1995 although the percent of variability explained in these models ranged between 3 and 5 percent. No significant associations were observed for each plant location in 1995. There were no significant negative associations between HDL and PFOS in 1997 for either the combined locations or each separate plant site.

Provided in Tables 11 through 14 are the analyses restricted to the 61 employees who participated in surveillance in both years. Table 11 provides the mean values for each parameter for the employees who participated in both exams compared to those who participated in only one of the two years. Overall, there were few differences. The mean age of the 61 employees was lower than that of the 1995 employees who didn't participate in 1997. Conversely, the mean age of the 61 employees was higher than that of the 1997 employees who didn't participate in 1995. Cholesterol and LDL were significantly higher in the 61 participants in 1997. Tables 12 and 13 present the mean values by plant location for 1995 and 1997, respectively. Of these 61 employees, 27 were from Antwerp and 34 from Decatur. Of noteworthy importance are the differences

between the 27 Antwerp employees and their fellow employees in 1997 (Table 13). The 27 Antwerp employees had significantly higher mean PFOS exposures, were significantly older, had greater BMI's and higher cholesterol values. Multivariable regression analyses for the 61 employees are presented in Table 14. The only significant association with PFOS appeared to be with serum creatinine (quadratic) in 1995.

Regardless of plant location, mean PFOS levels were higher for those employees who were selected for hormone measurements in 1995 (Table 15). This was expected as these employees were selected with the *a priori* belief that their serum measurements would be higher due to their workplace experience. For example, of the 42 employees in 1995 whose serum PFOS levels were ≥ 3 ppm, 76% had hormone measurements.

Presented in Table 16 are the mean values for PFOS, demographic, serum chemistries and hematology for those employees who had hormone measurements compared to those employees who did not in 1995. Those employees who had hormone measurements were younger, higher users of alcohol (Antwerp only) and cigarettes (both locations), and had lower serum creatinine (Antwerp only) and higher WBC levels (both locations). The latter observation is confounded by cigarette smoking as among non-smokers, those selected for hormone measurements had a mean WBC of 6.24 compared to 6.03 for non-selected employees ($p = .36$). Among smokers, those selected had a mean WBC of 8.69 compared to 8.06 for non-selected employees ($p = .23$). All other clinical parameters were comparable, by PFOS exposure categories, between subjects who had hormone measurements and those who did not in 1995 (Tables 17 and 18).

The Pearson correlation coefficients between PFOS and the hormones tested among the 88 employees were the following: cortisol (.07), DHEAS (-.13), estradiol

(.09), FSH (.06), 17-hydroxyprogesterone (-.04), LH (.03), prolactin (.06), SHBG (.11), free testosterone (-.06), bound testosterone (.06), TSH (.01). None were statistically significant.

Presented in Table 19 are the mean, median, standard deviation and range of the various hormones by the four PFOS categories: 0- <1 ppm, 1 - < 3 ppm, 3 - < 6 ppm and $\geq$ 6 ppm. Several observations are noteworthy. First, the mean age of the lowest PFOS exposure category was 10 years less than that of the highest exposure category. Therefore it was not unexpected to observe that the mean DHEAS, 17-HP, free testosterone and bound testosterone levels of this lowest exposure category were greater than the means of the higher PFOS exposure categorizations. Adjusting for the differences in age (as well as the other three potential confounders) in the regression models (Table 20) resulted in no significant associations between PFOS and the hormones analyzed, except for estradiol. With estradiol, a quadratic model provided the best fit of the data and both PFOS terms were significant. Upon residual diagnostics it was determined that this estradiol model was influenced by one specific employee (employee A). The influence of employee A is best seen in Figures 1 and 2 which are simple scatter plots of both the linear and quadratic fits of estradiol and PFOS, with and without employee A, respectively. Employee A had a 12.83 ppm serum level of PFOS which was the highest value recorded in 1995. His estradiol value was 92 pg/dl (see upper right hand corner of Figure 1). Employee's A estradiol value was also influenced by the fact that his body mass index was 33 kg/m^2. Exclusion of this employee resulted in a nonsignificant quadratic equation. The variability (R^2) of the data explained went from 7.6 percent to 2.1 percent upon exclusion of this employee. The slope of the linear equation changed from

positive to negative although it was nonsignificant in both Figures 1 and 2. Finally, it should be noted that the estradiol models in Table 20, with and without employee A, did predict the known positive assocation between estradiol and body mass index.

DISCUSSION

We conducted two cross-sectional analyses of surveillance data to examine the associations between serum PFOS levels and several hematological, clinical chemistry and hormonal parameters in male fluorochemical production employees. For both years, 95 percent of the measured serum PFOS levels were below 6 ppm. Because the Antwerp and Decatur employees were dissimilar by age, body mass indices and self-reported alcohol use, we conducted combined as well as separate analyses by plant location. These three demographic differences likely explain why the Antwerp employees had lower mean serum levels of alkaline phosphatase, HDL, triglycerides and blood glucose [Davern and Scharschmidt, 1993; Lewis, 1994; Friedman, 1998; Fu, 1998; Wolf, 1998].

In the present study, alkaline phosphatase, GGT, AST and ALT values were not significantly associated with the measured serum PFOS levels. This was an *a priori* question due to the fact that PFOS: 1) is a peroxisome proliferator in the rat [Ikeda et al., 1987; Sohlenius et al., 1993]; 2) resulted in slight to marked increases in plasma glutamic oxalacetic and pryuvic transaminase levels in a 90 day study of rats fed diets which contained PFOS at 100 ppm along with hypertrophy and liver necrosis observed at histopathology [Goldenthal, 1978a]; and 3) increased SGOT and decreased alkaline phosphatase levels in monkeys after administration, by oral gavage, for 30 days of doses of 4.5 mg/kg/day of PFOS [Goldenthal, 1978b]. On the other hand, SGPT values

remained constant and no histopathologic abnormalities were noted in the livers of these monkeys which died by the 7th week of the study. No significant liver enzymatic or histopathology changes occurred in monkeys in the 0.5 and 1.5 mg/kg/day dose groups.

We did observe a quadratic association with total bilirubin among only the Decatur employees. We do not suspect this is a biological association because the bilirubin levels were within the normal reference range. Also, the percent variability explained of total bilirubin by PFOS in the regression models was low. The Antwerp employees' total bilirubin levels were significantly higher than the Decatur employees'levels. We offer several possible explanations for this observation. First, we suspect there may be a greater prevalence of Gilbert's syndrome [Lidofsky and Scharschmidt, 1993; Friedman, 1998] among the Antwerp employees. In 1995, 15 (17%) Antwerp employees had total bilirubin values $\geq$ 1.2 mg/dl compared to 3 (3%) Decatur employees' levels. In 1997, there were 9 (15%) Antwerp and 2 (2%) Decatur employees with total bilirubin values $\geq$ 1.2 mg/dl. However, there was not a concomitant decline in bilirubin conjugation (i.e., direct bilirubin levels) as might be expected among individuals diagnosed with Gilbert's syndrome. Nevertheless, exclusion of these possible Gilbert's syndrome employees still resulted in higher mean total bilirubin values among the Antwerp employees in both years. Secondly, there were four Antwerp employees who self-reported hepatitis A histories and one employee self-reported a history of Hepatitis B. Fish and shellfish consumption is likely much greater in Antwerp than Decatur due to its vicinity near the North Atlantic. Third, bilirubin is a tetrapyrrole that is an end-product of heme degradation [Lidofsky and Scharschmidt, 1993]. Bilirubin levels may be increased due to disorders of bilirubin metabolism, liver

disease and obstruction of the bile ducts. Other hematological and clinical chemistry results did not suggest these conditions existed among the Decatur employees. Fourth, post-collection procedures may result in error. Total bilirubin determination may be falsely depressed if hemolysis is present because of increased absorbence in the blank [Kaplan and Pesce, 1984]. Bilirubin is also sensitive to and destroyed by light and heat. We are uncertain whether these factors could have contributed to the lower total bilirubin levels in the Decatur samples in both years. Finally, the linear component of the quadratic association observed among Decatur employees is negative in direction in relation with their measured PFOS levels. That is, total bilirubin levels declined with increasing PFOS levels. We would expect a positive association if PFOS impaired bilirubin conjugation. The trend upwards in the quadratic appears to occur at levels 6 ppm and higher where the data are sparse. We conclude that the association observed among only the Decatur employees is unlikely to be related to serum levels of PFOS.

We did observe a positive association between serum PFOS and serum cholesterol levels in the 1997 time period for Decatur employees. This result is unlikely to have a biological explanation as PFOS is a known peroxisome proliferator in the rat and was shown to have hypolipidemic properties in rhesus monkeys [Ikeda et al., 1987; Sohlenius et al., 1993; Goldenthal 1978b; 1979]. Rhesus monkeys fed PFOS at 4.5 mg/kg in their chow had serum cholesterol values reduced from 183 mg/L to 99 mg/L within 30 days. Rhesus monkeys fed 1.5 mg/kg in the chow had cholesterol levels reduced from 195 mg/kg to 111 mg/kg within 90 days [Goldenthal 1978b]. As for HDL, although the multivariable analyses were suggestive of a negative association between HDL and PFOS

in Antwerp (but not Decatur), the scatter plots presented in Appendix C do not support the notion of a biological association between PFOS and HDL.

It should be noted that total organic fluorine levels, primarily consisting of perfluorooctanoic acid (PFOA, $C_7F_{15}COO^-$), a seven carbon perfluorinated carboxylic acid, were reported to reduce the effect that alcohol has on HDL levels among higher exposed male PFOA production workers in Cottage Grove, Minnesota [Gilliland and Mandel, 1995]. However, this finding was not observed in subsequent analyses of these employees (Olsen et al., unpublished findings). This observation by Gilliland and Mandel was testable in the present study as both Antwerp and Decatur employees had measurable quantities of PFOA. We did not observe a significant negative modulation of the effect of alcohol consumption on HDL levels among Antwerp and Decatur employees with higher serum PFOA levels although their serum levels were approximately 3 to 5-fold less, on average, than that reported in Cottage Grove employees [Olsen et al., 1998]. The Antwerp and Decatur employees were exposed to PFOA, not in its actual production, but rather in its use as a surfactant in the production of fluoropolymers. In 1995 the mean serum PFOA level among the Antwerp and Decatur employees combined was 1.46 ppm (range 0 - 13.20 ppm) and in 1997 the mean serum level was 1.57 ppm (range 0.11 - 11.10). Stratified by plant location, the 1995 and 1997 mean serum PFOA levels were 1.19 and 1.78 ppm in the Antwerp employees and 1.72 and 1.40 ppm in the Decatur employees, respectively.

The multivariable regression models showed a negative association between PFOS and platelet counts at PFOS levels above 6 ppm in 1995 and this trend was also apparent, although to a lesser extent, in 1997. Nevertheless, platelet levels were well

within the normal reference range in both time periods. This association is not supported by a 90 day subchronic toxicity study which showed no decline in platelet counts for monkeys fed 0.5, 1.5 or 4.5 mg/kg for up to 90 days [Goldenthal, 1978b]. Mean platelet counts among the 1.5 mg/kg/day and 0.5 mg/kg/day dose groups were 226 and 231 (10^3/cmm) compared to 218 in the control group [Goldenthal, 1978b]. There were no platelet counts reported in the 90 day rat study although at the end of 3 months of study there were slight to moderate decreases in hemoglobin, hematocrit and erythrocyte counts observed for male and female rats in the 100 ppm dose group [Goldenthal, 1978a]. No consistent associations were observed between PFOS and hemoglobin, hematocrit or RBC values in the present epidemiologic investigation. In a prior subchronic rhesus monkey study that was aborted early due to all animals died by the 20th day, mean platelet counts were 203, 219, 136, 172 and 185 for the 300 mg/kg/day, 100 mg/kg/day, 30 mg/kg/day, 10 mg/kg/day and control groups, respectively [Goldenthal, 1979].

After controlling for age, a confounder for male testosterone hormone levels [Dali et al., 1981; Griffin and Wilson, 1994], we observed no significant associations with serum PFOS measurements. We did observe a quadratic association between estradiol and PFOS. Upon further examination, this finding was influenced by one particular employee who had the highest PFOS level but was confounded by the individual's large body mass index. Exclusion of this employee resulted in nonsignificant findings. Thus, any interpretation with estradiol is difficult because of the influence this one employee has on the statistical analyses.

It should be noted that perfluorooctanoic acid (PFOA), at approximately 50 - 100 ppm levels in serum, enhances the aromatase conversion of testosterone to estradiol in the

rat [Cook et al., 1992; Biegel et al., 1995]. However, PFOA production workers in Cottage Grove with serum levels up to 30 ppm appeared not to have altered serum estradiol levels [Olsen et al., 1998]. Again, like HDL, this was a testable hypothesis among the Antwerp and Decatur employees although their serum PFOA levels were lower than Cottage Grove employees. We did not observe any significant positive association between estradiol and serum PFOA levels in these Antwerp and Decatur employees.

Several methodological issues should be considered in evaluating the results from this study. First, the cross-sectional design does not allow for a direct analysis of the temporality of an association. Second, the voluntary participation rates in medical surveillance were not ideal as among eligible employees we had 88 and 65 percent participation in Antwerp for 1995 and 1997, respectively, but only 35 to 40 percent in Decatur for both years. Third, given the suspected long half-life of PFOS (at least two years), it may be conceivable that there may be some biological accommodation to the effects of PFOS which would minimize the possibility of finding an association. Fourth, it is known in laboratory animals that PFOS concentrates primarily in the liver. Serum measurements of PFOS may not adequately reflect body burden. Fifth, the two cross-sectional analyses cannot be viewed as independent populations as 61 employees were studied in both years. This was due, in part, to a large turnover of employees at both plants between examinations. Sixth, there could be measurement error in important confounding variables. Analysis of the data of the 61 subjects who participated in both years showed that there was excellent correlation for the confounding factors of BMI ($r = .92$, $p = .0001$), self-reported aspects of alcohol consumption ($r = .88$, $p = .0001$) and

cigarette smoking ($r = .79$, $p = .0001$). As expected, these 61 employees' serum PFOS levels for the two years were highly correlated ($r = .92$, $p = .0001$). Seventh, the quality of medical surveillance data, prior to its use for studying an *a priori* hypothesis, can often be evaluated by whether known positive associations are observed. In this regard, we observed various expected associations including cigarette smoking and elevated white blood cell counts and large body mass indices associated with elevated liver transaminase levels [Olsen et al., 1991; Burns et al., 1997]. Finally, the pulsatile nature of some of the hormones studied (e.g., FSH, LH, testosterone) has resulted in prior recommendations that mean hormone measurements should be the result of pooled blood from multiple samples taken at short intervals [Goldzieher et al., 1976]. In our study multiple samples were not feasible because of the low probability of employees voluntarily giving three serum samples over a 45 -60 minute period of time.

In summary, we conducted two cross-sectional analyses and did not observe consistent associations by plant location or time for several hematological parameters, serum chemistries and reproductive hormones with measured serum PFOS levels in male fluorochemical production employees. Ninety-five percent of the employees had serum PFOS levels below 6 ppm. Our findings suggest that, among these Antwerp and Decatur male fluorochemical production employees, significant hematological, clinical chemistry and hormonal abnormalities were not associated with serum PFOS concentrations less than 6 ppm. Any inferences derived from the few employees with serum PFOS levels ≥ 6 ppm would be tenuous, at best. Limitations of this study include its cross-sectional design, the voluntary participation rates, the few subjects exposed at the highest levels,

and the lower levels of serum PFOS measured among these employees compared to those that caused effects in two species of laboratory animals.

Acknowledgements

The authors gratefully acknowledge the assistance of Michele Burlew, Martha McGough, Jane Quarfoth and the helpful comments of Drs. John Butenhoff, Marvin Case and Andrew Seacat.

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Table 1

Distribution of Employees by Year, Location and PFOS Exposure Level (ppm)

	1995 Data						1997 Data					
	All Employees		Antwerp		Decatur		All Employees		Antwerp		Decatur	
PFOS	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
0 - < 1 ppm	45	25	34	39	11	12	60	40	31	48	29	35
1 - < 3 ppm	91	51	32	36	59	66	63	43	25	38	38	45
3 - < 6 ppm	35	20	19	22	16	18	21	14	9	14	12	14
>= 6 ppm	7	4	3	3	4	4	5	3	0	0	5	6
	178	(100)	88	(100)	90	(100)	149	(100)	65	(100)	84	(100)

Table 2

Mean, Median, Standard Deviation and Range of Study Parameters, Both Locations, 1995 and 1997

	1995 Data				1997 Data			
Variable	Mean	Median	Std Dev	Range	Mean	Median	Std. Dev.	Range
PFOS	2.19	1.70	1.87	0 - 12.83	1.75	1.30	1.60	0.10 - 9.93
Age	40.6	40.0	8.76	21 - 60	39.3	40.0	9.7	21 - 63
Alcohol	0.7	0.1	1.1	0 - 6.0	0.5	0.1	1.0	0 - 7.1
BMI	26.6	25.8	5.1	17.9 - 60.7	27.1	26.0	5.2	18.1 - 48.5
Cigarettes	6.3	0.0	10.7	0 - 40	6.1	0.0	10.3	0 - 40
Alk Phos	86.2	85.0	24.6	31 - 191	79.8	77.0	20.8	29 - 163
GGT	44.4	36.0	32.1	2 - 293	31.6	.24.0	25.9	10 - 179
AST	27.6	26.0	10.9	13 - 96	26.2	25.0	7.0	13 - 56
ALT	45.9	42.0	18.6	18 - 183	32.6	30.0	14.4	10 - 89
T. Bilirubin	0.72	0.70	0.37	0.20 - 2.90	0.67	0.60	0.32	0.30 - 2.30
D. Bilirubin	0.21	0.20	0.05	0.10 - 0.40	0.13	0.10	0.06	0.10 - 0.40

Table 2
(Continued)

Variable	Mean	Median	Std Dev	Range	Mean	Median	Std. Dev.	Range
BUN	15.9	15.0	3.8	8 - 26	14.4	14.0	3.0	6 - 26
Creatinine	1.0	1.0	0.2	0.6 - 1.6	0.9	0.9	0.1	0.6 - 1.4
Glucose	86.7	85.0	18.8	60 - 260	90.7	86.0	29.9	58 - 303
Cholesterol	215.9	214.0	42.5	100 - 340	211.2	213.0	40.7	110 - 365
LDL	136.6	134.0	39.1	28 - 261	135.3	135.0	35.0	50 - 290
HDL	48.5	48.0	12.7	23 - 94	45.5	45.0	10.6	19 - 74
Triglycerides	151.0	126.0	99.9	34 - 651	156.5	122.0	130.0	38 - 1209
Hematocrit	46.3	47.0	2.7	38.3 - 52.0	45.8	46.0	2.6	39 - 52.9
Hemoglobin	15.3	15.3	0.9	13 - 17.4	15.4	15.5	0.9	12.5 - 17.3
RBC	4.9	4.9	0.3	4.0 - 5.74	5.1	4.8	0.3	4.1 - 5.9
MCH	31.1	31.0	1.5	26.0 - 36.9	30.5	31.0	1.5	26.2 - 34.1
MCHC	33.1	33.0	0.7	31.3 - 34.7	33.6	34.0	0.5	31.8 - 34.9
MCV	93.7	94.0	4.9	79.7 - 114.6	90.7	91.0	.42	80.0 - 101.0
WBC	6.9	6.6	1.9	3.6 - 15.5	6.5	6.2	1.7	3.8 - 13.2
Platelets	226.4	223.0	45.4	122 - 367	225.7	230.0	50.4	106 - 406

Table 3

Mean Values of PFOS, Demographic, Serum Chemistry and Hematologic Parameters for Antwerp and Decatur, 1995 and 1997 Examinations

	1995 Data		1997 Data	
Variable	Antwerp	Decatur	Antwerp	Decatur
PFOS (ppm)	1.93	2.44	1.48	1.96
Age	37***	45	33***	44
BMI	23.9***	29.2	23.5***	30.0
Cigarettes	4.7*	7.9	5.5	6.6
Alcohol	1.3***	0.2	1.1***	0.1
Alk Phosphatase	75***	97	70***	87
GGT	41	48	26*	36
AST	26*	29	27	26
ALT	44	47	31	34
Total bilirubin	0.86***	0.58	0.80***	0.58
Direct bilirubin	0.22	0.21	0.15***	0.12
BUN	17.0***	14.8	14.9	14.1
Creatinine	0.9***	1.1	0.9**	1.0
Glucose	81***	92	81***	98
Cholesterol	214	218	206	215
LDL	138	136	134	137
HDL	54***	43	50***	42
Triglycerides	115***	187	111***	192

Table 3
(continued)

	1995 Data		1997 Data	
Variable	Antwerp	Decatur	Antwerp	Decatur
Hematocrit	47***	46	46*	45
Hemoglobin	15.4	15.2	15.4	15.3
RBC	4.9	5.0	5.1	5.1
MCH	31.4***	30.7	30.5	30.4
MCHC	32.9***	33.4	33.3***	33.7
MVC	95.7***	91.8	91.6*	90.0
WBC	6.4***	7.5	6.5	6.4
Platelets	224	229	237*	217

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

Table 4

Correlation Coefficients Between PFOS and Selected Variables by Location and Year of Examination

	1995 Data			1997 Data		
Variable	Both Locations	Antwerp	Decatur	Both Locations	Antwerp	Decatur
Age	.12	.10	.04	.20*	.41***	-.01
Alcohol	.09	.25*	.06	.10	.40***	-.07
BMI	.01	-.14	-.05	.18*	.22	.09
Cigarettes	.14	.19	.08	-.03	.08	-.08
BUN	-.05	-.04	.01	.01	.13	-.01
Creatinine	.05	-.37***	.28**	.08	-.12	.12
Glucose	-.02	-.17	-.02	.10	.04	.06
Alkaline Phosphatase	.06	.07	-.06	.07	.09	-.02
GGT	.01	.02	-.04	.07	.26*	-.06
AST	.06	.06	.0002	.003	.03	.001

Table 4
(continued)

	1995 Data			1997 Data		
Variable	Both Locations	Antwerp	Decatur	Both Locations	Antwerp	Decatur
ALT	-.01	-.03	-.03	.16*	.11	.16
Total Bilirubin	-.15*	-.13	-.07	-.13	-.12	-.07
Direct Bilirubin	-.03	-.13	.09	-.18*	-.13	-.17
Cholesterol	-.02	.02	-.08	.25**	.34**	.19
LDL	.01	.02	.02	.22**	.30*	.17
HDL	-.17*	-.14	-.12	-.07	-.05	.0005
Triglycerides	.04	.11	-.10	.10	.39***	-.01
Hematocrit	.002	.10	-.0003	-.16*	-.05	-.20
Hemoglobin	-.01	.05	-.02	-.15	-.05	-.20
Red Blood Cells	-.03	-.11	.01	-.11	-.15	-.10
MCH	.04	.21*	-.04	-.04	.17	-.10

Table 4
(continued)

Variable	1995 Data			1997 Data		
	Both Locations	Antwerp	Decatur	Both Locations	Antwerp	Decatur
MCHC	-.03	-.11	-.09	.01	-.03	-.06
MCV	.05	.25*	-.01	-.03	.20	-.09
White Blood Cells	.18*	.27**	.04	.01	.18	-.09
Platelets	-.15*	-.06	-.25*	-.11	-.06	-.10

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

Table 5

Mean, Median, Standard Deviation (SD) of Mean and Range of PFOS, Demographic, Serum Chemistries and Hematological for Antwerp and Decatur Employees Combined, 1995 (N=178) and 1997 (N=147)

PFOS* (ppm)	1995 Data				1997 Data			
	Mean	Median	SD	Range	Mean	Median	SD	Range
				PFOS (ppm)				
0 - < 1ppm	0.49[1]	0.5	0.27	000 - 0.90	0.52[1]	0.52	0.27	0.10 - 0.97
1 - < 3ppm	1.82[1]	1.77	0.58	1.00 - 2.91	1.78[1]	1.64	0.56	1.02 - 2.89
3 - < 6ppm	4.12[1]	3.97	0.81	3.00 - 5.80	3.87[1]	3.59	0.70	3.09 - 5.30
≥ 6ppm	8.17[1]	7.73	2.52	6.06 - 12.83	7.20[1]	6.68	1.59	6.05 - 9.3
	F value = 321.9, p < .0001				F value = 367.6, p < .0001			
				Age (yrs)				
0 - < 1 ppm	37	36	8	21 - 58	36	34	11	21 - 62
1 - < 3 ppm	42[2]	41	9	25 - 60	42[2]	41	9	24 - 63
3 - < 6 ppm	40	40	7	26 - 55	41	42	5	32 - 54
≥ 6 ppm	45	43	7	37 - 56	42	45	9	29 - 52
	F value = 3.7, p = .02				F value = 5.1, p = .002			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				Alcohol (drinks/day)				
0 - < 1ppm	0.8	0.6	0.9	0.0 - 3.6	0.5	0.1	0.8	0 - 4.3
1 - < 3 ppm	0.5	0.1	0.7	0.0 - 3.6	0.5	0.1	0.8	0 - 5.0
3 - < 6 ppm	1.2	0.3	1.9	0.0 - 6.0	1.0	0.1	1.8	0 - 7.1
≥ 6ppm	0.7	0.0	1.1	0.0 - 2.9	0.2	0.1	0.2	0.1 - 0.8
	F value = 4.0, p = .009				F value = 1.8, p = .15			
				BMI (kg/m^2)				
0 - < 1 ppm	25.5	24.8	4.2	17.9 - 38.7	26.0	24.9	4.9	20.1 - 41.7
1 - < 3 ppm	27.7	26.3	5.8	19.6 - 60.7	27.7	26.4	5.7	18.1 - 48.5
3 - < 6 ppm	24.9[3]	25.0	3.8	17.9 - 32.5	27.3	27.9	4.4	19.1 - 36.0
≥ 6 ppm	27.7	29.4	4.2	20.6 - 33.0	30.8	29.7	4.0	26.1 - 36.2
	F value = 3.7, p = .02				F value = 2.1, p = .10			
				Cigarettes (per day)				
0 - < 1 ppm	2.6	0.0	6.4	0.0 - 25.0	4.7	0.0	9.4	0 - 40
1 - < 3 ppm	6.8	0.0	11.3	0.0 - 40.0	8.2	0.0	11.3	0 - 40
3 - < 6 ppm	10.6	8.0	12.4	0.0 - 40.0	4.1	0.0	8.3	0 - 30
≥ 6 ppm	0.4	0.0	1.1	0.0 - 3.0	6.0	0.0	13.4	0 - 30
	F value = 4.8, p = .003				F value = 1.5, p = .23			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				BUN				
0 - < 1ppm	16.5	15	3.5	11 - 26	14.5	14.0	2.8	9.0 - 21.0
1 - <3 ppm	15.4	15.0	4.0	8.0 - 26.0	14.2	14.0	3.2	6.0 - 26.0
3 - < 6 ppm	16.4	16.0	3.7	10.0 - 23.0	15.0	15.0	2.9	9.0 - 20.0
≥ 6 ppm	15.1	14.0	4.2	10.0 - 21.0	13.8	12.0	4.1	9.0 - 19.0
	F value = 1.1, p = .36				F value = 0.5, p = 0.67			
				Creatinine				
0 - < 1ppm	1.0	1.0	0.2	0.7 - 1.6	0.9	0.9	0.1	0.6 - 1.2
1 - <3 ppm	1.0	1.0	0.2	0.7 - 1.6	0.9	0.9	0.1	0.7 - 1.3
3 - < 6 ppm	0.9	0.9	0.2	0.7 - 1.2	0.9	0.9	0.1	0.7 - 1.1
≥ 6 ppm	1.1	1.2	0.3	0.6 - 1.6	1.0	0.9	0.2	0.8 - 1.4
	F value = 2.3, p = .08				F value = 0.4, p = 0.78			
				Glucose				
0 - < 1 ppm	85	85	15	66 - 170	87	85	17	58 - 174
1 - <3 ppm	86	86	22	60 - 260	93	84	39	65 - 303
3 - < 6 ppm	84	83	12	66 - 114	95	89	25	74 - 192
≥ 6 ppm	84	83	14	71 - 105	89	88	7	80 - 97
	F value = 0.9, p = .44				F value = 0.6, p = .59			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				Alkaline Phosphatase				
0 - < 1 ppm	80	78	22	31 - 158	77	73	17	49 - 132
1 - <3 ppm	89	89	27	49 - 191	83	79	23	41 - 163
3 - < 6 ppm	86	85	21	32 - 124	76	74	22	29 - 120
≥ 6 ppm	88	85	24	63 - 136	88	84	18	65 - 114
	F value = 1.3, p = .28				F value = 1.17, p = .32			
				GGT				
0 - < 1 ppm	43	31	28	16 - 155	28	22	20	10 - 142
1 - <3 ppm	47	36	39	2 - 293	36	25	33	10 - 179
3 - < 6 ppm	40	39	15	21 - 80	28	27	14	13 - 71
≥ 6 ppm	43	33	18	28 - 79	33	37	12	17 - 48
	F value = 0.5, p = .71				F value = 1.1, p = .34			
				AST				
0 - < 1 ppm	27	25	13	15 - 96	27	25	7	13 - 53
1 - <3 ppm	29	26	12	14 - 90	26	25	7	15 - 56
3 - < 6 ppm	25	24	5	13 - 37	25	23	7	14 - 43
≥ 6 ppm	33	33	6	26 - 43	29	28	3	26 - 34
	F value - 1.8, p = .14				F value = 0.5, p = .67			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				ALT				
0 - < 1 ppm	48	43	20	27 - 118	31	30	11	13 - 60
1 - <3 ppm	46	42	21	18 - 183	33	29	16	10 - 89
3 - < 6 ppm	42	41	7	30 - 59	34	31	18	14 - 82
≥ 6 ppm	51	49	17	29 - 82	41	45	10	25 - 49
	F value = 1.0, p = .38				F value = 0.9, p = .46			
				Total Bilirubin				
0 - < 1 ppm	0.88	0.70	0.50	0.40 - 2.90	0.77	0.60	0.40	0.30 - 2.30
1 - <3 ppm	0.66[2]	0.60	0.30	0.20 - 1.50	0.61[2]	0.60	0.21	0.30 - 1.30
3 - < 6 ppm	0.64[2]	0.60	0.28	0.20 - 1.40	0.63	0.50	0.31	0.40 - 1.30
≥ 6 ppm	0.76	0.70	0.23	0.50 - 1.20	0.58	0.50	0.24	0.40 - 1.00
	F value = 4.4, p = .005				F value = 2.9, p = .04			
				Direct Bilirubin				
0 - < 1 ppm	0.22	0.20	0.05	0.02 - 0.40	0.15	0.10	0.07	0.10 - 0.40
1 - <3 ppm	0.21	0.20	0.06	0.10 - 0.40	0.12[2]	0.10	0.04	0.10 - 0.20
3 - < 6 ppm	0.21	0.20	0.04	0.20 - 0.30	0.12	0.10	0.04	0.10 - 0.20
≥ 6 ppm	0.20	0.20	0.02	0.10 0.30	0.10	0.10	0.00	0.10 - 0.10
	F value = 0.6, p = .58				F value = 3.5, p = .02			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				Cholesterol				
0 - <1 ppm	219	215	47	100 - 340	198	197	40	110 - 280
1 - <3 ppm	216	213	43	118 - 315	216	219	42	116 - 365
3 - <6 ppm	214	214	35	128 - 278	229[2]	224	29	192 - 321
≥ 6 ppm	213	221	36	160 - 251	229	238	26	186 - 250
	F value = 0.1, p =.96				F value = 4.3, p =.006			
				LDL				
0 - <1 ppm	140	137	43	29 - 261	124	128	34	50 - 205
1 - < 3 ppm	134	134	40	44 - 234	141	134	38	61 - 290
3 - <6 ppm	137	135	34	65 - 190	148[2]	142	24	111 - 196
≥ 6 ppm	142	136	32	95 - 178	145	156	26	103 - 164
	F value = 0.2 , p =.87				F value = 3.7, p =.01			
				HDL				
0 - <1 ppm	53	53	13	31 - 94	46	48	11	19 - 74
1- <3 ppm	48	47	13	26 -94	44	45	10	28 - 69
3 - <6 ppm	45	46	11	23 - 74	48	47	10	32 - 69
≥ 6 ppm	45	46	9	34 - 61	40	38	4	37 - 45
	F value = 2.9, p =.04				F value = 1.1, p =.34			
				Triglycerides				
0 - <1 ppm	129	96	98	41 - 622	148	107	162	38 - 1209
1- <3 ppm	161	133	107	41 - 651	156	122	108	44 - 534
3 - <6 ppm	158	142	88	34 - 413	166	158	92	45 - 394
≥ 6 ppm	132	151	45	64 - 187	220	191	83	149 - 352
	F value = 1.1, p =.35				F value = 0.5, p =.67			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				Hematocrit				
0 - <1 ppm	47	47	2	43 - 51	46	46	2	40 - 52
1 - <3 ppm	46	46	3	38 - 52	45	46	3	39 - 53
3 - <6 ppm	47	47	2	41 - 52	46	44	3	39 - 50
≥ 6 ppm	47	48	2	44 - 49	45	44	2	42 - 47
	F value = 2.4, p =.07				F value = 2.1, p = .11			
				Hemoglobin				
0 - <1 ppm	15.5	15.5	0.7	14.0 - 16.7	15.5	15.5	0.8	13.5 - 17.0
1 - <3 ppm	15.2	15.2	1.0	13.0 - 17.4	15.4	15.5	0.9	13.3 - 17.3
3 - <6 ppm	15.5	15.5	0.8	13.6 - 17.4	15.0	14.7	1.0	12.5 - 16.7
≥ 6 ppm	15.5	15.4	0.7	14.7 - 16.2	15.1	15.0	0.7	14.1 - 16.2
	F value = 2.2, p =.10				F value = 1.8, p =.15			
				RBC				
0 - <1 ppm	5.0	5.0	0.3	4.3 - 5.7	5.1	5.2	0.3	4.3 - 5.9
1 - <3 ppm	4.9	4.9	0.3	4.3 - 5.7	5.0	5.1	0.3	4.1 - 5.5
3 - <6 ppm	5.0	5.0	0.2	4.6 - 5.5	5.0	5.0	0.3	4.4 - 5.7
≥ 6 ppm	5.0	4.9	0.5	4.0 - 5.7	5.0	4.9	0.3	4.7 - 5.5
	F value = 0.4, p = .75				F value = 1.4, p = .25			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				MCH				
0 - <1 ppm	31.3	31.2	1.6	27.7 - 34.3	30.4	30.3	1.5	27.6 - 34.1
1 - <3 ppm	30.9	30.9	1.4	26.4 - 34.3	30.6	30.5	1.2	26.7 - 33.8
3 - <6 ppm	31.2	31.3	1.5	26.0 - 33.6	30.2	31.2	1.9	26.2 - 32.9
≥ 6 ppm	31.2	30.5	2.8	28.2 - 36.9	30.5	30.5	2.1	27.5 - 33.4
	F value = 0.9 , p =.45				F value = 0.6, p = .65			
				MCHC				
0 - <1 ppm	33.1	33.2	0.7	31.9 - 34.7	33.6	33.6	0.5	32.2 - 34.9
1 - <3 ppm	33.2	33.1	0.6	31.7 - 34.5	33.6	33.6	0.5	31.8 - 34.6
3 - <6 ppm	33.1	32.6	0.7	31.3 - 34.3	33.5	33.5	0.7	32.0 - 34.4
≥ 6 ppm	33.1	33.3	0.6	32.2 - 34.0	33.9	33.9	0.5	33.4 - 34.6
	F value = 0.2, p = .90				F value = 0.7, p = .56			
				MCV				
0 - <1 ppm	94	95	5.2	85-106	90	90	4.4	83 - 101
1 - <3 ppm	93	94	4.3	80-104	91	91	3.6	81 - 99
3 - <6 ppm	94	94	4.8	81-104	90	91	5.2	80 - 97
≥ 6 ppm	94	92	9.7	85-115	90	91	5.7	81 - 96
	F value = 1.1, p = .35				F value = 0.6, p = .59			

Table 5 (continued)

PFOS (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
				WBC				
0 - <1 ppm	6.1	6.0	1.3	4.1 - 9.4	6.1	5.8	1.4	3.8 - 10.3
1 - <3 ppm	7.0[2]	6.8	2.0	3.6 - 15.5	6.9	6.6	1.9	3.8 - 13.2
3 - <6 ppm	7.6[2]	6.9	2.2	4.1 - 13.3	6.2	6.1	1.5	4.0 - 10.0
≥ 6 ppm	7.0	6.9	0.6	6.4 - 7.8	6.2	7.1	1.5	4.2 - 7.4
	F value = 4.3, p =.006				F value = 2.2, p =.09			
				Platelets				
0 - <1 ppm	226	224	40	159 - 309	227	220	53	106 - 406
1 - <3 ppm	229	224	47	122 - 367	229	223	49	124 - 359
3 - <6 ppm	228	226	45	132 - 344	220	221	45	147 - 316
≥ 6 ppm	185	182	50	132 - 277	199	191	58	146 - 295
	F value = 2.1, p =.10				F value = 0.6, p = 0.60			

1. Mean is significantly different ($p < .05$, Bonferroni (Dunn) test) than the mean of the other PFOS categories.
2. Mean is significantly different ($p < .05$, Bonferroni (Dunn) test) than the mean of 0 - < 1 ppm PFOS category.
3. Mean is significantly different ($p < .05$, Bonferroni (Dunn) test) than the mean of 1 - < 3 ppm category.

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* Sample Size	1995 Data	1997 Data
0 - <1 ppm	45	60
1 - <3 ppm	91	63
3 - <6 ppm	35	21
≥ 6 ppm	7	5

Table 6

Mean, Median (Med), Standard Deviation (SD) of Mean and Range of PFOS, Demographic, Serum Chemistries and Hematological Values by Plant Location, 1995

PFOS* (ppm)	1995 Data: Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				PFOS				
0 < 1	0.46[1]	0.45	0.29	0.00 - 0.90	0.60[1]	0.63	0.19	0.25 - 0.88
1 < 3	1.69[1]	1.50	0.57	1.00 - 2.90	1.89[1]	1.89	0.58	1.00 - 2.91
3 < 6	3.96[1]	3.70	0.79	3.00 - 5.60	4.31[1]	4.23	0.82	3.11 - 5.80
≥ 6	8.17[1]	8.50	1.92	6.10 - 9.90	8.17[1]	6.90	3.20	6.06 - 12.83
	F value = 241.0, p = .0001				F value = 114.5, p = .0001			
				Age				
0 < 1	36	36	7	21 - 52	40	39	11	29 - 58
1 < 3	36	34	9	25 - 60	46	46	7	30 - 58
3 < 6	37	37	7	28 - 51	44	44	7	26 - 55
≥ 6	40	37	6	37 - 47	48	47	7	42 - 56
	F value = 0.5, p = .71				F value = 2.0, p = .12			
				Alcohol				
0 < 1	1.0	0.7	1.0	0.0 - 3.6	0.1	0.0	0.3	0.0 - 0.9
1 < 3	1.0	0.8	0.9	0.0 - 3.6	0.2	0.0	0.4	0.0 - 2.0
3 < 6	2.0	1.3	2.2	0.0 - 6.0	0.4	0.0	0.9	0.0 - 3.4
≥ 6	1.7	1.4	1.1	0.7 - 2.9	0.0	0.0	0.0	0.0 - 0.1
	F value = 2.9, p = .04				F value = 1.1, p = .37			
				BMI				
0 < 1	24.1	24.3	2.4	17.9 - 28.1	30.1	28.0	5.3	22.8 - 38.7
1 < 3	24.3	23.8	2.4	19.6 - 31.6	29.6	28.3	6.2	22.3 - 60.7
3 < 6	23.1	23.0	3.3	17.9 - 31.4	27.0	27.5	3.4	19.1 - 32.5
≥ 6	23.7	24.7	2.8	20.6 - 25.8	30.7	30.2	1.6	29.4 - 33.0
	F value = 0.9, p = .47				F value = 1.1, p = .35			

Table 6
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				Cigarettes				
0 < 1	3.0	0.0	7.0	0 - 25	1.4	0.0	3.8	0 - 13
1 < 3	4.1	0.0	7.0	0 - 23	8.3	0.0	12.9	0 - 40
3 < 6	9.1[3]	7.5	9.0	0 - 25	12.5	0.0	15.7	0 - 40
≥ 6	1.0	0.0	1.7	0 - 3	0	0.0	0	0 - 0
	F = 3.1, p = .03				F value = 2.3, p = .09			
				Alkaline Phosphatase				
0 < 1	75	75	16	31 - 104	96	99	29	47 - 158
1 < 3	73	66	19	49 - 108	98	95	27	49 - 191
3 < 6	79	78	20	32 -12195	95	96	18	58 - 124.
≥ 6	74	74	11	63 - 85	98	91	27	73 - 136
	F value = 0.5, p = .69				F value = 0.1, p = .98			
				GGT				
0 < 1	39	29	22	16 - 111	55	41	41	21 - 155
1 < 3	48	30	58	12 - 293	46	40	24	2 - 118
3 < 6	34	34	11	21 - 55	47	48	16	21 - 80
≥ 6	31	32	3	28 - 33	52	49	20	30 - 79
	F value = 0.7, p = .55				F value = 0.5, p = .71			
				AST				
0 < 1	26	23	13	15 - 96	32	31	9	19 - 52
1 < 3	27	26	14	14 - 90	29	27	10	17 - 85
3 < 6	23	22	5	13 - 35	27	26	5	21 - 37
≥ 6	33	35	6	26 - 37	34	32	7	28 - 43
	F value = 0.9, p = .45				F value = 0.9, p = .44			

Table 6
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				ALT				
0 < 1	46	42	18	27 - 108	55	47	24	37 - 118
1 < 3	45	40	18	26 - 122	47	42	22	18 - 183
3 < 6	40	39	6	30 - 52	43	42	9	30 - 59
≥ 6	50	38	28	29 - 82	52	53	8	41 - 59
	F value = 0.7, p = .59				F value = 0.8, p = .49			
				Total Bilirubin				
0 < 1	0.96	0.80	0.55	0.40 - 2.90	0.65	0.60	0.16	0.40 - 0.90
1 < 3	0.83	0.80	0.26	0.40 - 1.30	0.57	0.50	0.28	0.20 - 1.50
3 < 6	0.75	0.70	0.30	0.30 - 1.40	0.51	0.50	0.18	0.20 - 1.00
≥ 6	0.93	0.90	0.25	0.70 - 1.20	0.63	0.65	0.10	0.50 - 0.70
	F value = 1.2, p = .31				F value = 0.7, p = .54			
				Direct Bilirubin				
0 < 1	0.23	0.20	0.06	0.20 - 0.40	0.20	0.20	0.00	0.20 - 0.20
1 < 3	0.22	0.20	0.04	0.20 - 0.30	0.20	0.20	0.06	0.10 - 0.40
3 < 6	0.21	0.20	0.03	0.20 - 0.30	0.20	0.20	0.04	0.20 - 0.30
≥ 6	0.20	0.20	0.00	0.20 - 0.20	0.20	0.20	0.08	0.10 - 0.30
	F value = 0.7, p = .55				F value = 0.4, p = .74			
				BUN				
0 < 1	17.0	17.0	3.6	12.0 - 26.0	14.8	15.0	2.7	11.0 - 21.0
1 < 3	16.7	16.0	3.8	11.0 - 26.0	14.7	14.0	4.0	8.0 - 24.0
3 < 6	17.3	17.0	3.8	10.0 - 23.0	15.2	15.0	3.1	10.0 - 23.0
≥ 6	17.3	21.0	6.4	10.0 - 21.0	13.5	13.5	0.06	13.0 - 14.0
	F value = 0.1, p = .95				F value = 0.2, p = .87			
				Creatinine				
0 < 1	1.0	0.9	0.2	0.8 - 1.6	1.1	1.1	0.2	0.7 - 1.3
1 < 3	0.9	0.9	0.1	0.7 - 1.1	1.1	1.1	0.2	0.9 - 1.6
3 < 6	0.9[3]	0.9	0.1	0.7 - 1.0	1.1	1.1	0.1	0.8 - 1.2
≥ 6	0.8	0.8	0.2	0.6 - 0.9	1.3	1.3	0.2	1.2 - 1.6
		F value = 4.7, p = .004			F value = 3.8, p = .01			

Table 6
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				Glucose				
0 <1	83	83	8	66 - 103	90	86	28	66 -170
1 <3	82	81	13	60 - 126	93	89	25	67 - 260
3 <6	80	82	9	66 - 101	89	89	14	66 -114
≥6	72	72	2	71 - 74	93	92	12	83 - 105
	F value = 1.3, p = .29				F value = 0.1, p = .94			
				Cholesterol				
0 <1	220	219	50	100 - 340	215	208	39	154 - 276
1 <3	206	211	49	118 - 315	221	218	39	132 - 300
3 <6	217	215	30	178 - 266	209	213	42	128 - 278
≥6	223	221	16	208 - 240	206	206	47	160 - 251
	F value = 0.6, p = .61				F value = 0.5, p = .69			
				LDL				
0 <1	140	138	45	29 - 261	139	130	38	79 - 192
1 <3	131	124	46	44 - 220	136	136	36	62 - 234
3 <6	143	139	27	99 - 189	131	128	41	65 - 190
≥6	144	136	20	130 - 168	139	142	42	95 - 178
	F value = 0.4, p = .76				F value = 0.1, p = .94			
				HDL				
0 <1	56	57	13	31 - 94	43	41	9	31 - 59
1 <3	53	51	13	33 - 79	45	44	12	26 - 94
3 <6	50	49	11	31 - 74	39	39	9	23 - 51
≥6	53	49	7	48 - 61	39	39	5	34 - 46
	F value = 1.1, p = .35				F value = 1.4, p = .25			
				Triglycerides				
0 <1	117	93	98	41 - 622	167	151	94	62 - 307
1 <3	105	75	65	41 - 368	191	146	114	61 - 651
3 <6	126	112	64	34 - 278	199	198	99	78 - 413
≥6	129	116	52	85 - 187	135	153	48	64 - 168
	F value = 0.3, p = .81				F value = 0.5, p = .67			

Table 6
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				Hematocrit				
0 < 1	47	47	2	43 -51	46	45	2	43 - 50
1 < 3	46	47	2	42 - 51	45	45	3	38 - 52
3 < 6	48	47	2	44 - 51	46	46	3	41 - 52
≥ 6	47	48	1	46 - 48	46	46	2	44 - 49
	F value = 1.5, p = 23.				F value = 0.3, p = .83			
				Hemoglobin				
0 < 1	15.5	15.5	0.8	14.0 - 16.7	15.5	15.4	0.7	14.5 - 16.4
1 < 3	15.2	15.3	0.7	13.8 - 16.6	15.1	15.1	1.1	13.0 - 17.4
3 < 6	15.6	15.6	0.5	14.6 - 16.7	15.3	15.3	1.0	13.6 - 17.4
≥ 6	15.4	15.4	0.6	14.8 - 16.0	15.5	15.6	0.8	14.7 - 16.2
	F value = 1.4, p = .26				F value = 0.7, p = .58			
				RBC				
0 < 1	4.9	5.0	0.3	4.3 - 5.7	5.1	5.1	0.2	4.8 - 5.5
1 < 3	4.9	4.9	0.2	4.3 - 5.4	4.9	4.9	0.3	4.3 -5.7
3 < 6	5.0	5.0	0.2	4.7 - 5.3	5.0	4.9	0.3	4.6 - 5.5
≥ 6	4.7	4.9	0.6	4.0 - 5.2	5.2	5.1	0.4	4.8 - 5.7
	F value = 0.9, p = .46				F value = 1.1, p = .35			
				MCH				
0 < 1	31.5	31.3	1.5	27.7 - 34.3	30.7	30.7	1.6	28.7 - 33.5
1 < 3	31.2	31.0	1.2	29.5 - 34.3	30.7	30.9	1.5	26.4 - 33.1
3 < 6	31.5	31.9	1.2	29.1 - 33.3	30.9	31.2	1.7	26.0 - 33.6
≥ 6	33.0	32.5	3.7	29.6 - 36.9	29.9	30.4	1.2	28.2 - 30.7
	F value = 1.4, p = .25				F value = 0.4, p = .74			
				MCHC				
0 < 1	32.9	33.0	0.6	31.9 - 34.5	33.8	33.9	0.6	32.9 - 34.7
1 < 3	32.9	32.8	0.6	31.7 - 33.8	33.3	33.3	0.5	31.9 - 34.5
3 < 6	32.8	32.7	0.7	31.3 - 34.2	33.4	33.4	0.6	32.1 - 34.3
≥ 6	32.6	32.4	0.5	32.2 - 33.1	33.5	33.4	0.3	33.3 - 34.0
	F value = 0.4, p = .78				F value = 2.2, p = .10			

Table 6
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				MCV				
0 < 1	96	96	5	85 -106	91	90	4	85 - 99
1 < 3	95	95	3	90 - 104	92	93	4	80 - 100
3 < 6	96	97	4	88 - 104	92	92	5	81 - 101
≥ 6	101	98	12	91 - 115	89	90	3	85 - 92
	F value = 1.8, p = .16				F value = 0.8, p = .50			
				WBC				
0 < 1	5.9	5.7	1.3	4.1 - 9.4	6.8	6.9	1.1	5.0 - 9.0
1 < 3	6.1	6.1	1.3	3.8 - 8.8	7.5	7.0	2.2	3.6 - 15.5
3 < 6	7.5[2]	6.9	2.5	4.1 - 13.3	7.7	7.4	1.9	4.9 - 11.5
≥ 6	6.5	6.4	0.2	6.4 - 6.7	7.4	7.4	0.4	6.9 - 7.8
	F value = 4.5, p = .006				F value = 0.5, p = .72			
				Platelets				
0 < 1	224	222	42	159 - 309	233	246	35	162 - 271
1 < 3	222	220	41	153 - 318	233	225	50	122 - 367
3 < 6	237[4]	234	52	132 - 344	218	214	34	172 - 287
≥ 6	162	151	36	132 - 202	202	194	56	143 - 277
	F value = 2.6, p = .06				F value = 1.0, p = .40			

*Sample sizes:

FC95 Level	Antwerp	Decatur
0 < 1 ppm	34	11
1 < 3 ppm	32	59
3 < 6 ppm	19	16
≥ 6 ppm	3	4
	88	90

1. Significantly different (p < .05, Bonferroni (Dunn) t-test) than the remaining three PFOS exposure categories.
2. Significantly different (p < .05, Bonferroni (Dunn) t-test) than the 0 - < 1 ppm and the 1 - < 3 ppm categories.
3. Significantly different (p < .05, Bonferroni (Dunn) t-test) than the 0 - < 1 ppm category.
4. Significantly different (p < .05, Bonferroni (Dunn) t-test) than the 3 - < 6 ppm category.

Table 7

Mean, Median (Med), Standard Deviation (SD) of Mean and Range of PFOS, Demographic, Serum Chemistries and Hematological Values by Plant Location, 1997

PFOS* (ppm)	1997 Data							
	Antwerp				Decatur			
	Mean	Med	SD	Range	Mean	Med	SD	Range
				PFOS				
0 - < 1	0.46[1]	0.37	0.27	0.10 - 0.94	0.60[1]	0.59	0.26	0.10 - 0.97
1 - < 3	1.89[1]	1.79	0.61	1.02 - 2.89	1.71[1]	1.53	0.52	1.04 - 2.85
3 - < 6	3.87[1]	3.66	0.59	3.22 - 4.83	3.87[1]	3.51	0.81	3.09 - 5.30
≥ 6	-	-	-	-	7.20[1]	6.68	1.59	6.05 - 9.93
	F value = 195.3, p = .0001				F value = 218.1, p = .0001			
				Age				
0 - < 1	29	28	6	21 - 50	43	44	9	23 - 62
1 - < 3	37[3]	37	9	24 - 63	45	45	8	31 - 62
3 - < 6	37[3]	37	3	32 - 40	45	44	4	36 - 54
≥ 6	-	-	-	-	42	45	9	29 - 52
	F value = 10.4, p = .0001				F value = 0.5, p = .69			
				Alcohol				
0 - < 1	0.8	0.5	1.0	0.0 - 4.3	0.2	0.1	0.4	0.1 - 2.0
1 - < 3	1.0	0.7	1.1	0.0 - 5.0	0.1	0.1	0.1	0.1 - 0.3
3 - < 6	2.2[3]	1.4	2.3	0.0 - 7.1	0.1	0.1	0.1	0.1 - 0.3
≥ 6	-	-	-	-	0.2	0.1	0.3	0.1 - 0.8
	F value = 4.3, p = .02				F value = 0.8, p = .49			
				BMI				
0 - < 1	22.9	21.9	2.1	20.2 - 28.3	29.3	28.9	4.9	22.4 - 41.7
1 - < 3	24.2	23.9	2.8	18.1 - 30.4	30.0	29.0	6.0	20.2 - 48.5
3 - < 6	23.6	24.9	3.1	19.2 - 28.3	30.0	29.3	3.0	25.4 - 36.0
≥ 6	-	-	-	-	30.8	29.7	4.0	26.1 - 36.2
	F value = 2.0, p = .15				F value = 0.2, p = .91			

Table 7
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				Cigarettes				
0 - < 1	4.2	0.0	6.7	0 - 20	5.3	0.0	11.6	0 - 40
1 - < 3	7.3	2.0	8.1	0 - 20	8.7	0.0	13.0	0 - 40
3 - < 6	5	0.0	7.8	0 - 20	3.3	0.0	9.0	0 - 30
≥ 6	-	-	-	-	6.0	0.0	13.4	0 - 30
	F = 1.3, p = .28				F value = 0.8, p = .51			
				Alkaline Phosphatase				
0 - < 1	69	68	14	49 - 110	86	84	16	55 - 132
1 - < 3	74	74	16	41 - 113	88	83	26	41 - 163
3 - < 6	64	59	24	29 - 120	85	83	15	61 - 109
≥ 6	-	-	-	-	88	84	18	65 - 114
	F value = 1.5, p = .22				F value = 0.1, p = .96			
				GGT				
0 - < 1	21	17	10	10 - 50	36	32	25	13 - 142
1 - < 3	34	24	34	10 - 144	37	27	33	13 - 179
3 - < 6	25	22	10	14 - 43	31	28	15	13 - 71
≥ 6	-	-	-	-	33	37	12	17 - 48
	F value = 2.5, p = .09				F value = 0.2, p = .91			
				AST				
0 - < 1	27	26	7	17 - 53	26	25	7	13 - 48
1 - < 3	27	25	7	15 - 48	26	25	7	18 - 56
3 - < 6	25	24	4	19 - 30	25	23	9	14 -43
≥ 6	-	-	-	-	29	28	3	26 - 34
	F value = 0.2, p = .80				F value = 0.4, p = .77			

Table 7
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
ALT								
0 - < 1	30	25	12	13 - 60	33	31	11	17 - 57
1 - < 3	33	31	16	13 - 87	33	28	16	10 - 89
3 - < 6	28	23	10	14 - 46	38	33	21	17 - 82
≥ 6	-	-	-	-	41	45	10	25 - 49
	F value = 0.6, p = .58				F value = 0.9, p = .45			
Total Bilirubin								
0 - < 1	0.90	0.80	0.46	0.40 - 2.30	0.63	0.60	0.30	0.30 - 1.40
1 - < 3	0.68	0.70	0.23	0.30 - 1.30	0.56	0.50	0.18	0.30 - 1.00
3 - < 6	0.79	0.70	0.40	0.30 - 1.30	0.51	0.50	0.16	0.30 - 0.90
≥ 6	-	-	-	-	0.58	0.50	0.24	0.40 - 1.00
	F value = 2.3, p = .11				F value = 1.0, p = .41			
Direct Bilirubin								
0 - < 1	0.16	0.20	0.08	0.10 - 0.40	0.13	0.10	0.06	0.10 - 0.30
1 - < 3	0.13	0.10	0.05	0.10 - 0.20	0.11	0.10	0.03	0.10 - 0.20
3 - < 6	0.14	0.10	0.05	0.10 - 0.20	0.11	0.10	0.03	0.10 - 0.20
≥ 6	-	-	-	-	0.10	0.10	0.00	0.10 - 0.10
	F value = 2.2, p = .12				F value= 1.3, p = .28			
BUN								
0 - < 1	14.3	14.0	2.1	11.0 - 19.0	14.7	14.0	3.3	9.0 - 21.0
1 - < 3	15.2	15.0	2.6	10.0 - 20.0	13.5	13.5	3.5	6.0 - 26.0
3 - < 6	16.0	16.0	2.7	12.0 - 20.0	14.3	14.0	3.0	9.0 - 19.0
≥ 6	-	-	-	-	13.8	12.0	4.1	9.0 - 19.0
	F value = 2.1, p = .13				F value = 0.7, p = .56			
Creatinine								
0 - < 1	0.9	0.9	0.1	0.7 - 1.2	1.0	1.0	0.1	0.6 - 1.2
1 - < 3	0.9	0.9	0.1	0.7 - 1.3	1.0	1.0	0.1	0.7 - 1.3
3 - < 6	0.9	0.9	0.1	0.8 - 1.1	1.0	1.0	0.1	0.7 - 1.1
≥ 6	-	-	-	-	1.0	0.9	0.2	0.8 - 1.4
	F value = 0.3, p = .76				F value = 0.2, p = .89			

Table 7
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				Glucose				
0 - < 1	81	82	10	63 - 114	93	91	21	58 - 174
1 - < 3	79	78	9	65 - 102	102	89	47	75 - 303
3 - < 6	84	85	8	74 - 96	103	93	30	79 - 192
≥ 6	-	-	-	-	89	88	7	80 - 97
	F value = 0.8, p = .47				F value = 0.5, p = .67			
				Cholesterol				
0 - < 1	193	190	41	110 - 277	204	208	38	145 - 277
1 - < 3	213	205	48	116 - 365	218	226	39	152 - 290
3 - < 6	228	223	38	192 - 321	230	230	23	197 - 280
≥ 6	-	-	-	-	229	238	26	186 - 250
	F value = 2.9, p = .07				F value = 2.0, p = .13			
				LDL				
0 - < 1	122	114	35	57 - 205	127	133	33	50 - 178
1 - < 3	143	134	42	67 - 290	139	135	35	61 - 196
3 - < 6	147	141	24	111 - 195	149	144	25	113 - 196
≥ 6	-	-	-	-	145	156	26	103 - 164
	F value = 3.0, p = .06				F value = 1.6, p = .19			
				HDL				
0 - < 1	51	50	12	19 - 74	42	41	9	26 - 59
1 - < 3	48	46	10	34 - 68	42	41	10	28 - 69
3 - < 6	51	50	10	39 - 69	45	45	10	32 - 62
≥ 6	-	-	-	-	40	38	4	37 - 45
	F value = 0.8, p = .47				F value = 0.5, p = .67			
				Triglycerides				
0 - < 1	99	92	41	38 - 175	200	128	219	46 - 1209
1 - < 3	112	95	58	44 - 290	185	147	124	63 - 534
3 - < 6	150	122	88	65 - 362	179	183	98	45 - 394
≥ 6	-	-	-	-	220	191	83	149 - 352
	F value = 2.9, p = .06				F value = 0.1, p = .95			

Table 7
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				Hematocrit				
0 - < 1	47	47	3	42 - 52	46	45	2	40 - 50
1 - < 3	46	47	3	40 - 53	46	46	3	39 - 51
3 - < 6	46	45	3	42 - 50	44	44	2	39 - 48
≥ 6	-	-	-	-	45	44	2	42 - 47
	F value = 0.7, p = .51				F value = 1.6, p = .18			
				Hemoglobin				
0 - < 1	15.6	15.5	0.8	14.2 - 17.0	15.4	15.4	0.7	13.5 - 16.9
1 - < 3	15.4	15.6	1.0	13.3 - 17.3	15.4	15.5	0.9	13.5 - 17.3
3 - < 6	15.2	14.7	1.0	14.0 - 16.7	14.8	14.7	1.0	12.5 - 16.5
≥ 6	-	-	-	-	15.1	15.0	0.8	14.1 - 16.2
	F value = 0.7, p = .48				F value = 1.7, p = .18			
				RBC				
0 - < 1	5.1	5.2	0.4	4.6 - 5.9	5.1	5.1	0.3	4.3 - 5.7
1 - < 3	5.0	5.1	0.3	4.1 - 5.5	5.1	5.1	0.3	4.2 - 5.5
3 - < 6	4.9	4.8	0.4	4.4 - 5.7	5.0	5.0	0.3	4.5 - 5.4
≥ 6	-	-	-	-	5.0	4.9	0.3	4.7 - 5.5
	F value = 1.7, p = .19				F value = 0.4, p = .78			
				MCH				
0 - < 1	30.4	30.4	1.3	27.9 - 33.5	30.3	30.2	1.8	27.6 - 34.1
1 - < 3	30.6	30.5	0.9	29.2 - 32.8	30.6	30.6	1.4	26.7 - 33.8
3 - < 6	30.9	31.4	1.4	28.8 - 32.7	29.7	30.5	2.2	26.2 - 32.9
≥ 6	-	-	-	-	30.5	30.5	2.1	27.5 - 33.4
	F value = 0.9, p = .40				F value = 1.0, p = .41			
				MCHC				
0 - < 1	33.4	33.4	0.5	32.2 - 34.0	33.8	33.7	0.5	32.8 - 34.9
1 - < 3	33.3	33.2	0.5	31.8 - 34.1	33.8	33.8	0.5	32.7 - 34.6
3 - < 6	33.4	33.5	0.5	32.4 - 34.3	33.6	33.9	0.8	32.0 - 34.4
≥ 6	-	-	-	-	33.9	33.9	0.5	33.4 - 34.6
	F value = 0.6, p = .54				F value = 0.6, p = .62			

Table 7
(continued)

PFOS (ppm)	Antwerp Mean	Med	SD	Range	Decatur Mean	Med	SD	Range
				MCV				
0 - < 1	91	91	4	84 - 101	90	89	5	83 - 101
1 - < 3	92	92	3	87 - 99	91	90	4	81 - 99
3 - < 6	93	95	5	86 - 97	88	89	5	80 - 96
≥ 6	-	-	-	-	90	91	6	81 - 96
	F value = 1.3, p = .29				F value = 0.9, p = .45			
				WBC				
0 - < 1	6.0	5.7	1.3	3.8 - 8.8	6.3	5.9	1.6	4.0 - 10.3
1 - < 3	7.1	6.8	2.2	4.4 - 13.2	6.7	6.6	1.6	3.8 - 10.1
3 - < 6	6.4	6.0	1.8	4.2 - 10.0	6.1	6.1	1.3	4.0 - 8.9
≥ 6	-	-	-	-	6.2	7.1	1.5	4.2 - 7.4
	F value = 2.6, p = .08				F value = 0.8, p = .51			
				Platelets				
0 - < 1	237	232	55	126 - 406	215	207	50	106 - 363
1 - < 3	243	232	48	151 - 359	219	210	48	124 - 323
3 - < 6	215	225	41	147 - 263	224	219	50	159 - 316
≥ 6	-	-	-	-	199	191	58	146 - 295
	F value = 1.1, p = .35				F value = 0.3, p = .80			

*Sample sizes:

FC95 Level	Antwerp	Decatur
0 - < 1 ppm	31	29
1 - < 3 ppm	25	38
3 - < 6 ppm	9	12
≥ 6 ppm	0	5
	65	84

1. Significantly different ($p < .05$, Bonferroni (Dunn) t-test) than the remaining three PFOS exposure categories.
2. Significantly different ($p < .05$, Bonferroni (Dunn) t-test) than the 0 - < 1 ppm and the 1 - < 3 ppm categories.
3. Significantly different ($p < .05$, Bonferroni (Dunn) t-test) than the 0 - < 1 ppm category.

Table 8

Multivariable Regression of Serum Chemistries and Hematological Parameters - Examination of the Effect of PFOS Adjusting for Age, Alcohol, BMI and Cigarettes, Antwerp and Decatur Data Combined, 1995 and 1997 Examinations

Alkaline Phosphatase

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	52.99	11.14	.0001	40.87	9.60	.0001
PFOS	0.32	0.89	.72	0.19	1.03	.86
Age	0.08	0.20	.68	0.45	0.18	.01
Alcohol	-5.43	1.53	.0005	-2.09	1.61	.20
BMI	1.04	0.34	.002	0.69	0.34	.04
Cigarettes	0.85	0.15	.0001	0.49	0.15	.002
	$R^2 = .26$	Adj $R^2 = .24$		$R^2 = .19$	Adj $R^2 = .16$	

ln GGT

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	2.3816	0.2711	.0001	2.0471	0.2592	.0001
PFOS	0.0032	0.0217	.88	0.0178	0.0280	.53
Age	0.0040	0.0048	.41	0.0036	0.0049	.47
Alcohol	0.0605	0.0373	.11	0.0747	0.0438	.09
BMI	0.0372	0.0082	.0001	0.0365	0.0091	.0001
Cigarettes	0.0076	0.0038	.05	0.0030	0.0042	.48
	$R^2 = .14$	Adj $R^2 = .12$		$R^2 = .15$	Adj $R^2 = .12$	

AST

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	12.62	5.52	.02	23.25	3.50	.0001
PFOS	0.42	0.44	.35	-0.11	0.38	.77
Age	0.0005	0.10	.99	-0.07	0.07	.29
Alcohol	0.70	0.76	.36	0.40	0.59	.50
BMI	0.54	0.17	.002	0.23	0.12	.07
Cigarettes	-0.11	0.08	.14	-0.07	0.06	.20
	$R^2 = .08$	Adj $R^2 = .05$		$R^2 = .04$	Adj $R^2 = .00$	

Table 8 (continued)

ALT

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	28.54	9.46	.003	11.60	6.78	.09
PFOS	0.09	0.76	.91	0.97	0.73	.19
Age	-0.18	0.17	.28	-0.19	0.13	.14
Alcohol	-0.16	1.30	.90	0.31	1.14	.79
BMI	0.96	0.29	.001	1.00	0.24	.0001
Cigarettes	-0.14	0.13	.28	-0.09	0.11	.40
	$R^2 = .08$	Adj $R^2 = .05$		$R^2 = .13$	Adj $R^2 = .10$	

ln Total Bilirubin

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.2742	0.1958	.16	-0.1395	0.1945	.47
PFOS	-0.0984	0.0368	.008	-0.1620	0.0515	.002
$PFOS^2$	0.0086	0.0039	.03	0.0188	0.0070	.009
Age	0.0052	0.0035	.14	0.0015	0.0037	.70
Alcohol	0.0738	0.0268	.007	0.1220	0.0327	.0003
BMI	-0.0273	0.0059	.0001	-0.0097	0.0068	.16
Cigarettes	-0.0158	0.0028	.0001	-0.0054	0.0031	.09
	$R^2 = .32$	Adj $R^2 = .30$		$R^2 = .18$	Adj $R^2 = .14$	

Direct Bilirubin

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.2196	0.0259	.0001	0.1929	0.0264	.0001
PFOS	-0.0009	0.0021	.68	-0.0061	0.0029	.03
Age	0.0006	0.0005	.17	-0.0002	0.0005	.69
Alcohol	0.0074	0.0036	.04	0.0106	0.0045	.02
BMI	-0.0012	0.0008	.13	-0.0017	0.0009	.07
Cigarettes	-0.0007	0.0004	.06	-0.0009	0.0004	.05
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .14$	Adj $R^2 = .11$	

Table 8 (continued)

BUN

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	18.64	1.94	.0001	13.22	1.47	.0001
PFOS	-0.02	0.15	.91	-0.08	0.16	.60
Age	-0.03	0.03	.39	0.08	0.03	.005
Alcohol	0.37	0.27	.17	0.50	0.25	.05
BMI	-0.05	0.06	.42	-0.07	0.05	.20
Cigarettes	-0.08	.03	.004	-0.05	0.02	.05
	$R^2 = .08$	Adj $R^2 = .05$		$R^2 = .09$	Adj $R^2 = .06$	

Creatinine

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.5744	0.0779	.0001	0.9478	0.0602	.0001
PFOS	-0.0223	0.0146	.13	-0.0302	0.0159	.06
$PFOS^2$	0.0033	0.0016	.04	0.0055	0.0022	.01
Age	0.0059	0.0013	.0001	0.0027	0.0012	0.02
Alcohol	-0.0260	0.0106	.02	-0.0242	0.0101	.02
BMI	0.0086	0.0023	.0003	-0.0022	0.0021	.30
Cigarettes	-0.0005	0.0011	.65	-0.0019	0.0010	.05
	$R^2 = .29$	Adj $R^2 = .27$		$R^2 = .16$	Adj $R^2 = .13$	

ln Glucose

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	3.8943	0.0732	.0001	3.8597	0.0919	.0001
PFOS	-0.0039	0.0058	.51	0.0014	0.0098	.89
Age	0.0045	0.0013	.0006	0.0025	0.0017	.15
Alcohol	-0.0026	0.0101	.79	-0.0068	0.0154	.66
BMI	0.0143	0.0022	.0001	0.0195	0.0032	.0001
Cigarettes	-0.0003	0.0010	.78	-0.0013	0.0015	.39
	$R^2 = .31$	Adj $R^2 = .29$		$R^2 = .30$	Adj $R^2 = .27$	

Table 8 (continued)

Cholesterol

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	190.1	22.1	.0001	155.5	19.0	.0001
PFOS	-0.99	1.77	.58	4.66	2.04	.02
Age	0.74	0.39	.06	1.39	0.36	.0002
Alcohol	-0.40	3.04	.90	7.50	3.18	.02
BMI	-0.04	0.67	.95	-0.40	0.67	.55
Cigarettes	-0.18	0.31	.56	-0.08	0.30	.80
	$R^2 = .02$	Adj $R^2 = .00$		$R^2 = .17$	Adj $R^2 = .14$	

LDL

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	135.26	20.27	.0001	114.69	17.06	.0001
PFOS	0.50	1.61	.76	4.01	1.82	.03
Age	0.58	0.36	.11	1.04	0.32	.002
Alcohol	-3.33	2.78	.23	4.29	2.84	.13
BMI	-6.67	0.61	.28	-1.09	0.60	.07
Cigarettes	-0.52	0.28	.07	-0.02	0.28	.95
	$R^2 = .05$	Adj $R^2 = .02$		$R^2 = .13$	Adj $R^2 = .10$	

HDL

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	70.82	5.73	.0001	66.71	4.52	.0001
PFOS	-1.17	0.46	.01	-0.22	0.49	.65
Age	-0.11	0.10	.27	0.12	0.09	.17
Alcohol	3.53	0.79	.0001	2.01	0.76	.009
BMI	-0.63	0.17	.0004	-0.95	0.16	.0001
Cigarettes	-0.17	0.08	0.03	-0.16	0.07	.03
	$R^2 = .28$	Adj $R^2 = .26$		$R^2 = .29$	Adj $R^2 = .26$	

Table 8 (continued)

Triglycerides

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	-103.29	45.97	.03	-187.99	58.18	.002
PFOS	-1.78	3.68	.63	-0.33	6.28	.96
Age	1.54	0.82	.06	1.37	1.11	.22
Alcohol	-0.43	6.32	.95	14.68	9.82	.14
BMI	6.71	1.39	.0001	10.06	2.05	.0001
Cigarettes	2.70	0.64	.0001	1.87	0.94	.05
	$R^2 = .24$	Adj $R^2 = .22$		$R^2 = .23$	Adj $R^2 = .20$	

Hematocrit

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	48.01	1.36	.0001	46.73	1.28	.0001
PFOS	-0.06	0.11	.57	-0.25	0.14	.07
Age	0.0005	0.02	.98	-0.03	0.02	.20
Alcohol	0.10	0.19	.58	0.15	0.22	0.50
BMI	-0.08	0.04	.06	0.01	0.05	0.75
Cigarettes	0.05	0.02	.007	0.04	0.02	.04
	$R^2 = .08$	Adj $R^2 = .05$		$R^2 = .08$	Adj $R^2 = .04$	

Hemoglobin

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	15.78	0.45	.0001	15.43	0.43	.0001
PFOS	-0.02	0.04	.53	-0.08	0.05	.07
Age	0.004	0.008	.57	-0.006	0.01	.46
Alcohol	-0.02	0.06	.77	0.01	0.07	.85
BMI	-0.03	0.01	.06	0.008	0.02	.59
Cigarettes	0.02	0.006	.02	0.02	0.007	.03
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .06$	Adj $R^2 = .03$	

Table 8 (continued)

RBC

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	4.8766	0.1559	.0001	5.1416	0.1626	.0001
PFOS	-0.0026	0.0123	.83	-0.0208	0.1756	.24
Age	-0.0022	0.0028	.42	-0.0068	0.0031	.03
Alcohol	-0.0323	0.0213	.13	-0.0111	0.0274	.69
BMI	0.0069	0.0047	.14	0.0089	0.0057	.12
Cigarettes	-0.0006	0.0022	.77	-0.0025	0.0026	.35
	$R^2 = .04$	Adj $R^2 = .01$		$R^2 = .06$	Adj $R^2 = .02$	

MCH

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	32.292	0.725	.0001	30.062	0.706	.0001
PFOS	-0.015	0.058	.79	-0.047	0.076	.54
Age	0.23	0.013	.08	0.028	0.013	.04
Alcohol	0.189	0.099	.06	0.095	0.119	.43
BMI	-0.093	0.022	.0001	-0.035	0.025	.16
Cigarettes	0.0347	0.010	.001	0.046	0.011	.0001
	$R^2 = .20$	Adj $R^2 = .18$		$R^2 = .13$	Adj $R^2 = .10$	

MCHC

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	32.8525	0.3341	.0001	33.0109	0.2675	.0001
PFOS	-0.0015	0.0266	.96	-0.0092	0.0289	.75
Age	0.0097	0.0059	.11	0.0101	0.0051	.05
Alcohol	-0.1121	0.0458	.02	-0.0589	0.0451	.19
BMI	-0.0006	0.0100	.95	0.0072	0.0094	.45
Cigarettes	-0.0041	0.0047	.39	0.0016	0.0043	.72
	$R^2 = .07$	Adj $R^2 = .05$		$R^2 = .07$	Adj $R^2 = .04$	

Table 8 (continued)

MCV

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	98.29	2.29	.0001	90.91	1.98	.0001
PFOS	-0.03	0.18	.88	-0.09	0.21	.67
Age	0.04	0.04	.33	0.06	0.04	.15
Alcohol	0.88	0.31	.01	0.49	0.33	.14
BMI	-0.28	0.07	.0001	-0.12	0.07	.08
Cigarettes	0.12	0.03	.0005	0.13	0.03	.0001
	$R^2 = .23$	Adj $R^2 = .21$		$R^2 = .15$	Adj $R^2 = .12$	

Platelets

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	272.49	23.37	.0001	260.92	25.27	.0001
PFOS	-3.37	1.86	.07	-2.91	2.73	.29
Age	-0.88	0.41	.04	-0.25	0.48	.61
Alcohol	-4.80	3.20	.14	2.37	4.26	.58
BMI	-0.04	0.70	.95	-0.73	0.89	.41
Cigarettes	0.21	0.33	0.52	-0.30	0.41	.46
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .03$	Adj $R^2 = .00$	

WBC

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	3.9538	0.8120	.0001	5.1296	0.6927	.0001
PFOS	0.0893	0.0646	.17	-0.0048	0.0748	.95
Age	0.0214	0.0144	.14	0.0139	0.0132	.30
Alcohol	-0.0860	0.1111	.44	0.2471	0.1169	.04
BMI	0.0492	0.0244	.05	0.0045	0.0244	.86
Cigarettes	0.1009	0.0115	.0001	0.0878	0.0111	.0001
	$R^2 = .36$	Adj $R^2 = .34$		$R^2 = .33$	Adj $R^2 = .31$	

Table 9

Multivariable Regression of Total Bilirubin, Direct Bilirubin, Creatinine Cholesterol, LDL, HDL, Heamtocrit, Hemoglobin and Platelets - Examination of the Effect of PFOS Adjusting for Age, Alcohol, BMI and Cigarettes, by Location, 1995 and 1997

ln Total Bilirubin - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.2742	0.1958	.16	-0.1395	0.1945	.47
PFOS	-0.0984	0.0368	.008	-0.1620	0.0515	.002
$PFOS^2$	0.0086	0.0039	.03	0.0188	0.0070	.009
Age	0.0052	0.0035	.14	0.0015	0.0037	.70
Alcohol	0.0738	0.0268	.007	0.1220	0.0327	.0003
BMI	-0.0273	0.0059	.0001	-0.0097	0.0068	.16
Cigarettes	-0.0158	0.0028	.0001	-0.0054	0.0031	.09
	$R^2 = .32$	Adj $R^2 = .30$		$R^2 = .18$	Adj $R^2 = .14$	

ln Total Bilirubin - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	-0.0776	0.0475	.85	-0.3130	0.5586	0.58
PFOS	-0.0473	0.0575	.41	-0.2157	0.1779	.23
$PFOS^2$	0.0035	0.0072	.63	0.0336	0.0385	.39
Age	0.0062	0.0055	.27	-0.0036	0.0081	.66
Alcohol	0.0398	0.0316	.21	0.0826	0.0441	.07
BMI	-0.0115	0.0161	.48	0.0114	0.0222	.61
Cigarettes	-0.0176	0.0056	.002	-0.0102	0.0074	.17
	$R^2 = .15$	Adj $R^2 = .08$		$R^2 = .14$	Adj $R^2 = .05$	

ln Total Bilirubin - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	-0.4462	0.3154	.16	-0.9486	0.2932	.002
PFOS	-0.0862	0.0509	.09	-0.1160	0.0578	.05
$PFOS^2$	0.0081	0.0048	.10	0.0144	0.0072	.05
Age	0.0128	0.0048	.01	0.0134	0.0046	.005
Alcohol	-0.0045	0.0828	.59	0.1708	0.1607	.29
BMI	-0.0179	0.0068	.01	-0.0045	0.0073	.54
Cigarettes	-0.0117	0.0031	.0004	-0.0031	0.0032	.33
	$R^2 = .29$	Adj $R^2 = .24$		$R^2 = .17$	Adj $R^2 = .10$	

Table 9
(continued)

HDL - Both Locations

	1995 Data (N = 178)			1997 Data (N = 149)		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	70.82	5.73	.0001	66.71	4.52	.0001
PFOS	-1.17	0.46	.01	-0.22	0.49	.65
Age	-0.11	0.10	.27	0.12	0.09	.17
Alcohol	3.53	0.79	.0001	2.01	0.76	.009
BMI	-0.63	0.17	.0004	-0.95	0.16	.0001
Cigarettes	-0.17	0.08	0.03	-0.16	0.07	.03
	$R^2 = .28$	Adj $R^2 = .26$		$R^2 = .28$	Adj $R^2 = .26$	

HDL - Antwerp Only

	1995 Data (N = 86)			1997 Data (N = 63)		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	73.44	12.69	.0001	57.30	12.12	.0001
PFOS	-1.55	0.73	.04	-2.26	1.17	.06
Age	0.01	0.17	.93	0.43	0.17	.01
Alcohol	3.31	0.98	.001	2.78	0.99	.007
BMI	-0.87	0.50	.09	-0.82	0.48	.10
Cigarettes	-0.19	0.17	.28	-0.45	0.16	.007
	$R^2 = .16$	Adj $R^2 = .11$		$R^2 = .28$	Adj $R^2 = .21$	

HDL - Decatur Only

	1995 Data (N = 85)			1997 Data (N = 83)		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	66.35	9.42	.0001	69.17	7.01	.0001
PFOS	-0.75	0.60	.22	0.17	0.50	.73
Age	-0.14	0.14	.32	0.01	0.11	.96
Alcohol	4.71	2.48	.06	-3.07	3.87	.43
BMI	-0.49	0.21	.02	-0.90	0.18	.0001
Cigarettes	-0.16	0.09	.09	-0.04	0.08	.61
	$R^2 = .14$	Adj $R^2 = .09$		$R^2 = .27$	Adj $R^2 = .22$	

Table 9
(continued)

Platelets - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	272.49	23.37	.0001	260.92	25.27	.0001
PFOS	-3.37	1.86	.07	-2.91	2.73	.29
Age	-0.88	0.41	.04	-0.25	0.48	.61
Alcohol	-4.80	3.20	.14	2.37	4.26	.58
BMI	-0.04	0.70	.95	-0.73	0.89	.41
Cigarettes	0.21	0.33	.52	-0.30	0.41	.46
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .03$	Adj $R^2 = .00$	

Platelets, Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	294.81	48.19	.0001	258.21	66.58	.0003
PFOS	-2.57	2.77	.36	-1.99	6.44	.76
Age	-0.35	0.65	.60	0.41	0.91	.65
Alcohol	-3.65	3.74	.33	-0.87	5.42	.87
BMI	-2.23	1.91	.25	-1.16	2.65	.66
Cigarettes	0.82	0.65	.21	-0.70	0.90	.44
	$R^2 = .06$	Adj $R^2 = .00$		$R^2 = .02$	Adj $R^2 = .00$	

Platelets, Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	353.90	39.04	.0001	225.66	42.96	.0001
PFOS	-6.08	2.50	.02	-2.75	3.09	.38
Age	-1.99	0.59	.001	-0.16	0.69	.82
Alcohol	5.36	10.14	.60	8.45	23.70	.72
BMI	-0.64	0.84	.45	0.14	1.10	.90
Cigarettes	-0.35	0.40	.38	-0.19	0.47	.69
	$R^2 = .19$	Adj $R^2 = .14$		$R^2 = .01$	Adj $R^2 = .00$	

Table 9
(continued)

Creatinine - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.5744	0.0779	.0001	0.9478	0.0602	.0001
PFOS	-0.0223	0.0146	.13	-0.0302	0.0159	.06
$PFOS^2$	0.0033	0.0016	.04	0.0055	0.0022	.01
Age	0.0059	0.0013	.0001	0.0027	0.0012	0.02
Alcohol	-0.0260	0.0106	.02	-0.0242	0.0101	.02
BMI	0.0086	0.0023	.0003	-0.0022	0.0021	.30
Cigarettes	-0.0005	0.0011	.65	-0.0019	0.0010	.05
	$R^2 = .29$	Adj $R^2 = .27$		$R^2 = .16$	Adj $R^2 = .13$	

Creatinine - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.7319	0.1382	.0001	0.8600	0.1430	.0001
PFOS	-0.0324	0.0195	.10	-0.0453	0.0455	.32
$PFOS^2$	0.0008	0.0024	.74	0.0074	0.0099	.46
Age	0.0044	0.0019	.02	0.0033	0.0021	.11
Alcohol	-0.0055	0.0107	.61	-0.0142	0.0113	.21
BMI	0.0037	0.0055	.50	-0.0012	0.0057	.83
Cigarettes	0.0017	0.0019	.36	0.0041	0.0019	.04
	$R^2 = .20$	Adj $R^2 = .14$		$R^2 = .14$	Adj $R^2 = .05$	

Creatinine - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.8641	0.1300	.0001	1.1363	0.1021	.0001
PFOS	-0.0093	0.0206	.65	-0.0430	0.0201	.04
$PFOS^2$	0.0036	0.0019	.07	0.0067	0.0025	.009
Age	0.0032	0.0020	.11	0.0006	0.0016	.72
Alcohol	0.0082	0.0336	.81	-0.1133	0.0559	.05
BMI	0.0032	0.0028	.26	-0.0038	0.0026	.14
Cigarettes	-0.0030	0.0013	.02	-0.0034	0.0011	.003
	$R^2 = .23$	Adj $R^2 = .18$		$R^2 = .27$	Adj $R^2 = .22$	

Table 9
(continued)

Cholesterol - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	190.1	22.1	.0001	155.5	19.0	.0001
PFOS	-0.99	1.77	.58	4.66	2.04	.02
Age	0.74	0.39	.06	1.39	0.36	.0002
Alcohol	-0.40	3.04	.90	7.50	3.18	.02
BMI	-0.04	0.67	.95	-0.40	0.67	.55
Cigarettes	-0.18	0.31	.56	-0.08	0.30	.80
	$R^2 = .02$	Adj $R^2 = .00$		$R^2 = .17$	Adj $R^2 = .14$	

Cholesterol - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	62.17	43.72	.16	93.11	49.20	.06
PFOS	-1.22	2.51	.63	2.37	4.74	.62
Age	2.60	0.59	.0001	2.54	0.67	.0004
Alcohol	1.13	3.39	.74	7.49	3.98	.06
BMI	2.28	1.73	.19	0.78	1.95	.69
Cigarettes	0.81	0.59	.17	-0.23	0.66	.72
	$R^2 = .25$	Adj $R^2 = .20$		$R^2 = .33$	Adj $R^2 = .27$	

Cholesterol - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	304.27	33.14	.0001	207.01	31.55	.0001
PFOS	-1.03	2.19	.64	4.26	2.27	.06
Age	-1.05	0.51	.04	0.48	0.51	.35
Alcohol	-21.16	8.88	.02	19.54	17.41	.27
BMI	-1.03	.73	.17	-.78	0.81	.34
Cigarettes	-0.40	0.33	.23	-0.11	.35	.75
	$R^2 = .14$	Adj $R^2 = .09$		$R^2 = .07$	Adj $R^2 = .01$	

Table 9
(continued)

LDL

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	135.26	20.27	.0001	114.69	17.06	.0001
PFOS	0.50	1.61	.76	4.01	1.82	.03
Age	0.58	0.36	.11	1.04	0.32	.002
Alcohol	-3.33	2.78	.23	4.29	2.84	.13
BMI	-6.67	0.61	.28	-1.09	0.60	.07
Cigarettes	-0.52	0.28	.07	-0.02	0.28	.95
	$R^2 = .05$	Adj $R^2 = .02$		$R^2 = .13$	Adj $R^2 = .10$	

LDL - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	12.14	41.44	.77	40.88	42.42	.34
PFOS	0.24	2.38	.92	1.50	4.08	.71
Age	2.15	0.56	.0003	2.22	0.58	.0003
Alcohol	-3.04	3.21	.35	4.12	3.43	.23
BMI	2.04	1.64	.22	0.48	1.68	.78
Cigarettes	0.35	0.56	.53	0.26	0.57	.65
	$R^2 = .20$	Adj $R^2 = .15$		$R^2 = .29$	Adj $R^2 = .23$	

LDL - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	218.24	30.58	.0001	160.50	28.17	.0001
PFOS	1.06	1.96	.59	3.55	2.03	.08
Age	-0.79	0.46	.09	0.20	0.45	.65
Alcohol	-22.95	8.04	.006	-12.68	28.72	.66
BMI	-1.38	0.67	.04	-1.27	0.72	.08
Cigarettes	-0.65	0.30	.03	-0.13	0.31	.67
	$R^2 = .20$	Adj $R^2 = .15$		$R^2 = .07$	Adj $R^2 = .01$	

Table 9
(continued)

Hematocrit - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	48.01	1.36	.0001	46.73	1.28	.0001
PFOS	-0.06	0.11	,57	-0.25	0.14	.07
Age	0.0005	0.02	.98	-0.03	0.02	.20
Alcohol	0.10	0.19	.58	0.15	0.22	0.50
BMI	-0.08	0.04	.06	0.01	0.05	0.75
Cigarettes	0.05	0.02	.007	0.04	0.02	.04
	$R^2 = .08$	Adj $R^2 = .05$		$R^2 = .08$	Adj $R^2 = .04$	

Hematocrit - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	44.00	2.30	.0001	45.63	3.63	.0001
PFOS	0.06	0.13	.63	-0.29	0.35	.42
Age	0.06	0.03	.06	0.04	0.50	.37
Alcohol	-0.12	0.18	.51	0.06	0.30	.84
BMI	0.02	0.09	.80	-0.02	0.14	.89
Cigarettes	0.05	0.03	.14	0.01	0.05	.79
	$R^2 = .08$	Adj $R^2 = .03$		$R^2 = .01$	Adj $R^2 = .00$	

Hematocrit - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	45.56	2.62	.0001	45.69	1.95	.0001
PFOS	-0.05	0.17	.79	-0.28	0.14	.05
Age	0.01	0.04	.89	-0.05	0.03	.09
Alcohol	-0.56	0.68	.41	-1.52	1.08	.16
BMI	-0.02	0.06	.71	0.08	0.05	.11
Cigarettes	0.08	0.03	.004	0.06	0.02	.006
	$R^2 = .10$	Adj $R^2 = .04$		$R^2 = .19$	Adj $R^2 = .13$	

Table 9
(continued)

Hemoglobin - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	15.78	0.45	.0001	15.43	0.43	.0001
PFOS	-0.02	0.04	.53	-0.08	0.05	.07
Age	0.004	0.008	.57	-0.006	0.01	.46
Alcohol	-0.02	0.06	.77	0.01	0.07	.85
BMI	-0.03	0.01	.06	0.008	0.02	.59
Cigarettes	0.02	0.006	.02	0.02	0.007	.03
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .06$	Adj $R^2 = .03$	

Hemoglobin - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	14.72	0.74	.0001	15.32	1.15	.0001
PFOS	0.008	0.04	.86	-0.10	0.11	.40
Age	0.02	0.01	.02	0.02	0.02	.33
Alcohol	-0.04	0.06	.51	0.02	0.09	.81
BMI	-0.007	0.03	.81	-0.01	0.05	.81
Cigarettes	0.005	0.01	.61	-0.006	0.02	.70
	$R^2 = .08$	Adj $R^2 = .02$		$R^2 = .03$	Adj $R^2 = .00$	

Hemoglobin - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	15.87	0.90	.0001	15.58	0.71	.0001
PFOS	-0.03	0.06	.63	-0.10	0.05	.07
Age	-0.004	0.01	.79	-0.02	0.01	.12
Alcohol	-0.22	0.23	.35	-0.47	0.39	.23
BMI	-0.02	0.02	.32	0.02	0.02	.25
Cigarettes	0.02	0.009	.01	0.02	0.008	.004
	$R^2 = .10$	Adj $R^2 = .04$		$R^2 = .17$	Adj $R^2 = .12$	

Table 9
(continued)

Direct Bilirubin - Both Locations

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.2196	0.0259	.0001	0.1929	0.0264	.0001
PFOS	-0.0009	0.0021	.68	-0.0061	0.0029	.03
Age	0.0006	0.0005	.17	-0.0002	0.0005	.69
Alcohol	0.0074	0.0036	.04	0.0106	0.0045	.02
BMI	-0.0012	0.0008	.13	-0.0017	0.0009	.07
Cigarettes	-0.0007	0.0004	.06	-0.0009	0.0004	.05
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .14$	Adj $R^2 = .11$	

Direct Bilirubin - Antwerp Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.1794	0.0461	.0002	0.1963	0.0813	.02
PFOS	-0.0034	0.0026	.21	-0.0077	0.0079	.33
Age	0.00004	0.0006	.95	-0.0017	0.0011	.13
Alcohol	0.0102	0.0036	.006	0.0112	0.0066	.10
BMI	0.0017	0.0018	.36	0.0006	0.0032	.84
Cigarettes	-0.0016	0.0006	0.009	-0.0017	0.0011	.12
	$R^2 = .17$	Adj $R^2 = .12$		$R^2 = .14$	Adj $R^2 = .06$	

Direct Bilirubin - Decatur Only

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.1972	0.0478	.0001	0.1205	0.0347	.0008
PFOS	0.0025	0.0032	.44	-0.0038	0.0025	.13
Age	0.0012	0.0007	0.11	0.0014	0.0006	.02
Alcohol	-0.0114	0.0128	.37	-0.0042	0.0191	.83
BMI	-0.0016	0.0011	.13	-0.0018	0.0009	.04
Cigarettes	-0.0001	0.0005	.79	-0.0004	0.0004	.27
	$R^2 = .07$	Adj $R^2 = .02$		$R^2 = .15$	Adj $R^2 = .10$	

Table 10

Summaries of Simple Linear and Quadratic Regression Models for Total and Unconjugated Bilirubin, 1995 and 1997

	1995 Data				1997 Data			
	Total Bilirubin		Unconjugated		Total Bilirubin		Unconjugated	
	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Both Locations								
R^2	.002	.052	.024	.059	.016	.046	.012	.046
Intercept	0.78247	0.86532	0.56837	0.65239	0.8175	0.78963	0.57745	0.64247
PFOS(p value)	-0.02927 (.047)	-0.00918 (.03)	-0.0285 (.04)	-0.09941 (.002)	-0.02583 (.12)	-0.10456 (.01)	-0.01940 (.18)	-0.09138 (.01)
$PFOS^2$ (p value)		0.00846 (.02)		0.00858 (.01)		0.01200 (.03)		0.01097 (.03)
Antwerp								
R^2	.018	.028	.017	.028	.014	.052	.012	.050
Intercept	0.92001	0.96548	0.69447	0.73919	0.85170	0.96350	0.69161	0.78708
PFOS (p value)	-0.02927 (.21)	-0.07872 (.18)	-0.02604 (.23)	-0.07468 (.17)	-0.03647 (.35)	-0.22847 (.08)	-0.02872 (.39)	-0.19268 (.09)
$PFOS^2$ (p value)		0.00697 (.31)		0.00686 (.32)		0.04620 (.20)		0.03945 (.13)
Decatur								
R^2	.004	.010	.008	.029	0.009	.071	.002	.077
Intercept	0.59712	0.66974	0.39803	0.48279	0.59609	0.68287	0.47268	0.55440
PFOS (p value)	-0.014363 (.53)	-0.05867 (.09)	-0.01166 (.39)	-0.06966 (.03)	-0.00894 (.53)	-0.09408 (.02)	-0.00489 (.69)	-0.08508 (.01)
$PFOS^2$ (p value)		0.00518 (.12)		0.00605 (.05)		0.001143 (.02)		0.01076 (.01)

Table 11

Mean Values of PFOS, Demographic, Serum Chemistry and Hematologic Parameters for Antwerp and Decatur Combined Locations, 1995 and 1997 Examinations for Employees Who Participated and Did Not Participate in Both Years

	1995 Data		1997 Data	
Variable	Both Years (N = 61)	Only 1995 (N = 117)	Both Years (N = 61)	Only 1997 (N = 88)
PFOS (ppm)	2.40	2.08	2.34***	1.34
Age	39*	42	41*	38
BMI	27.1	26.3	27.3	26.9
Cigarettes	5.4	6.7	5.2	6.8
Alcohol	0.8	0.6	0.4*	0.4
Alk Phosphatase	87	86	79	80
GGT	44	44	37*	27
AST	29	27	26	26
ALT	46	46	33	32
Total bilirubin	0.71	0.72	0.65	0.69
Direct bilirubin	0.21	0.22	0.13	0.13
BUN	16.2	15.7	14.6	14.3
Creatinine	1.0	1.0	1.0	1.0
Glucose	86	87	93	89
Cholesterol	212	213	225***	201
LDL	142	134	145***	128
HDL	50	47	46	45

Table 11
(continued)

Variable	1995 Data		1997 Data	
	Antwerp	Decatur	Antwerp	Decatur
Triglycerides	139	157	167	149
Hematocrit	45	47	46	46
Hemoglobin	15.0	15.5	15.3	15.4
RBC	4.9	5.0	5.0*	5.1
MCH	30.8	31.2	30.8*	30.2
MCHC	33.2	33.1	33.6	33.6
MVC	93	94	92**	90
WBC	6.6	7.0	6.5	6.4
Platelets	226	227	228	224

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

Table 12

Mean Values of PFOS, Demographic, Serum Chemistry and Hematologic Parameters
for Antwerp and Decatur, 1995 Examinations
for Employees Who Participated and Did not Participate in Both 1995 and 1997

	Antwerp		Decatur	
Variable	Both Years (N = 27)	Only 1995 (N = 61)	Both Years (N = 34)	Only 1995 (N = 56)
PFOS (ppm)	2.30	1.76	2.48	2.42
Age	34	37	42*	46
BMI	24.0	23.9	29.6	29.0
Cigarettes	5.4	4.3	5.4	9.4
Alcohol	1.7*	1.0	0.1	0.2
Alk Phosphatase	75	75	96	98
GGT	46	39	43	50
AST	28	25	30	29
ALT	43	45	48	47
Total bilirubin	0.91	0.84	0.54	0.59
Direct bilirubin	0.23	0.22	0.19	0.21
BUN	17.7	16.7	15.0	15.0
Creatinine	0.9	0.9	1.1	1.1
Glucose	78*	83	92	92
Cholesterol	209	216	232**	209
LDL	133	140	150**	128
HDL	56	53	46	42

Table 12
(continued)

Variable	1995 Data		1997 Data	
	Antwerp	Decatur	Antwerp	Decatur
Triglycerides	100	122	170	197
Hematocrit	46	47	44**	46
Hemoglobin	15.3	15.5	14.8**	15.4
RBC	4.9	4.9	4.9*	5.0
MCH	31.2	31.5	30.5	30.8
MCHC	33.0	32.8	33.4	33.4
MVC	95	96	91	92
WBC	6.4	6.3	6.8*	7.8
Platelets	222	225	23.0	228

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

Table 13

Mean Values of PFOS, Demographic, Serum Chemistry and Hematologic Parameters
for Antwerp and Decatur, 1997 Examinations
for Employees Who Participated and Did not Participate in Both Years

	Antwerp		Decatur	
Variable	Both Years (N = 27)	Only 1997 (N = 38)	Both Years (N = 34)	Only 1997 (N = 50)
PFOS (ppm)	2.33***	0.88	2.35	1.69
Age	37***	30	45	44
BMI	24.4*	22.8	29.5	29.9
Cigarettes	5.9	5.2	4.7	7.9
Alcohol	1.0	0.7	0.1	0.2
Alk Phosphatase	72	69	85	88
GGT	33*	21	41	32
AST	27	26	26	26
ALT	32	30	34	34
Total bilirubin	0.77	0.81	0.56	0.59
Direct bilirubin	0.14	0.16	0.12	0.11
BUN	15.2	14.6	14.1	14.0
Creatinine	0.9	0.9	1.0	1.0
Glucose	80	81	103	95
Cholesterol	224***	192	226*	208
LDL	148	123	143	132
HDL	51	49	43	42

Table 13
(continued)

Variable	1995 Data		1997 Data	
	Antwerp	Decatur	Antwerp	Decatur
Triglycerides	125	101	201	185
Hematocrit	46	46	45	46
Hemoglobin	15.5	15.4	15.2	15.4
RBC	5.0	5.1	4.9**	5.1
MCH	30.8	30.4	30.9	30.0
MCHC	33.4	33.3	33.7	33.8
MVC	92	91	91*	89
WBC	6.8	6.3	6.4	6.5
Platelets	241	234	218	217

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

Table 14

Multivariable Regression of Serum Chemistries and Hematological Parameters - Examination of the Effect of PFOS Adjusting for Age, Alcohol, BMI and Cigarettes, Antwerp and Decatur Employees (N = 61) Who Participated in Both the 1995 and 1997 Examinations

Alkaline Phospatase

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	55.23	22.22	.02	45.74	22.07	.04
PFOS	-1.71	1.77	.34	0.46	1.71	.79
Age	0.42	0.43	.33	0.33	0.37	.37
Alcohol	-5.34	2.47	.04	-2.93	2.36	.22
BMI	0.70	0.67	.30	0.62	0.61	.31
Cigarettes	0.82	0.34	.02	0.76	0.32	.02
	$R^2 = .24$	Adj $R^2 = .17$		$R^2 = .15$	Adj $R^2 = .07$	

ln GGT

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	2.5359	0.5561	.0001	2.5660	0.5965	.0001
PFOS	-0.0028	0.0443	.95	-0.0357	0.0461	.44
Age	-0.0078	0.0107	.47	-0.0095	0.0010	.35
Alcohol	0.0795	0.0619	.20	0.0673	0.0638	.30
BMI	0.0469	0.0167	.007	0.0463	0.0165	.007
Cigarettes	0.0023	0.0084	.79	-0.0025	0.0087	.77
	$R^2 = .14$	Adj $R^2 = .06$		$R^2 = .14$	Adj $R^2 = .07$	

SGOT

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	15.27	11.19	.18	21.68	6.80	.002
PFOS	0.40	0.89	.65	-0.22	0.53	.67
Age	0.17	0.22	.42	0.001	0.11	.99
Alcohol	1.01	1.25	.42	0.47	.73	52
BMI	0.24	0.34	.47	0.17	0.19	.38
Cigarettes	-0.26	0.17	.13	0.07	0.10	.49
	$R^2 = .08$	Adj $R^2 = .00$		$R^2 = .03$	Adj $R^2 = .00$	

Table 14
(continued)

SGPT

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	26.32	17.83	.15	15.34	13.86	.27
PFOS	-0.03	1.42	.98	0.27	1.07	.80
Age	-0.20	0.34	.57	-0.34	0.23	.14
Alcohol	0.13	1.98	.95	0.22	1.48	.88
BMI	1.05	0.54	.06	1.15	0.38	.004
Cigarettes	-0.25	0.27	.35	-0.04	0.20	.83
	$R^2 = .10$	Adj $R^2 = .02$		$R^2 = .18$	Adj $R^2 = .11$	

ln Total Bilirubin

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.7086	0.3971	.08	-0.3739	0.3996	.35
PFOS	-0.0874	0.0806	.28	0.0202	0.0308	.51
$PFOS^2$	0.0081	0.0068	.24	-0.0014	0.0026	.58
Age	-0.0030	0.0073	.69	0.0072	0.0068	.29
Alcohol	0.0344	0.0436	.43	0.1045	0.0426	.02
BMI	-0.0319	0.0115	.01	-0.0182	0.0112	.11
Cigarettes	-0.0130	0.0060	.03	-0.0105	0.0058	.08
	$R^2 = .23$	Adj $R^2 = .14$		$R^2 = .19$	Adj $R^2 = .10$	

Direct Bilirubin

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.2579	0.0469	.0001	0.1711	0.0462	.0005
PFOS	-0.0027	0.0037	.47	-0.0026	0.0036	.47
Age	-0.0019	0.0009	.04	0.0004	0.0008	.60
Alcohol	0.0049	0.0052	.35	0.0089	0.0049	.08
BMI	0.0010	0.0014	.49	-0.0021	0.0013	.10
Cigarettes	-0.0005	0.0007	.50	-0.0008	0.0007	.22
	$R^2 = .13$	Adj $R^2 = .05$		$R^2 = .14$	Adj $R^2 = .07$	

Table 14
(continued)

BUN

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	18.33	3.62	.0001	14.06	3.09	.0001
PFOS	-0.09	0.29	.75	0.29	0.24	.22
Age	-0.01	0.07	.87	0.07	0.05	.16
Alcohol	0.59	0.40	.15	0.18	0.33	.59
BMI	-0.04	0.11	.71	-0.12	0.09	.18
Cigarettes	-0.15	0.05	.007	-0.03	0.04	.55
	$R^2 = .16$	Adj $R^2 = .09$		$R^2 = .08$	Adj $R^2 = .00$	

Creatinine

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	0.5185	0.1308	.0002	0.8785	0.1333	.0001
PFOS	-0.0515	0.0264	.06	0.0168	0.0103	.11
$PFOS^2$	0.0068	0.0022	.004	-0.0005	0.0009	.57
Age	0.0073	0.0024	.004	0.0036	0.0023	.12
Alcohol	-0.0100	0.0143	.49	-0.0266	0.0142	.07
BMI	0.0099	0.0038	.01	-0.0030	0.0037	.43
Cigarettes	-0.0003	0.0019	.89	-0.0028	0.0020	.15
	$R^2 = .49$	Adj $R^2 = .43$		$R^2 = .18$	Adj $R^2 = .09$	

ln Glucose

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	3.7479	0.1311	.0001	3.4111	0.2013	.0001
PFOS	-0.0017	0.0103	.87	0.0036	0.0156	.82
Age	0.0008	0.0025	.74	0.0063	0.0034	.07
Alcohol	-0.0050	0.0145	.73	0.0005	0.0215	.98
BMI	0.0236	0.0039	.0001	0.0306	0.0056	.0001
Cigarettes	0.0023	0.0020	.26	-0.0051	0.0029	.09
	$R^2 = .46$	Adj $R^2 = .41$		$R^2 = .48$	Adj $R^2 = .43$	

Table 14
(continued)

Cholesterol

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	184.37	34.59	.0001	179.50	38.87	.0001
PFOS	-1.15	2.76	.68	3.75	3.01	.22
Age	1.37	0.67	.04	0.73	0.65	.27
Alcohol	-2.72	3.85	.48	6.57	4.16	.12
BMI	-0.24	1.04	.81	0.09	1.07	.94
Cigarettes	-0.82	0.52	.12	-0.07	0.57	.90
	$R^2 = .13$	Adj $R^2 = .05$		$R^2 = .09$	Adj $R^2 = .01$	

LDL

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	115.89	30.35	.0004	150.88	34.90	.0001
PFOS	0.36	2.38	.88	2.68	2.70	.33
Age	1.26	0.58	.88	0.44	0.58	.45
Alcohol	-3.74	3.35	.27	3.81	3.73	.31
BMI	-0.61	0.91	.51	-1.20	0.96	.22
Cigarettes	-0.72	0.45	.12	-0.10	0.51	.85
	$R^2 = .15$	Adj $R^2 = .07$		$R^2 = .07$	Adj $R^2 = .00$	

HDL

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	75.25	11.01	.0001	68.22	8.91	.0001
PFOS	-0.68	0.86	.44	-0.33	0.69	.63
Age	-0.0005	0.21	.99	0.11	0.15	.47
Alcohol	2.31	1.21	.06	2.10	0.95	.03
BMI	-0.86	0.33	.01	-0.97	0.25	.0002
Cigarettes	-0.30	0.17	.08	-0.12	0.13	.37
	$R^2 = .25$	Adj $R^2 = .18$		$R^2 = .34$	Adj $R^2 = .28$	

Table 14
(continued)

Triglycerides

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	-89.52	66.79	.19	-198.05	82.02	.02
PFOS	-3.78	5.32	.48	7.03	6.35	.27
Age	0.72	1.29	.58	0.87	1.37	.53
Alcohol	-1.93	7.43	.80	3.28	8.77	.71
BMI	7.50	2.00	.0004	11.26	2.26	.0001
Cigarettes	1.40	1.01	.17	0.73	1.19	.54
	$R^2 = .26$	Adj $R^2 = .19$		$R^2 = .38$	Adj $R^2 = .32$	

Hematocrit

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	50.87	2.15	.0001	46.61	2.56	.0001
PFOS	-0.03	0.17	.87	-0.20	0.20	.33
Age	-0.05	0.04	.19	-0.04	0.04	.38
Alcohol	0.09	0.24	.70	0.31	0.27	.26
BMI	-0.13	0.06	.04	0.02	0.07	.77
Cigarettes	0.05	0.04	.21	0.06	0.04	.14
	$R^2 = .20$	Adj $R^2 = .13$		$R^2 = .10$	Adj $R^2 = .02$	

Hemoglobin

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	17.09	0.72	.0001	15.55	0.88	.0001
PFOS	-0.02	0.06	.70	-0.07	0.07	.33
Age	-0.01	0.01	.36	-0.01	0.01	.44
Alcohol	-0.002	0.08	.98	0.05	0.09	.61
BMI	-0.06	0.02	.01	0.01	0.02	.70
Cigarettes	0.003	0.01	.79	0.02	0.01	.12
	$R^2 = .18$	Adj $R^2 = .10$		$R^2 = .07$	Adj $R^2 = .00$	

Table 14
(continued)

RBC

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	5.21	0.22	.0001	5.02	0.30	.0001
PFOS	0.002	0.018	.89	-0.003	0.024	.88
Age	-0.003	0.004	.55	-0.003	0.005	.53
Alcohol	-0.006	0.025	.81	0.025	0.033	.44
BMI	-0.007	0.007	.28	0.004	0.008	.64
Cigarettes	-0.005	0.004	.18	-0.005	0.004	.28
	$R^2 = .06$	Adj $R^2 = .03$		$R^2 = .04$	Adj $R^2 = .04$	

MCH

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	32.97	1.25	.0001	31.13	1.43	.0001
PFOS	-0.05	0.10	.60	-0.11	0.11	.31
Age	-0.01	0.02	.67	-0.004	0.024	.85
Alcohol	0.04	0.14	.79	-0.06	0.15	.71
BMI	-0.07	0.04	.07	-0.007	0.039	.86
Cigarettes	0.04	0.02	.06	0.07	0.02	.001
	$R^2 = .18$	Adj $R^2 = .10$		$R^2 = .19$	Adj $R^2 = .12$	

MCHC

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	33.55	0.53	.0001	33.40	0.50	.0001
PFOS	-0.03	0.04	.55	-0.005	0.039	.89
Age	0.01	0.01	.20	0.005	0.008	.55
Alcohol	-0.08	0.06	.18	-0.10	0.05	.07
BMI	-0.02	0.02	.17	0.001	0.014	.92
Cigarettes	-0.02	0.01	.01	0.003	0.007	.69
	$R^2 = .18$	Adj $R^2 = .10$		$R^2 = .09$	Adj $R^2 = .01$	

Table 14
(continued)

MCV

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	98.33	3.59	.0001	92.85	3.82	.0001
PFOS	-0.09	0.29	,76	-0.28	0.30	.34
Age	-0.07	0.07	.34	-0.02	0.06	.76
Alcohol	0.30	0.40	.45	0.19	0.41	.65
BMI	-0.15	0.11	.18	-0.03	0.11	.78
Cigarettes	0.19	0.06	.003	0.20	0.06	.0008
	$R^2 = .27$	Adj $R^2 = .20$		$R^2 = .22$	Adj $R^2 = .15$	

Platelets

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	295.55	37.09	.0001	392.12	48.22	.0001
PFOS	-3.96	2.96	.19	-3.84	3.73	.31
Age	-0.84	0.71	.24	-2.31	0.81	.006
Alcohol	-10.54	4.13	.01	-6.59	5.16	.21
BMI	-0.54	1.12	.63	-1.85	1.33	.17
Cigarettes	-0.78	0.63	.22	-0.82	0.70	.25
	$R^2 = .19$	Adj $R^2 = .11$		$R^2 = .21$	Adj $R^2 = .14$	

WBC

	1995 Data			1997 Data		
	Parameter	SE	p value	Parameter	SE	p value
Intercept	3.10	1.19	.01	4.46	1.36	.002
PFOS	0.03	0.09	.77	-0.04	0.11	.70
Age	0.002	0.023	.93	-0.007	0.02	.75
Alcohol	0.07	0.13	.62	0.21	0.15	.15
BMI	0.10	0.04	.007	0.06	0.04	.09
Cigarettes	0.12	0.02	.0001	0.11	0.02	.0001
	$R^2 = .43$	Adj $R^2 = .38$		$R^2 = .40$	Adj $R^2 = .34$	

Table 15

Employee Distribution as to Plant Location and Whether Hormones Were Measured, 1995

PFOS (ppm)	Total	Both Locations: Hormones Measured Yes	Both Locations: Hormones Measured No	By Location: Antwerp Hormones Measured Yes	By Location: Antwerp Hormones Measured No	By Location: Decatur Hormones Measured Yes	By Location: Decatur Hormones Measured No
0 - < 1	45	10 (22%)	35 (78%)	9 (27%)	25 (73%)	1 (9%)	10 (91%)
1 - < 3	91	46 (51%)	45 (49%)	21 (66%)	11 (34%)	25 (43%)	34 (57%)
3 - < 6	35	27 (77%)	8 (23%)	18 (95%)	1 (5%)	9 (56%)	7 (44%)
>= 6	7	5 (71%)	2 (29%)	2 (67%)	1 (33%)	3 (75%)	1 (25%)
	178	88	90	50	38	38	52

Table 16

Mean Values for PFOS, Demographic, Serum Chemistries and Hematology,
by Plant Location and Whether Hormones Were Measured, 1995

	Both Locations Hormones Measured		Antwerp Hormones Measured		Decatur Hormones Measured	
Variable	Yes N = 88	No N = 90	Yes N = 50	No N = 38	Yes N = 38	No N = 52
PFOS	2.87***	1.52	2.69***	0.92	3.10**	1.96
Age	38.4***	42.7	35.0*	38.4	42.9	45.9
Alcohol	1.0**	0.4	1.6**	0.8	0.2	0.2
BMI	26.5	26.7	23.6	24.4	30.3	28.5
Cigarettes	8.3*	4.3	6.7**	1.9	10.3	6.0
BUN	16.3	15.5	17.1	16.8	15.1	14.5
Creatinine	0.97*	1.02	0.87***	0.94	1.10	1.08
Glucose	86	88	80	84	94	90
AlkalinePhosphatase	86	86	77	73	99	96

Table 16
(continued)

Variable	Both Locations Hormones Measured Yes N = 88	Both Locations Hormones Measured No N = 90	Antwerp Hormones Measured Yes N = 50	Antwerp Hormones Measured No N = 38	Decatur Hormones Measured Yes N = 38	Decatur Hormones Measured No N = 52
GGT	47	42	45	37	50	46
AST	29	27	27	24	31	29
ALT	47	45	44	45	51	45
Total Bilirubin	0.7	0.8	0.8	0.9	0.5	0.6
Direct Bilirubin	0.2	0.2	0.2	0.2	0.2	0.2
Cholesterol	217	215	210	220	227	211
LDL	136	137	133	144	141	132
HDL	49	48	52	55	43	43
Triglycerides	158	144	124	104	205	174
Hematocrit	47	46	47	47	46	45
Hemoglobin	15.4	15.3	15.4	15.4	15.3	15.1

Table 16
(continued)

Variable	Both Locations Hormones Measured Yes N = 88	Both Locations Hormones Measured No N = 90	Antwerp Hormones Measured Yes N = 50	Antwerp Hormones Measured No N = 38	Decatur Hormones Measured Yes N = 38	Decatur Hormones Measured No N = 52
RBC	5.0	4.9	4.9	4.9	5.0	4.9
MCH	31.1	31.0	31.5	31.3	30.5	30.8
MCHC	33.0*	33.3	32.9	32.8	33.2*	33.5
MCV	94	93	96	95	92	92
WBC	7.3**	6.5	6.8***	5.7	8.0*	7.0
Platelets	230	223	233**	212	226	231

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

Table 17

Mean, Median (Med), Standard Deviation (SD) of Mean and Range of PFOS, Demographic, Serum Chemistries and Hematological Values for N = 88 Employees, Antwerp and Decatur Combined, who Had Hormone Measurements, 1995

PFOS (ppm)	Mean	Med	SD	Range
		PFOS		
0 - < 1	0.68[1]	0.75	0.21	0.37-0.90
1 - < 3	1.96[1]	1.96	0.62	1.00-2.90
3 - < 6	4.15[1]	3.97	0.85	3.00-5.80
≥ 6	8.67[1]	8.50	2.85	6.06-12.83
	F value = 121.3, p = .0001			
		Age		
0 - < 1	32.7	32.5	6.3	21.0-43.0
1 - < 3	38.7	39.0	8.4	25.0-58.0
3 - < 6	39.0	39.0	7.6	26.0-54.0
≥ 6	43.0	42.0	7.8	37.0-56.0
	F value = 2.4, p = .08			
		Alcohol		
0 - < 1	1.4	1.1	1.2	0.0-3.6
1 - < 3	0.6	0.2	0.8	0.0-3.6
3 - < 6	1.4	0.5	2.0	0.0-6.0
≥ 6	0.9	0.0	1.3	0.0-2.9
	F value = 2.1, p = .11			
		BMI		
0 - < 1	24.5	24.5	2.4	20.4-28.0
1 - < 3	27.9	26.2	7.2	19.6-60.7
3 - < 6	24.7	24.2	4.2	17.9-32.5
≥ 6	27.5	29.4	4.9	20.6-33.0
	F value = 2.1, p = .10			

Table 17
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		Cigarettes		
0 - < 1	6.0	0.0	10.5	0.0-25.0
1 - < 3	7.7	0.0	11.2	0.0-35.0
3 - < 6	11.6	12.0	11.8	0.0-40.0
≥ 6	0.6	0.0	1.3	0.0-3.0
	F = 1.8, p = .16			
		BUN		
0 - < 1	17.0	16.0	3.1	14.0-22.0
1 - < 3	15.8	15.0	3.8	8.0-26.0
3 - < 6	17.0	17.0	3.8	10.0-23.0
≥ 6	14.4	14.0	4.0	10.0-21.0
	F value = 1.1, p = .35			
		Creatinine		
0 - < 1	1.0	1.0	0.1	0.8-1.1
1 - < 3	1.0	0.9	0.2	0.7-1.6
3 - < 6	0.9	0.9	0.1	0.7-1.2
≥ 6	1.1	1.2	0.4	0.6-1.6
	F value = 2.7, p = .05			
		Glucose		
0 - < 1	82	82	7	70-93
1 - < 3	89	84	29	62-260
3 - < 6	81	82	12	66-112
≥ 6	87	83	16	71-105
	F value = 0.8, p = .52			
		Alkaline Phosphatase		
0 - < 1	82	82	14	66-103
1 - < 3	88	89	25	49-146
3 - < 6	85	82	21	32-124
≥ 6	88	74	29	63-136
	F value = 0.3, p = .84			

Table 17
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		GGT		
0 - < 1	38	28	27	23-111
1 - < 3	53	41	49	2-293
3 - < 6	39	39	15	21-80
≥ 6	48	49	19	32-79
	F value = 0.9, p = .44			
		AST		
0 - < 1	31	25	23	17-96
1 - < 3	30	27	14	14-90
3 - < 6	25	24	6	13-37
≥ 6	31	30	4	26-37
	F value = 1.2, p = .31			
		ALT		
0 - < 1	52	48	21	36-108
1 - < 3	48	43	24	25-183
3 - < 6	42	41	7	30-59
≥ 6	54	57	20	29-82
	F value =1.1, p = .36			
		Total Bilirubin		
0 - < 1	0.86	0.70	0.45	0.40-2.00
1 - < 3	0.67	0.65	0.28	0.20-1.30
3 - < 6	0.65	0.60	0.31	0.20-1.40
≥ 6	0.68	0.70	0.15	0.50-0.90
	F value = 1.2, p = .30			
		Direct Bilirubin		
0 - < 1	0.22	0.20	0.04	0.20-0.30
1 - < 3	0.20	0.20	0.05	0.10-0.30
3 - < 6	0.22	0.20	0.04	0.20-0.30
≥ 6	0.22	0.20	0.04	0.20-0.30
	F value = 0.6, p = .63			

Table 17
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		Cholesterol		
0 - < 1	213	207	33	180-290
1 - < 3	220	227	42	144-315
3 - < 6	217	214	29	171-270
≥ 6	200	208	34	160-240
	F value = 0.5, p = .69			
		LDL		
0 - < 1	129	128	22	106-177
1 - < 3	136	146	39	65-228
3 - < 6	139	135	29	84-190
≥ 6	129	130	29	95-172
	F value = 0.3, p = .85			
		HDL		
0 - < 1	52	57	12	31-63
1 - < 3	50	46	15	28-94
3 - < 6	46	48	12	23-74
≥ 6	45	46	10	34-61
	F value = 0.6, p = .64			
		Triglycerides		
0 - < 1	157	121	167	41-622
1 - < 3	163	129	118	41-651
3 - < 6	156	138	97	34-413
≥ 6	128	151	52	64-187
	F value = 0.1, p = .94			
		Hematocrit		
0 - < 1	47	48	2	44-49
1 - < 3	46	46	3	39-52
3 - < 6	47	47	2	43-52
≥ 6	47	48	1	45-49
	F value = 2.3, p = .08			

Table 17
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		Hemoglobin		
0 - < 1	15.6	15.8	0.5	14.6-16.1
1 - < 3	15.2	15.3	0.9	13.0-17.1
3 - < 6	15.6	15.6	0.7	13.8-17.4
≥ 6	15.5	15.4	0.7	14.8-16.2
	F value = 1.8, p = .16			
		RBC		
0 - < 1	4.9	5.0	0.3	4.3-5.2
1 - < 3	4.9	4.9	0.3	4.3-5.7
3 - < 6	5.0	5.0	0.2	4.6-5.4
≥ 6	5.0	5.2	0.7	4.0-5.7
	F value = 0.4, p = .74			
		MCH		
0 - < 1	32.0	31.7	1.1	30.8-33.9
1 - < 3	30.8	30.8	1.4	27.3-33.2
3 - < 6	31.2	31.8	1.5	26.0-33.3
≥ 6	31.1	30.2	3.4	28.2-36.9
	F value = 1.9, p = .14			
		MCHC		
0 - < 1	32.9	33.1	0.8	31.9-34.5
1 - < 3	33.0	33.1	0.7	31.7-34.5
3 - < 6	32.9	32.8	0.7	31.3-34.2
≥ 6	33.1	33.3	0.8	32.2-34.0
	F value = 0.2, p = .93			
		MCV		
0 - < 1	97	95	5	92-106
1 - < 3	93	93	4	83-101
3 - < 6	95	95	5	81-104
≥ 6	94	91	12	85-115
	F value = 1.9, p = .13			

Table 17
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		WBC		
0 - < 1	6.7	6.5	1.8	4.4-9.4
1 - < 3	7.3	6.9	2.2	3.6-15.5
3 - < 6	7.7	7.5	2.3	4.1-13.3
≥ 6	7.1	6.9	0.6	6.4-7.8
	F value = 0.7, p = .59			
		Platelets		
0 - < 1	243	230	43	189-309
1 - < 3	234	227	44	153-365
3 - < 6	229	230	50	132-344
≥ 6	177	182	29	143-205
	F value = 2.7, p = .05			

1. Significantly different ($p < .05$) than the remaining three PFOS exposure categories.
2. Significantly different ($p < .05$) than the 0 - < 1 ppm PFOS category.
3. Significantly different ($p < .05$) than the 1 - < 3 ppm PFOS category.
4. Significantly different ($p < .05$) than the 3 - < 6 ppm PFOS category.
5. Significantly different ($p < .05$) than the ≥ 6ppm PFOS category.

Sample sizes:

PFOS Level	Both Locations	Antwerp	Decatur
0 - < 1 ppm	10	9	1
1 - < 3 ppm	46	21	25
3 - < 6 ppm	27	18	9
≥ 6 ppm	5	2	3
	88	50	38

Table 18

Multivariable Regression of Serum Chemistries and Hematological Parameters in Relation to PFOS Adjusting for Age, Alcohol, BMI and Cigarettes, Antwerp and Decatur Data Combined, For Those Employees Who Had Hormone Measurements in 1995

Alkaline Phosphatase

Variable	Parameter	SE	p value
Intercept	64.57	15.23	.001
PFOS	0.002	1.11	.99
Age	0.13	0.30	.66
Alcohol	-4.17	1.75	.02
BMI	0.60	0.39	.13
Cigarettes	0.60	0.20	.004
	$R^2 = .22$	Adj $R^2 = .17$	

ln GGT

Variable	Parameter	SE	p value
Intercept	1.9570	0.4203	.0001
PFOS	0.0077	0.0301	.80
Age	0.0157	0.0084	.07
Alcohol	0.1043	0.0484	.03
BMI	0.0341	0.0107	.002
Cigarettes	0.0096	0.0056	.09
	$R^2 = .20$	Adj $R^2 = .15$	

AST

Variable	Parameter	SE	p value
Intercept	16.13	9.90	.11
PFOS	-0.13	.72	.86
Age	0.006	0.20	.98
Alcohol	1.02	1.14	.37
BMI	0.51	0.25	.04
Cigarettes	-0.20	0.13	.13
	$R^2 = .08$	Adj $R^2 = .02$	

Table 18
(continued)

ALT

Variable	Parameter	SE	p value
Intercept	25.19	14.22	.08
PFOS	-0.12	1.04	.90
Age	-0.04	0.28	.89
Alcohol	0.20	1.64	.90
BMI	0.95	0.36	.01
Cigarettes	-0.20	0.19	.29
	$R^2 = .10$	Adj $R^2 = .04$	

ln Total Bilirubin

Variable	Parameter	SE	p value
Intercept	0.6133	0.2726	.03
PFOS	-0.0885	0.0518	.09
$PFOS^2$	0.0073	0.0048	.13
Age	-0.0025	0.0054	.64
Alcohol	0.0235	0.0309	.45
BMI	-0.0270	0.0068	.0002
Cigarettes	-0.0162	0.0036	.0001
	$R^2 = .39$	Adj $R^2 = .34$	

Direct Bilirubin

Variable	Parameter	SE	p value
Intercept	0.225	0.0335	.0001
PFOS	0.001	0.002	.64
Age	0.0007	0.0007	.31
Alcohol	0.004	0.004	.26
BMI	-0.002	0.0009	0.05
Cigarettes	-0.0003	0.0004	.44
	$R^2 = .09$	Adj $R^2 = .03$	

Table 18
(continued)

BUN

Variable	Parameter	SE	p value
Intercept	18.73	2.72	.0001
PFOS	-0.10	0.20	.60
Age	-0.05	0.05	.35
Alcohol	0.37	0.31	.24
BMI	-0.003	0.07	.97
Cigarettes	-0.05	0.04	.14
	$R^2 = .08$	Adj $R^2 = .02$	

Creatinine

Variable	Parameter	SE	p value
Intercept	0.5031	0.1178	.0001
PFOS	-0.0488	0.0223	.03
$PFOS^2$	0.0051	0.0020	.01
Age	0.0086	0.0023	.0004
Alcohol	-0.0119	0.0133	.38
BMI	0.0090	0.0029	.003
Cigarettes	-0.0017	0.0016	.28
	$R^2 = .37$	Adj $R^2 = .32$	

ln Glucose

Variable	Parameter	SE	p value
Intercept	3.8241	0.1090	.0001
PFOS	-0.0029	0.0079	.71
Age	0.0051	0.0022	.02
Alcohol	-0.0052	0.0125	.68
BMI	0.0166	0.0028	.0001
Cigarettes	-0.0018	0.0014	.22
	$R^2 = .42$	Adj $R^2 = .38$	

Table 18
(continued)

Cholesterol

Variable	Parameter	SE	p value
Intercept	198.04	26.88	.0001
PFOS	-2.83	1.97	.15
Age	1.26	0.54	.02
Alcohol	-1.32	3.09	.67
BMI	-0.73	0.68	.29
Cigarettes	-0.07	0.35	.85
	$R^2 = .09$	Adj $R^2 = .03$	

LDL

Variable	Parameter	SE	p value
Intercept	152.37	23.90	.0001
PFOS	-0.45	1.74	.80
Age	0.70	0.48	.14
Alcohol	-5.58	2.75	.05
BMI	-1.19	0.61	.05
Cigarettes	-0.59	0.32	.07
	$R^2 = .14$	Adj $R^2 = .08$	

HDL

Variable	Parameter	SE	p value
Intercept	77.68	8.51	.0001
PFOS	-0.66	0.62	.29
Age	-0.31	0.17	.07
Alcohol	2.68	0.98	.008
BMI	-0.66	0.22	.003
Cigarettes	-0.07	0.11	.56
	$R^2 = .32$	Adj $R^2 = .28$	

Table 18
(continued)

Triglycerides

Variable	Parameter	SE	p value
Intercept	-178.52	71.97	.02
PFOS	-7.89	5.26	.14
Age	4.22	1.44	.005
Alcohol	9.90	8.28	.24
BMI	6.07	1.83	.001
Cigarettes	3.17	0.95	.001
	$R^2 = .32$	Adj $R^2 = .28$	

Hematocrit

Variable	Parameter	SE	p value
Intercept	48.03	1.66	.0001
PFOS	-0.05	0.12	.70
Age	0.02	0.03	.48
Alcohol	-0.003	0.19	.99
BMI	-0.10	0.04	.02
Cigarettes	0.04	0.02	.05
	$R^2 = .12$	Adj $R^2 = .06$	

Hemoglobin

Variable	Parameter	SE	p value
Intercept	15.76	0.58	.0001
PFOS	-0.02	0.04	.67
Age	-0.04	0.07	.28
Alcohol	0.01	0.01	.58
BMI	-0.03	0.01	.03
Cigarettes	0.009	0.008	.25
	$R^2 = .09$	Adj $R^2 = .03$	

Table 18
(continued)

MCH

Variable	Parameter	SE	p value
Intercept	33.52	1.05	.0001
PFOS	0.04	0.08	.59
Age	-0.006	0.02	.79
Alcohol	0.11	0.12	.35
BMI	-0.10	0.03	.0003
Cigarettes	0.03	0.01	.03
	$R^2 = .24$		Adj $R^2 = .20$

MCHC

Variable	Parameter	SE	p value
Intercept	32.87	0.50	.0001
PFOS	-0.001	.037	.98
Age	0.008	0.01	.42
Alcohol	-0.08	0.06	.19
BMI	-0.0006	0.01	.96
Cigarettes	-0.01	0.007	0.08
	$R^2 = .07$	Adj $R^2 = .02$	

MCV

Variable	Parameter	SE	p value
Intercept	101.97	3.36	.0001
PFOS	0.14	0.25	.56
Age	-0.04	0.07	.53
Alcohol	0.56	0.39	.15
BMI	-0.31	0.09	.0005
Cigarettes	0.12	0.04	0.007
	$R^2 = .28$	Adj $R^2 = .23$	

Table 18
(continued)

RBC

Variable	Parameter	SE	p value
Intercept	4.673	0.214	.0001
PFOS	-0.009	0.016	.58
Age	0.005	0.004	.28
Alcohol	-0.026	0.025	.29
BMI	0.006	0.005	.24
Cigarettes	-0.002	0.003	.48
	$R^2 = .08$	Adj $R^2 = .02$	

Platelets

Variable	Parameter	SE	p value
Intercept	320.83	32.21	.0001
PFOS	-6.73	2.36	.006
Age	-0.94	0.64	.15
Alcohol	-6.95	3.70	.06
BMI	-1.26	0.82	.13
Cigarettes	0.43	0.43	.32
	$R^2 = .18$	Adj $R^2 = .13$	

WBC

Variable	Parameter	SE	p value
Intercept	3.24	1.32	.02
PFOS	-0.03	0.10	.74
Age	0.07	0.03	.01
Alcohol	0.03	0.15	.82
BMI	0.03	0.03	.42
Cigarettes	0.09	0.02	.0001
	$R^2 = .35$	Adj $R^2 = .31$	

Table 19

Mean, Median (Med), Standard Deviation (SD) of Mean and Range of PFOS, Hormonal Measurements for N = 88 Employees, Antwerp and Decatur Combined, 1995

PFOS (ppm)	Mean	Med	SD	Range
		Cortisol		
0 - < 1	19.3	17.5	7.0-29.0	
1 - < 3	17.7	18.0	7.2	1.0-42.0
3 - < 6	21.4	23.0	7.2	7.0-31.0
≥ 6	17.0	19.0	6.2	9.0-23.0
	F = 1.7, p = .18			
		DHEA-S		
0 - < 1	388[3,5]	358	168	88-605
1 - < 3	234[2,4]	210	95	69-460
3 - < 6	316[3]	318	106	90-530
≥ 6	194[2]	190	19	176-215
	F = 8.3, p = .0001			
		Estradiol		
0 - < 1	67.1	67.0	12.8	50.0-87.0
1 - < 3	60.3	59.0	15.2	35.0-101.0
3 - < 6	60.5	61.0	10.1	42.0-81.0
≥ 6	64.8	65.0	18.7	47.0-92.0
	F = 0.8, p = .49			
		FSH		
0 - < 1	3.8	3.5	1.5	2.0-6.0
1 - < 3	5.6	4.0	4.2	1.0-26.0
3 - < 6	5.6	4.0	3.9	2.0-18.0
≥ 6	6.6	6.0	3.4	3.0-12.0
	F value = 0.8, p = 0.48			
		17-Hydroxyprogesterone		
0 - < 1	170	164	41	121-245
1 - < 3	131	123	52	53-294
3 - < 6	150	153	52	65-245
≥ 6	119	98	4590-197	
	F value = 2.4, p = .08			

Table 19
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		LH		
0 - < 1	3.8	4.0	0.9	2.0-5.0
1 - < 3	4.6	4.0	3.0	1.0-21.0
3 - < 6	4.6	5.0	1.9	2.0-9.0
≥ 6	4.8	5.0	1.3	3.0-6.0
	F value = 0.3, p = .81			
		Prolactin		
0 - < 1	13.5	13.0	7.0	6.0-29.0
1 - < 3	11.8	11.0	5.0	3.0-30.0
3 - < 6	13.4	10.0	7.9	5.0-39.0
≥ 6	13.6	10.0	6.3	9.0-24.0
	F value = 0.5, p = .67			
		SHBG		
0 - < 1	0.9	0.9	0.3	0.5-1.3
1 - < 3	1.0	0.9	0.4	0.4-1.9
3 - < 6	1.0	0.9	0.3	0.4-1.7
≥ 6	1.2	1.3	0.6	0.6-2.1
	F = 1.1, p = .35			
		Free testosterone		
0 - < 1	20.5[3]	20.2	5.2	10.2-28.2
1 - < 3	16.2[2]	16.1	3.3	8.9-27.1
3 - < 6	17.7	18.2	3.2	12.2-25.2
≥ 6	17.5	17.7	2.0	15.3-20.5
	F value = 4.5, p = .006			
		Bound testosterone		
0 - < 1	739[3]	757	175	5281094
1 - < 3	580[2,4]	589	110	278-762
3 - < 6	676[3]	659	171	410-1039
≥ 6	711	752	160	462-883
	F value = 5.2, p = .003			

Table 19
(continued)

PFOS (ppm)	Mean	Med	SD	Range
		TSH		
0 - < 1	1.9	1.4	1.3	0.6-4.5
1 - < 3	1.0	1.5	1.4	0.5-8.1
3 - < 6	1.5	1.4	0.8	0.5-3.4
≥ 6	2.0	1.6	1.2	0.7-3.8

F value = 0.6, p = .62

Sample sizes:

PFOS Level	Both Locations	Antwerp	Decatur
0 - < 1 ppm	10	9	1
1 - < 3 ppm	46	21	25
3 - < 6 ppm	27	18	9
≥ 6 ppm	5	2	3
	88	50	38

Table 20

Multivariable Regression Analysis of Hormones in Relation to PFOS
Adjusting for Age, Alcohol, BMI and Cigarettes,
Antwerp and Decatur Data Combined, 1995

Cortisol

Variable	Parameter	SE	p value
Intercept	27.13	4.84	.0001
PFOS	0.27	0.35	.45
Age	-0.10	0.10	.31
Alcohol	1.56	0.56	.006
BMI	-0.25	0.12	.04
Cigarettes	0.01	0.06	.87
	$R^2 = .22$	Adj $R^2 = .17$	

DHEAS

Variable	Parameter	SE	p value
Intercept	499.17	76.98	.0001
PFOS	-2.95	5.63	.60
Age	-5.30	1.54	.0009
Alcohol	17.88	8.84	.05
BMI	-1.82	1.95	.35
Cigarettes	2.25	1.01	.03
	$R^2 = .28$	Adj $R^2 = .24$	

Estradiol

Variable	Parameter	SE	p value
Intercept	53.56	9.76	.0001
PFOS	-3.82	1.85	.04
$PFOS^2$	0.44	0.17	.01
Age	-0.13	0.19	.51
Alcohol	2.42	1.10	.03
BMI	0.57	0.24	.02
Cigarettes	0.07	0.13	.58
	$R^2 = .18$	Adj $R^2 = .12$	

Table 20
(continued)

Estradiol (without employee C)

Variable	Parameter	SE	p value
Intercept	53.43	9.84	.0001
PFOS	-3.56	2.39	.14
$PFOS^2$	0.40	0.28	.15
Age	-0.13	0.19	.51
Alcohol	2.43	1.11	.03
BMI	0.56	0.25	.03
Cigarettes	0.69	0.13	.60
	$R^2 = .13$	Adj $R^2 = .06$	

FSH

Variable	Parameter	SE	p value
Intercept	3.64	2.79	.20
PFOS	0.02	0.20	.91
Age	0.14	0.06	.02
Alcohol	0.04	0.32	.89
BMI	-0.13	0.07	.07
Cigarettes	0.005	0.04	.90
	$R^2 = .10$	Adj $R^2 = .05$	

17-Hydroxyprogesterone

Variable	Parameter	SE	p value
Intercept	306.10	32.69	.0001
PFOS	-0.04	2.36	.99
Age	-2.13	0.67	.002
Alcohol	-0.76	3.68	.84
BMI	-3.47	0.82	.0001
Cigarettes	0.79	0.42	.07
	$R^2 = .33$	Adj $R^2 = .28$	

Table 20
(continued)

LH

Variable	Parameter	SE	p value
Intercept	5.65	1.86	.003
PFOS	0.05	0.13	.69
Age	-0.02	0.04	.69
Alcohol	-0.24	0.21	.26
BMI	-0.03	0.05	.56
Cigarettes	0.03	0.02	.21
	$R^2 = .04$	Adj $R^2 = .02$	

Prolactin

Variable	Parameter	SE	p value
Intercept	16.67	3.99	.0001
PFOS	0.34	0.29	.25
Age	-0.15	0.08	.07
Alcohol	1.75	0.46	.0003
BMI	0.004	0.10	.97
Cigarettes	-0.14	0.05	.01
	$R^2 = .31$	Adj $R^2 = .27$	

SHBG

Variable	Parameter	SE	p value
Intercept	0.03	0.24	.89
PFOS	0.005	0.02	.77
Age	0.02	0.005	.0001
Alcohol	-0.005	0.03	.86
BMI	0.005	0.006	.40
Cigarettes	0.004	0.003	.19
	$R^2 = .28$	Adj $R^2 = .23$	

Table 20
(continued)

Free Testosterone

Variable	Parameter	SE	p value
Intercept	27.37	2.57	.0001
PFOS	0.02	0.19	.90
Age	-0.14	0.05	.01
Alcohol	-0.11	0.30	.69
BMI	-0.19	0.06	.005
Cigarettes	0.01	0.03	.68
	$R^2 = .19$	Adj $R^2 = .14$	

Bound Testosterone

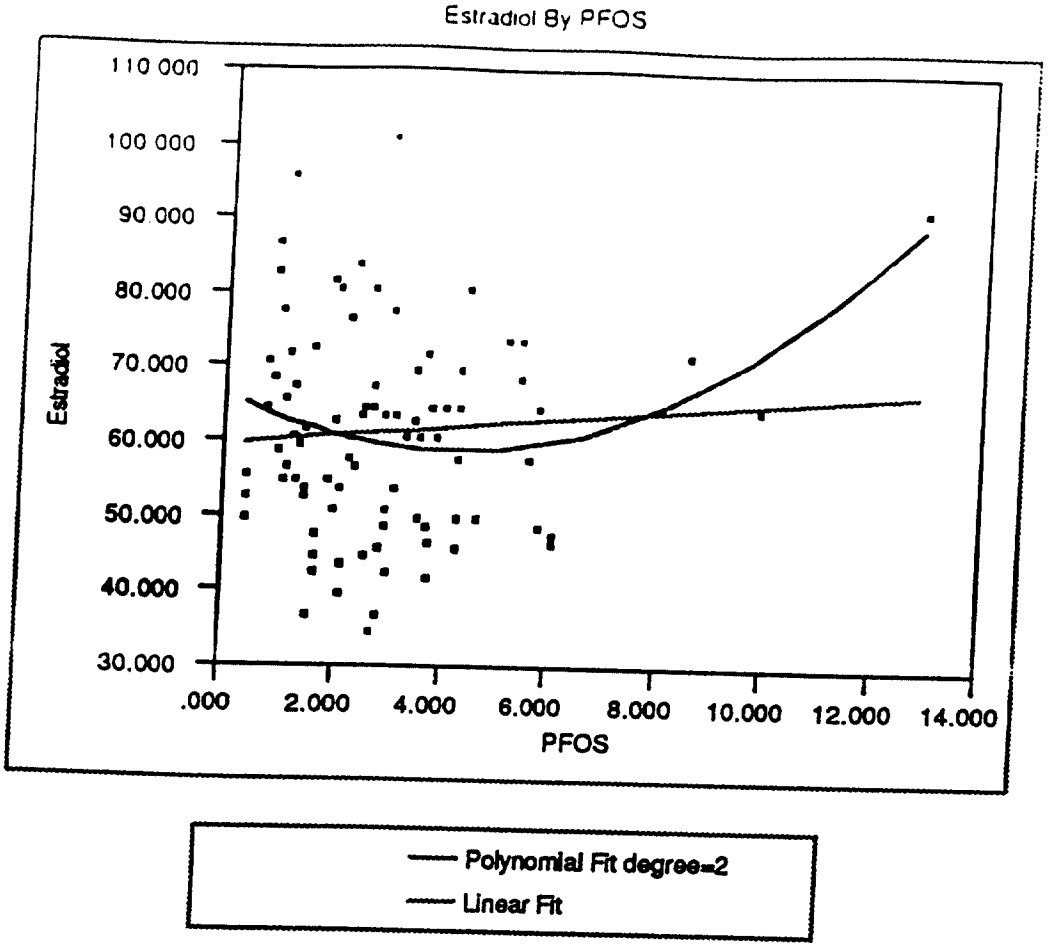
Variable	Parameter	SE	p value
Intercept	993.88	100.93	.0001
PFOS	6.91	7.28	.35
Age	-2.43	2.06	.24
Alcohol	7.41	11.37	.52
BMI	-11.43	2.52	.0001
Cigarettes	1.22	1.31	.35
	$R^2 = .28$	Adj $R^2 = .23$	

TSH

Variable	Parameter	SE	p value
Intercept	-0.873	0.826	.29
PFOS	0.004	0.060	.95
Age	0.003	0.016	.85
Alcohol	0.078	0.095	.41
BMI	0.096	0.021	.0001
Cigarettes	-0.011	0.011	.32
	$R^2 = .23$	Adj $R^2 = .18$	

FIGURE 1

Scatter Plot of Estradiol and PFOS, Both Locations Combined, 1995



Polynomial Fit degree=2

Estradiol = 66.4703 – 3.60448 PFOS + 0.42197 PFOS^2

Summary of Fit

RSquare	0.07616
RSquare Adj	0.054423
Root Mean Square Error	13.33314
Mean of Response	61.36364
Observations (or Sum Wgts)	88

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	1245.701	622.850	3.5036
Error	85	15110.663	177.773	Prob>F
C Total	87	16356.364		0.0345

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	66.470276	3.632698	18.30	<.0001
PFOS	-3.604477	1.7997	-2.00	0.0484
PFOS^2	0.4219692	0.167705	2.52	0.0137

Estradiol = 59.7222 + 0.57198 PFOS

Summary of Fit

RSquare	0.00735
RSquare Adj	-0.00419
Root Mean Square Error	13.74017
Mean of Response	61.36364
Observations (or Sum Wgts)	88

Analysis of Variance

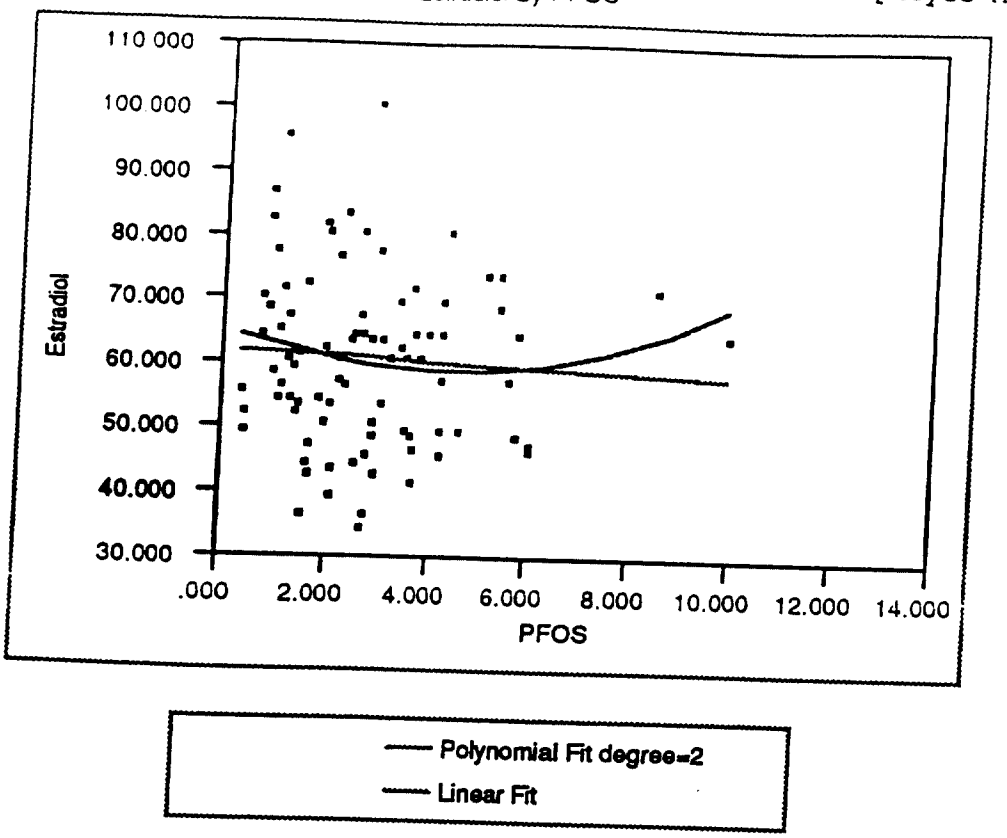
Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	120.226	120.226	0.6368
Error	86	16236.138	188.792	Prob>F
C Total	87	16356.364		0.4271

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	59.722236	2.525093	23.65	<.0001
PFOS	0.5719843	0.716766	0.80	0.4271

FIGURE 2

Scatter Plot of Estradiol and PFOS, Both Locations Cominbed, 1995 Without Employee A



Polynomial Fit degree=2

Estradiol = 65.8629 – 3.10569 PFOS + 0.34755 PFOS^2

Summary of Fit

RSquare	0.020552
RSquare Adj	-0.00277
Root Mean Square Error	13.40325
Mean of Response	61.01149
Observations (or Sum Wgts)	87

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	316.639	158.320	0.8813
Error	84	15090.349	179.647	Prob>F
C Total	86	15406.989		0.4180

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	65.862871	4.074112	16.17	<.0001
PFOS	-3.105693	2.339491	-1.33	0.1879
PFOS^2	0.3475472	0.278213	1.25	0.2151

Linear Fit

Estradiol = 62 0271 - 0 36861 PFOS

Summary of Fit

RSquare	0.002356
RSquare Adj	-0.00938
Root Mean Square Error	13.44737
Mean of Response	61.01149
Observations (or Sum Wgts)	87

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	36.295	36.295	0.2007
Error	85	15370.694	180.832	Prob>F
C Total	86	15406.989		0.6553

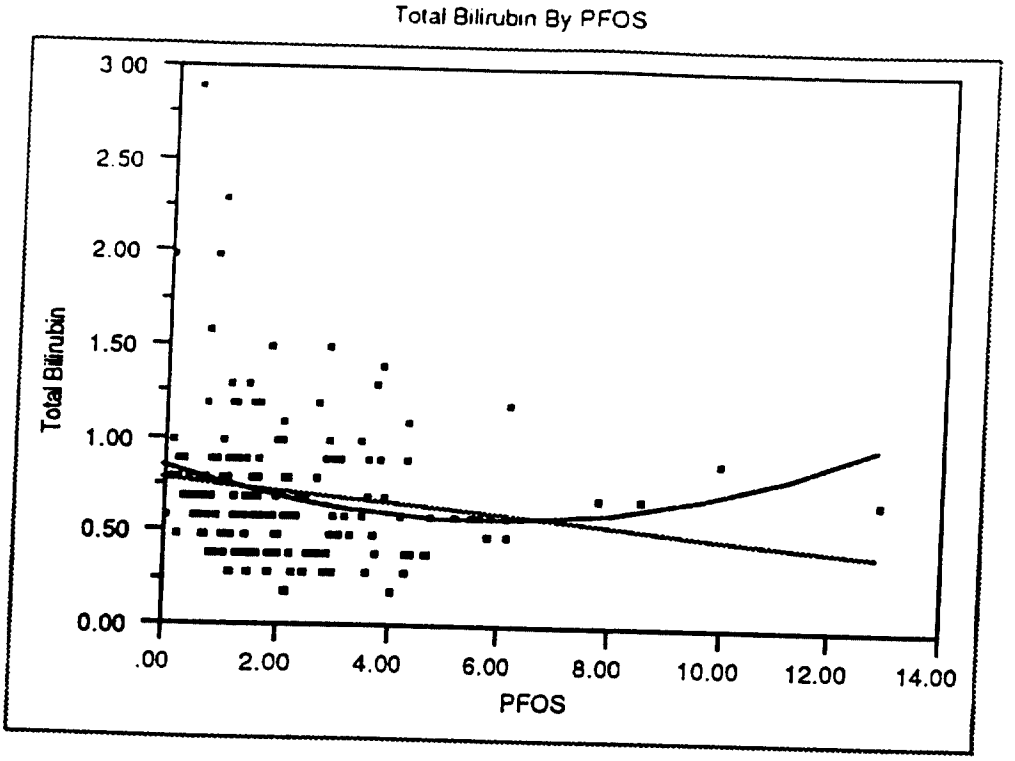
Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	62.027069	2.686488	23.09	<.0001
PFOS	-0.368607	0.822768	-0.45	0.6553

APPENDIX A

Total Bilirubin and PFOS Scatter Plots

Scatter Plot of Total Bilirubin and PFOS, Both Locations Combined, 1995



Linear Fit

Total Bilirubin = 0.78247 – 0.02927 PFOS

Summary of Fit

RSquare	0.022279
RSquare Adj	0.016692
Root Mean Square Error	0.363488
Mean of Response	0.718644
Observations (or Sum Wgts)	177

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.526856	0.526856	3.9876
Error	175	23.121618	0.132124	Prob>F
C Total	176	23.648475		0.0474

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.7824732	0.04205	18.61	<.0001
PFOS	-0.029269	0.014657	-2.00	0.0474

Polynomial Fit degree=2

Total Bilirubin = 0.86532 – 0.09918 PFOS + 0.00846 PFOS^2

Summary of Fit

RSquare	0.051674
RSquare Adj	0.040773
Root Mean Square Error	0.359009
Mean of Response	0.718644
Observations (or Sum Wgts)	177

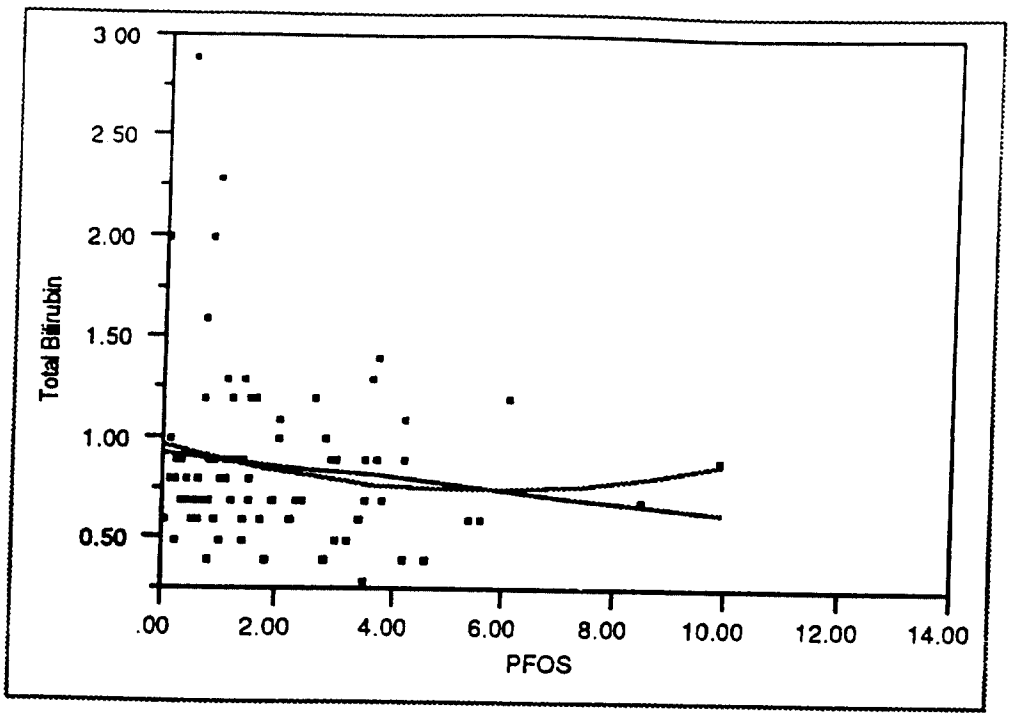
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	1.222006	0.611003	4.7406
Error	174	22.426468	0.128888	Prob>F
C Total	176	23.648475		0.0099

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.865318	0.054748	15.81	<.0001
PFOS	-0.099182	0.033404	-2.97	0.0034
PFOS^2	0.008459	0.003642	2.32	0.0214

Scatter Plot of Total Bilirubin and PFOS, Antwerp, 1995



Linear Fit

Total Bilirubin = 0.92001 – 0.02927 PFOS

Summary of Fit

RSquare	0.017786
RSquare Adj	0.006365
Root Mean Square Error	0.407279
Mean of Response	0.863636
Observations (or Sum Wgts)	88

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.258313	0.258313	1.5573
Error	86	14.265323	0.165876	Prob>F
C Total	87	14.523636		0.2155

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.9200069	0.062654	14.68	<.0001
PFOS	-0.029266	0.023452	-1.25	0.2155

Polynomial Fit degree=2

Total Bilirubin = 0.96548 – 0.07872 PFOS + 0.00697 PFOS^2

Summary of Fit

RSquare	0.027505
RSquare Adj	0.004623
Root Mean Square Error	0.407635
Mean of Response	0.863636
Observations (or Sum Wgts)	88

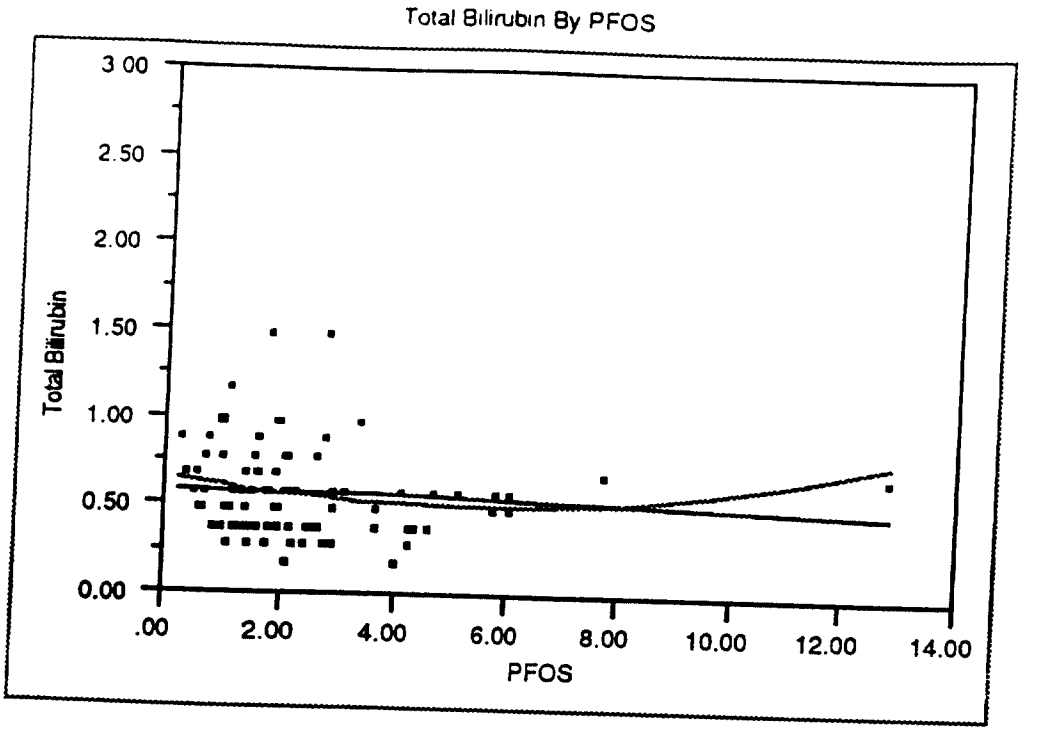
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.399470	0.199735	1.2020
Error	85	14.124166	0.166167	Prob>F
C Total	87	14.523636		0.3056

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.9654789	0.07979	12.10	<.0001
PFOS	-0.078719	0.058565	-1.34	0.1825
PFOS^2	0.0069749	0.007568	0.92	0.3593

Scatter Plot of Total Bilirubin and PFOS, Decatur, 1995



Linear Fit

Total Bilirubin = 0.59712 – 0.00898 PFOS

Summary of Fit

RSquare	0.004472
RSquare Adj	-0.00697
Root Mean Square Error	0.249626
Mean of Response	0.575281
Observations (or Sum Wgts)	89

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.0243540	0.024354	0.3908
Error	87	5.4212639	0.062313	Prob>F
C Total	88	5.4456180		0.5335

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.5971232	0.043827	13.62	<.0001
PFOS	-0.008979	0.014363	-0.63	0.5335

Polynomial Fit degree=2

Total Bilirubin = 0.66974 – 0.05867 PFOS + 0.00518 PFOS^2

Summary of Fit

RSquare	0.032545

RSquare Adj	0.010046
Root Mean Square Error	0.247508
Mean of Response	0.575281
Observations (or Sum Wgts)	89

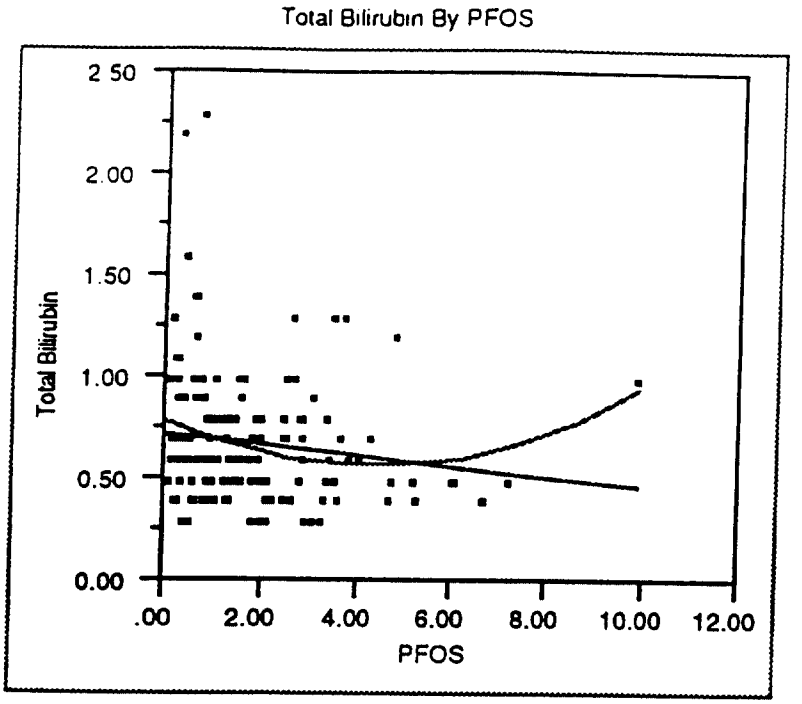
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.1772262	0.088613	1.4465
Error	86	5.2683918	0.061260	Prob>F
C Total	88	5.4456180		0.2411

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.6697418	0.063258	10.59	<.0001
PFOS	-0.058672	0.034531	-1.70	0.0929
PFOS^2	0.0051833	0.003281	1.58	0.1178

Scatter Plot of Total Bilirubin and PFOS, Both Locations Combined, 1997



Linear Fit

Total Bilirubin = 0.7185 – 0.02583 PFOS

Summary of Fit

RSquare	0.016221
RSquare Adj	0.009483
Root Mean Square Error	0.322046
Mean of Response	0.672973
Observations (or Sum Wgts)	148

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.249674	0.249674	2.4073
Error	146	15.142218	0.103714	Prob>F
C Total	147	15.391892		0.1229

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.7184974	0.039518	18.18	<.0001
PFOS	-0.025825	0.016645	-1.55	0.1229

Polynomial Fit degree=2

Total Bilirubin = 0.78963 – 0.10456 PFOS + 0.012 PFOS^2

Summary of Fit

RSquare	0.045789
RSquare Adj	0.032628

Root Mean Square Error	0.318261
Mean of Response	0 672973
Observations (or Sum Wgts)	148

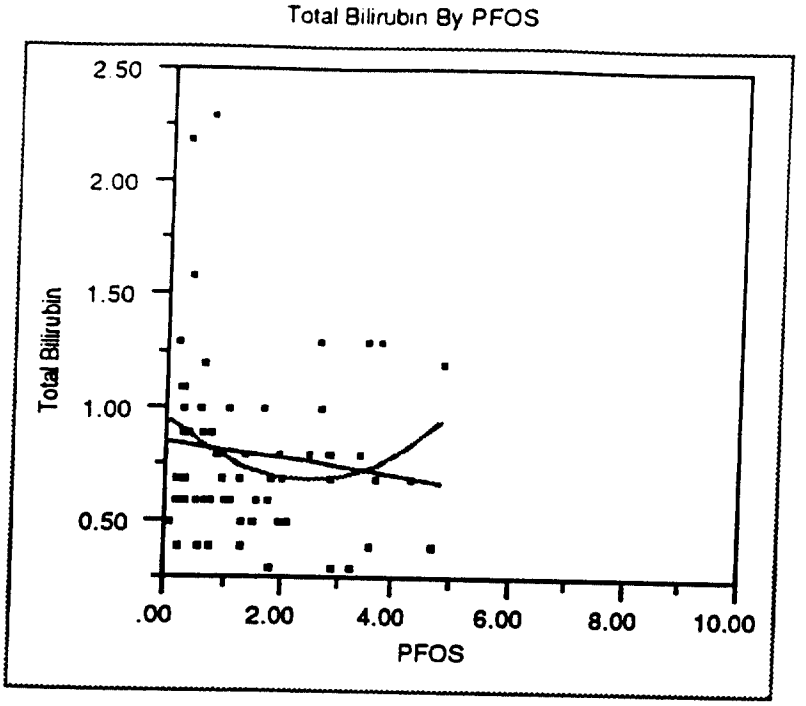
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.704787	0.352393	3.4790
Error	145	14.687105	0.101290	Prob>F
C Total	147	15.391892		0.0334

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.7896264	0.05149	15.34	<.0001
PFOS	-0.104564	0.040625	-2.57	0.0111
PFOS^2	0.0120049	0.005663	2.12	0.0357

Scatter Plot of Total Bilirubin and PFOS, Antwerp, 1997



Linear Fit

Total Bilirubin = 0.8517 – 0.03647 PFOS

Summary of Fit

RSquare	0.014291
RSquare Adj	-0.00161
Root Mean Square Error	0.385334
Mean of Response	0.796875
Observations (or Sum Wgts)	64

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.1334670	0.133467	0.8989
Error	62	9.2059080	0.148482	Prob>F
C Total	63	9.3393750		0.3468

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.8516999	0.075259	11.32	<.0001
PFOS	-0.036474	0.038471	-0.95	0.3468

Polynomial Fit degree=2

Total Bilirubin = 0.9635 – 0.22847 PFOS + 0.0462 PFOS^2

Summary of Fit

RSquare	0.051848
RSquare Adj	0.020761

Root Mean Square Error	0.318261
Mean of Response	0.672973
Observations (or Sum Wgts)	148

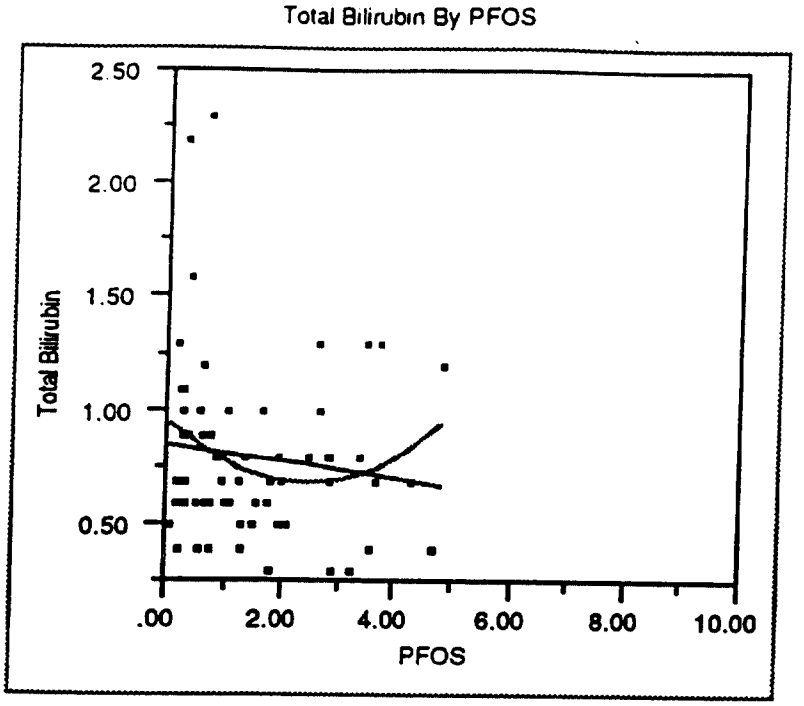
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.704787	0.352393	3.4790
Error	145	14.687105	0.101290	Prob>F
C Total	147	15.391892		0.0334

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.7896264	0.05149	15.34	<.0001
PFOS	-0.104564	0.040625	-2.57	0.0111
PFOS^2	0.0120049	0.005663	2.12	0.0357

Scatter Plot of Total Bilirubin and PFOS, Antwerp, 1997



Linear Fit

Total Bilirubin = 0.8517 – 0.03647 PFOS

Summary of Fit

RSquare	0.014291
RSquare Adj	-0.00161
Root Mean Square Error	0.385334
Mean of Response	0.796875
Observations (or Sum Wgts)	64

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.1334670	0.133467	0.8989
Error	62	9.2059080	0.148482	Prob>F
C Total	63	9.3393750		0.3468

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.8516999	0.075259	11.32	<.0001
PFOS	-0.036474	0.038471	-0.95	0.3468

Polynomial Fit degree=2

Total Bilirubin = 0.9635 – 0.22847 PFOS + 0.0462 PFOS^2

Summary of Fit

RSquare	0.051848
RSquare Adj	0.020761

Root Mean Square Error	0.381007
Mean of Response	0.796875
Observations (or Sum Wgts)	64

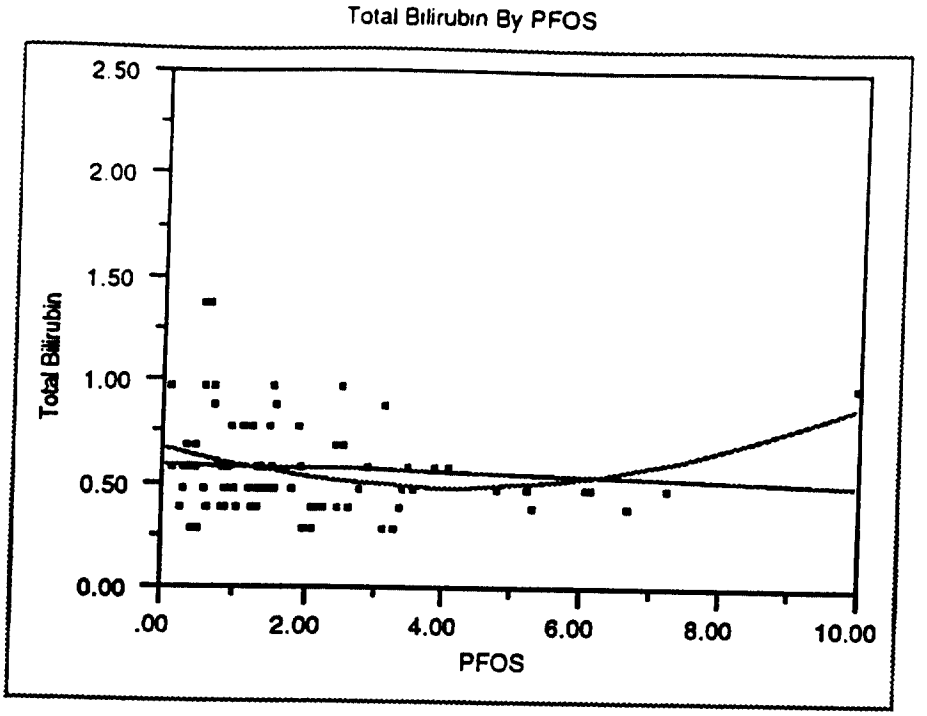
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.4842255	0.242113	1.6678
Error	61	8.8551495	0.145166	Prob>F
C Total	63	9.3393750		0.1971

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.963501	0.103492	9.31	<.0001
PFOS	-0.228466	0.129238	-1.77	0.0821
PFOS^2	0.0461951	0.029718	1.55	0.1253

Scatter Plot of Total Bilirubin and PFOS, Decatur, 1997



Linear Fit

Total Bilirubin = 0.59609 – 0.00894 PFOS

Summary of Fit

RSquare	0.004924
RSquare Adj	-0.00721
Root Mean Square Error	0.229
Mean of Response	0.578571
Observations (or Sum Wgts)	84

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.0212775	0.021278	0.4057
Error	82	4.3001510	0.052441	Prob>F
C Total	83	4.3214286		0.5259

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.5960926	0.037161	16.04	<.0001
PFOS	-0.008937	0.01403	-0.64	0.5259

Polynomial Fit degree=2

Total Bilirubin = 0.68287 – 0.09408 PFOS + 0.01143 PFOS^2

Summary of Fit

RSquare	0.071405
RSquare Adj	0.048477

001208

Root Mean Square Error	0.222579
Mean of Response	0.578571
Observations (or Sum Wgts)	84

Analysis of Variance

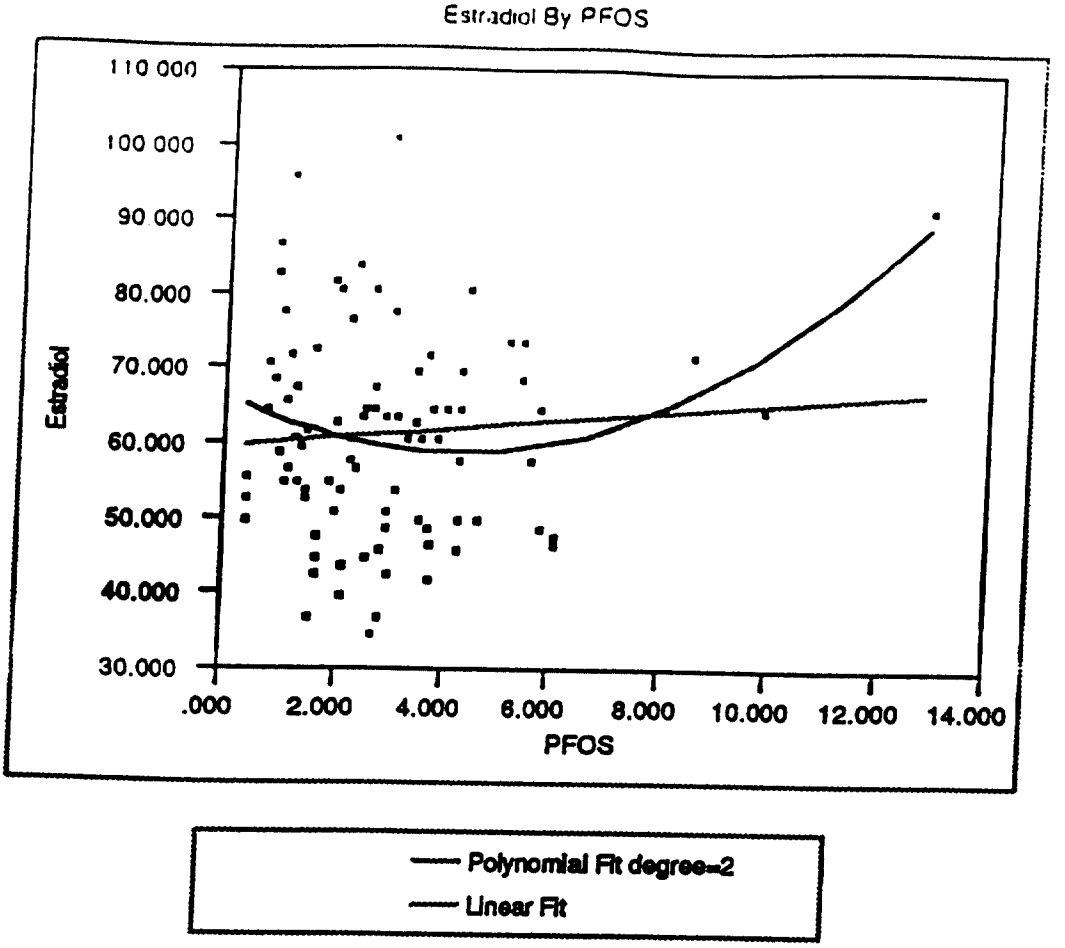
Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.3085734	0.154287	3.1143
Error	81	4.0128552	0.049541	Prob>F
C Total	83	4.3214286		0.0498

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.6828676	0.05102	13.38	<.0001
PFOS	-0.094082	0.037896	-2.48	0.0151
PFOS^2	0.011426	0.004745	2.41	0.0183

FIGURE 1

Scatter Plot of Estradiol and PFOS, Both Locations Combined, 1995



Polynomial Fit degree=2

Estradiol = 66.4703 – 3.60448 PFOS + 0.42197 PFOS^2

Summary of Fit

RSquare	0.07616
RSquare Adj	0.054423
Root Mean Square Error	13.33314
Mean of Response	61.36364
Observations (or Sum Wgts)	88

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	1245.701	622.850	3.5036
Error	85	15110.663	177.773	Prob>F
C Total	87	16356.364		0.0345

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	66.470276	3.632698	18.30	<.0001
PFOS	-3.604477	1.7997	-2.00	0.0484
PFOS^2	0.4219692	0.167705	2.52	0.0137

Estradiol = 59.7222 + 0.57198 PFOS

Summary of Fit

RSquare	0.00735
RSquare Adj	-0.00419
Root Mean Square Error	13.74017
Mean of Response	61.36364
Observations (or Sum Wgts)	88

Analysis of Variance

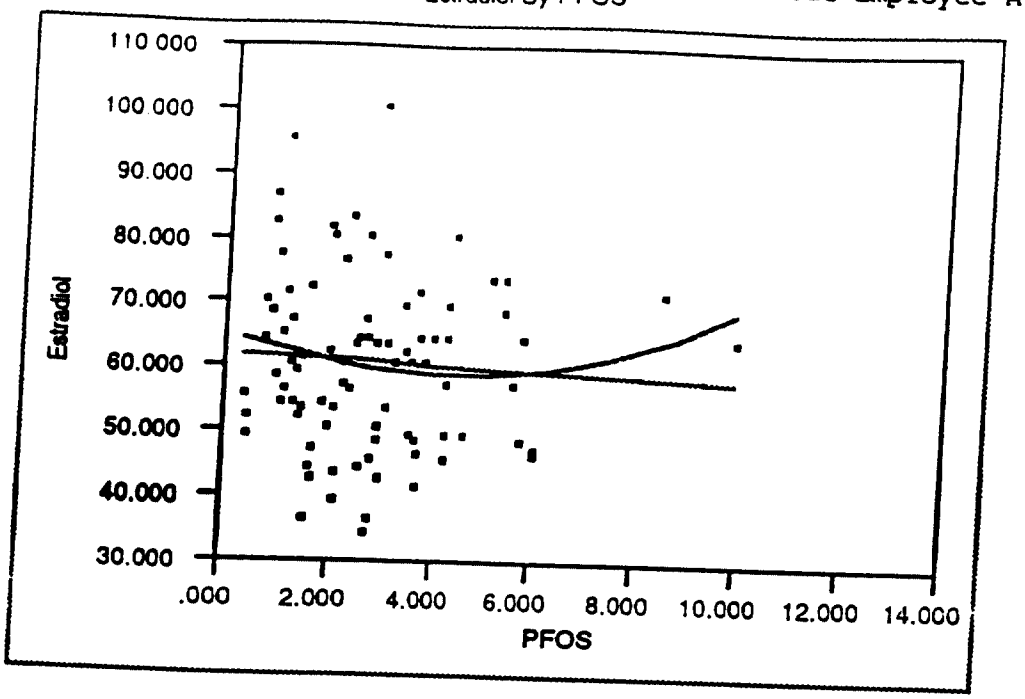
Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	120.226	120.226	0.6368
Error	86	16236.138	188.792	Prob>F
C Total	87	16356.364		0.4271

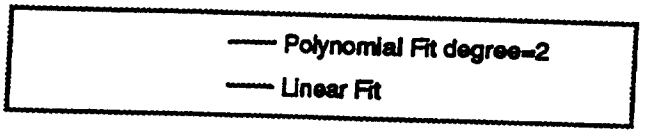
Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	59.722236	2.525093	23.65	<.0001
PFOS	0.5719843	0.716766	0.80	0.4271

FIGURE 2

Scatter Plot of Estradiol and PFOS, Both Locations Cominbed, 1995 Without Employee A





Polynomial Fit degree=2

Estradiol = 65.8629 – 3.10569 PFOS + 0.34755 PFOS^2

Summary of Fit

RSquare	0.020552
RSquare Adj	-0.00277
Root Mean Square Error	13.40325
Mean of Response	61.01149
Observations (or Sum Wgts)	87

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	316.639	158.320	0.8813
Error	84	15090.349	179.647	Prob>F
C Total	86	15406.989		0.4180

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	65.862871	4.074112	16.17	<.0001
PFOS	-3.105693	2.339491	-1.33	0.1879
PFOS^2	0.3475472	0.278213	1.25	0.2151

Linear Fit

Estradiol = 62.0271 - 0.36861 PFOS

Summary of Fit

RSquare	0.002356
RSquare Adj	-0.00938
Root Mean Square Error	13.44737
Mean of Response	61.01149
Observations (or Sum Wgts)	87

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	36.295	36.295	0.2007
Error	85	15370.694	180.832	Prob>F
C Total	86	15406.989		0.6553

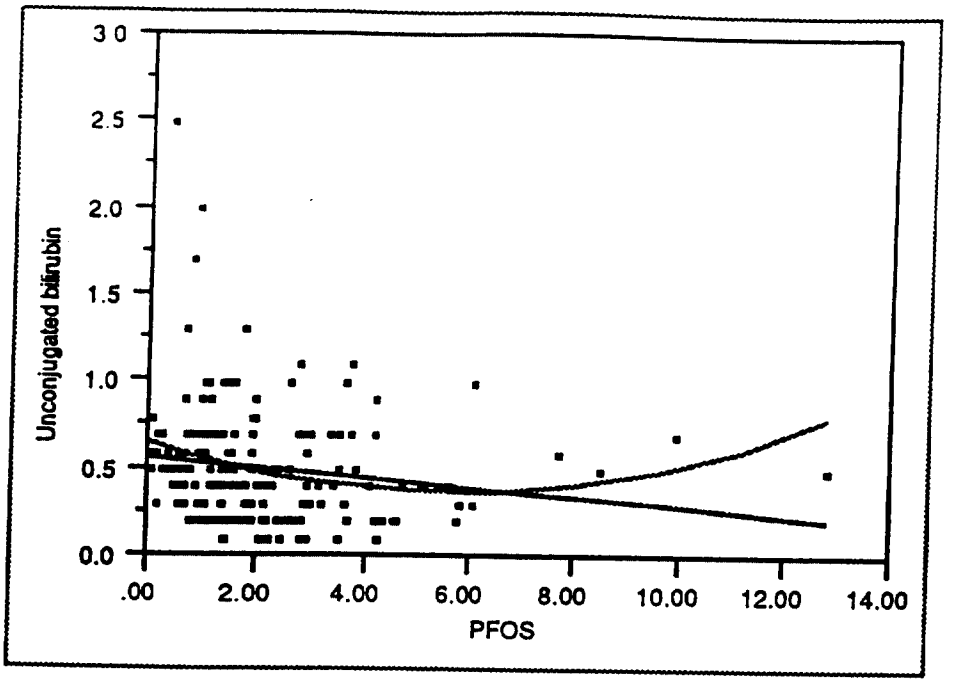
Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	62.027069	2.686488	23.09	<.0001
PFOS	-0.368607	0.822768	-0.45	0.6553

APPENDIX B

Unconjugated Bilirubin and PFOS Scatter Plots

Scatter Plot of Unconjugated Bilirubin and PFOS, Both Locations Combined, 1995



Linear Fit

Unconjugated bilirubin = 0.56837 – 0.0285 PFOS

Summary of Fit

RSquare	0.024418
RSquare Adj	0.018843
Root Mean Square Error	0.337753
Mean of Response	0.506215
Observations (or Sum Wgts)	177

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.499660	0.499660	4.3800
Error	175	19.963503	0.114077	Prob>F
C Total	176	20.463164		0.0378

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.5683746	0.039072	14.55	<.0001
PFOS	-0.028503	0.013619	-2.09	0.0378

Polynomial Fit degree=2

Unconjugated bilirubin = 0.65239 – 0.09941 PFOS + 0.00858 PFOS^2

Summary of Fit

RSquare	0.059356
RSquare Adj	0.048544

Root Mean Square Error	0.332602
Mean of Response	0.506215
Observations (or Sum Wgts)	177

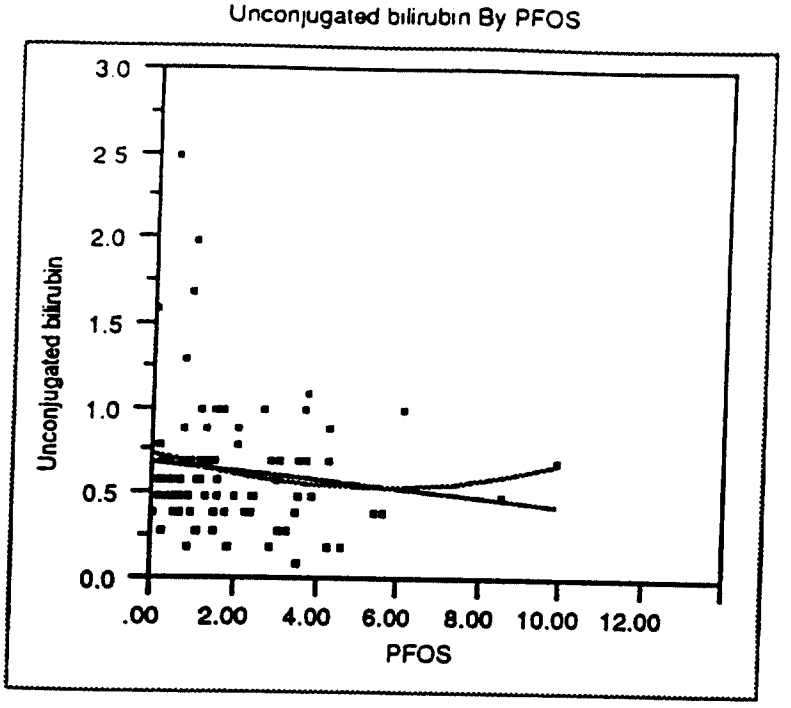
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	1.214616	0.607308	5.4898
Error	174	19.248548	0.110624	Prob>F
C Total	176	20.463164		0.0049

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.6523913	0.050721	12.86	<.0001
PFOS	-0.099406	0.030947	-3.21	0.0016
PFOS^2	0.0085787	0.003374	2.54	0.0119

Scatter Plot of Unconjugated Bilirubin and PFOS, Antwerp, 1995



Linear Fit

Unconjugated bilirubin = 0.69447 – 0.02604 PFOS

Summary of Fit

RSquare	0.016651
RSquare Adj	0.005217
Root Mean Square Error	0.374674
Mean of Response	0.644318
Observations (or Sum Wgts)	88

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.204426	0.204426	1.4562
Error	86	12.072733	0.140381	Prob>F
C Total	87	12.277159		0.2308

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.6944654	0.057638	12.05	<.0001
PFOS	-0.026035	0.021575	-1.21	0.2308

Polynomial Fit degree=2

Unconjugated bilirubin = 0.73919 – 0.07468 PFOS + 0.00686 PFOS^2

Summary of Fit

RSquare	0.027775
RSquare Adj	0.004899

Root Mean Square Error	0.374734
Mean of Response	0.644318
Observations (or Sum Wgts)	88

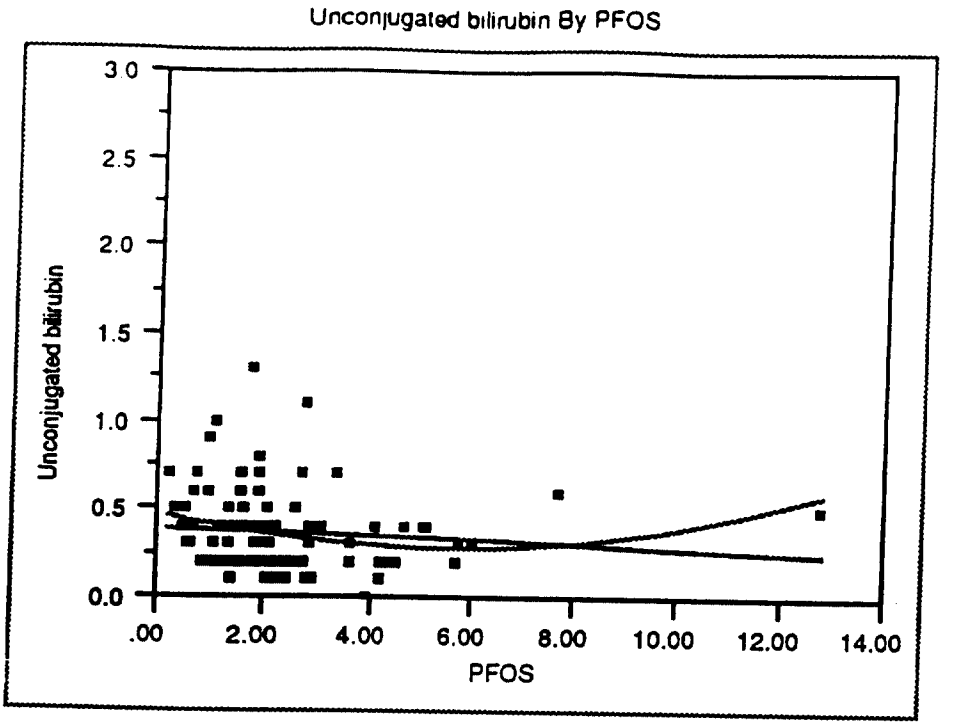
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.340994	0.170497	1.2141
Error	85	11.936165	0.140425	Prob>F
C Total	87	12.277159		0.3021

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.7391923	0.07335	10.08	<.0001
PFOS	-0.074678	0.053838	-1.39	0.1690
PFOS^2	0.0068606	0.006957	0.99	0.3268

Scatter Plot of Unconjugated Bilirubin and PFOS, Decatur, 1995



Linear Fit

Unconjugated bilirubin = 0.39803 – 0.01166 PFOS

Summary of Fit

RSquare	0.008475
RSquare Adj	-0.00292
Root Mean Square Error	0.235059
Mean of Response	0.369663
Observations (or Sum Wgts)	89

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.0410886	0.041089	0.7436
Error	87	4.8070013	0.055253	Prob>F
C Total	88	4.8480899		0.3909

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.3980339	0.04127	9.64	<.0001
PFOS	-0.011663	0.013525	-0.86	0.3909

Polynomial Fit degree=2

Unconjugated bilirubin = 0.48279 – 0.06966 PFOS + 0.00605 PFOS^2

Summary of Fit

RSquare	0.051431

RSquare Adj	0.029371
Root Mean Square Error	0.231244
Mean of Response	0.369663
Observations (or Sum Wgts)	89

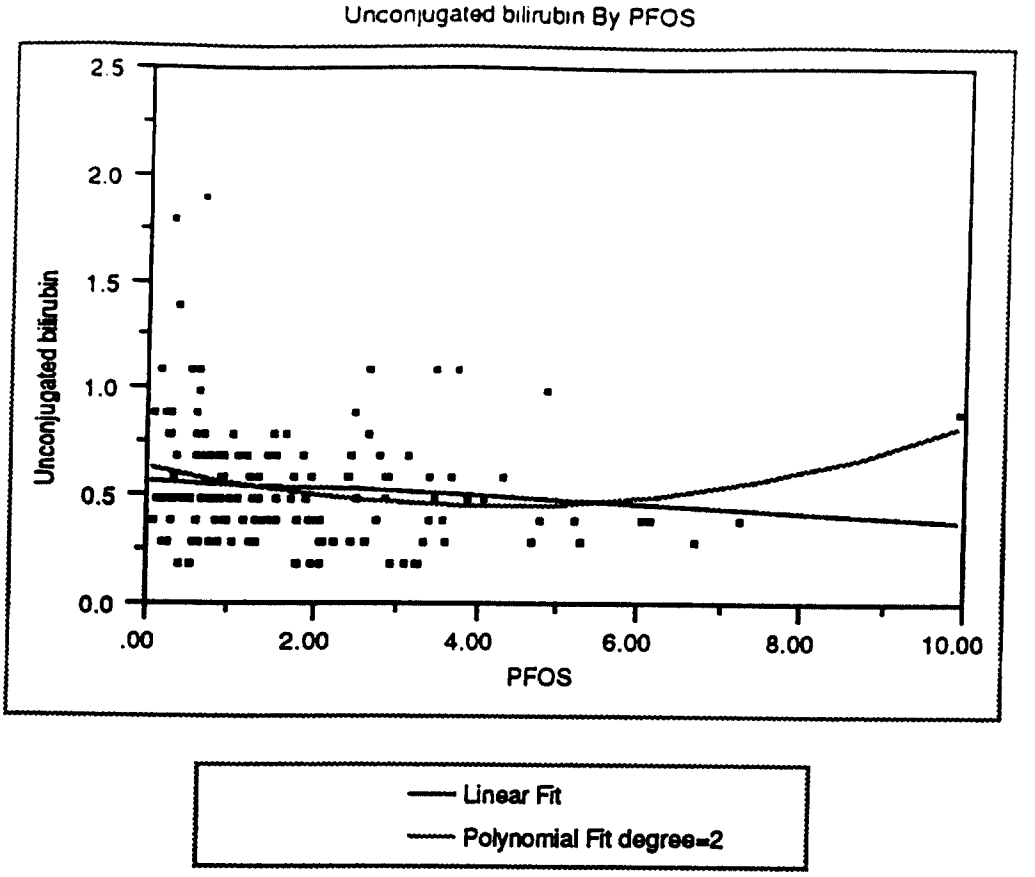
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.2493418	0.124671	2.3314
Error	86	4.5987481	0.053474	Prob>F
C Total	88	4.8480899		0.1033

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.4827917	0.059102	8.17	<.0001
PFOS	-0.069663	0.032262	-2.16	0.0336
PFOS^2	0.0060498	0.003066	1.97	0.0517

Scatter Plot of Unconjugated Bilirubin and PFOS, Both Locations Combined, 1997



Linear Fit

Unconjugated bilirubin = 0.57745 – 0.0194 PFOS

Summary of Fit

RSquare	0.012338
RSquare Adj	0.005573
Root Mean Square Error	0.277986
Mean of Response	0.543243
Observations (or Sum Wgts)	148

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.140939	0.140939	1.8238
Error	146	11.282304	0.077276	Prob>F
C Total	147	11.423243		0.1789

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.577447	0.034111	16.93	<.0001
PFOS	-0.019403	0.014368	-1.35	0.1789

Polynomial Fit degree=2

Unconjugated bilirubin = 0.64247 – 0.09138 PFOS + 0.01097 PFOS^2

Summary of Fit

RSquare	0.045634

001221

RSquare Adj	0.03247
Root Mean Square Error	0.274201
Mean of Response	0.543243
Observations (or Sum Wgts)	148

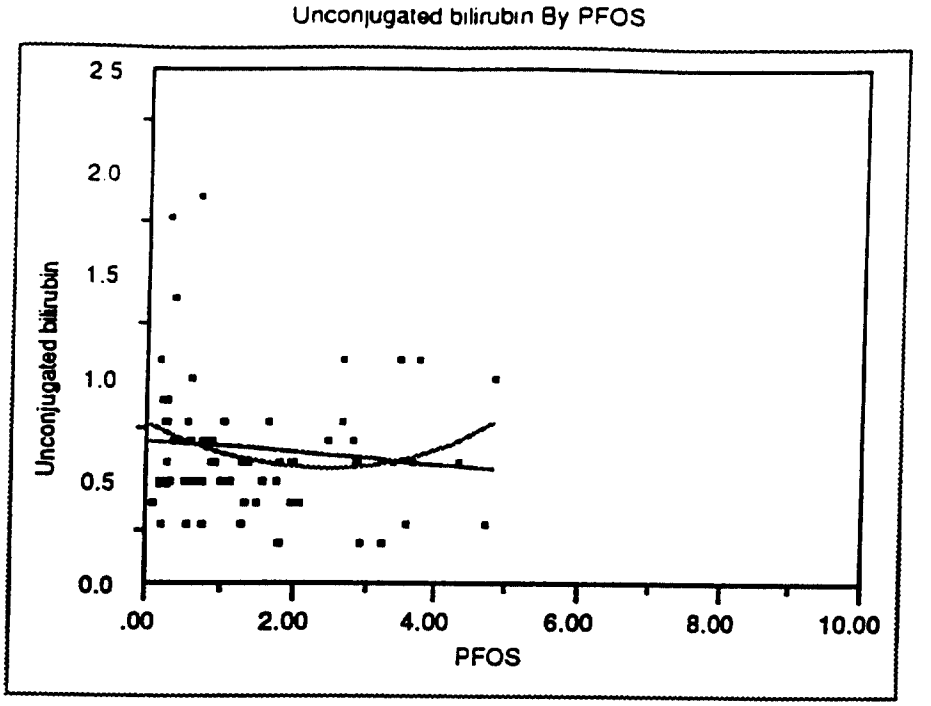
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.521284	0.260642	3.4666
Error	145	10.901959	0.075186	Prob>F
C Total	147	11.423243		0.0338

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.6424713	0.044361	14.48	<.0001
PFOS	-0.091384	0.035001	-2.61	0.0100
PFOS^2	0.0109746	0.004879	2.25	0.0260

Scatter Plot of Unconjugated Bilirubin and PFOS, Antwerp, 1997



Linear Fit

Unconjugated bilirubin = 0.69161 – 0.02872 PFOS

Summary of Fit

RSquare	0.01217
RSquare Adj	-0.00376
Root Mean Square Error	0.329151
Mean of Response	0.648438
Observations (or Sum Wgts)	64

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.0827520	0.082752	0.7638
Error	62	6.7170917	0.108340	Prob>F
C Total	63	6.7998437		0.3855

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.6916073	0.064286	10.76	<.0001
PFOS	-0.02872	0.032862	-0.87	0.3855

Polynomial Fit degree=2

Unconjugated bilirubin = 0.78708 – 0.19268 PFOS + 0.03945 PFOS^2

Summary of Fit

RSquare	0.049788
RSquare Adj	0.018634

Root Mean Square Error	0.325458
Mean of Response	0.648438
Observations (or Sum Wgts)	64

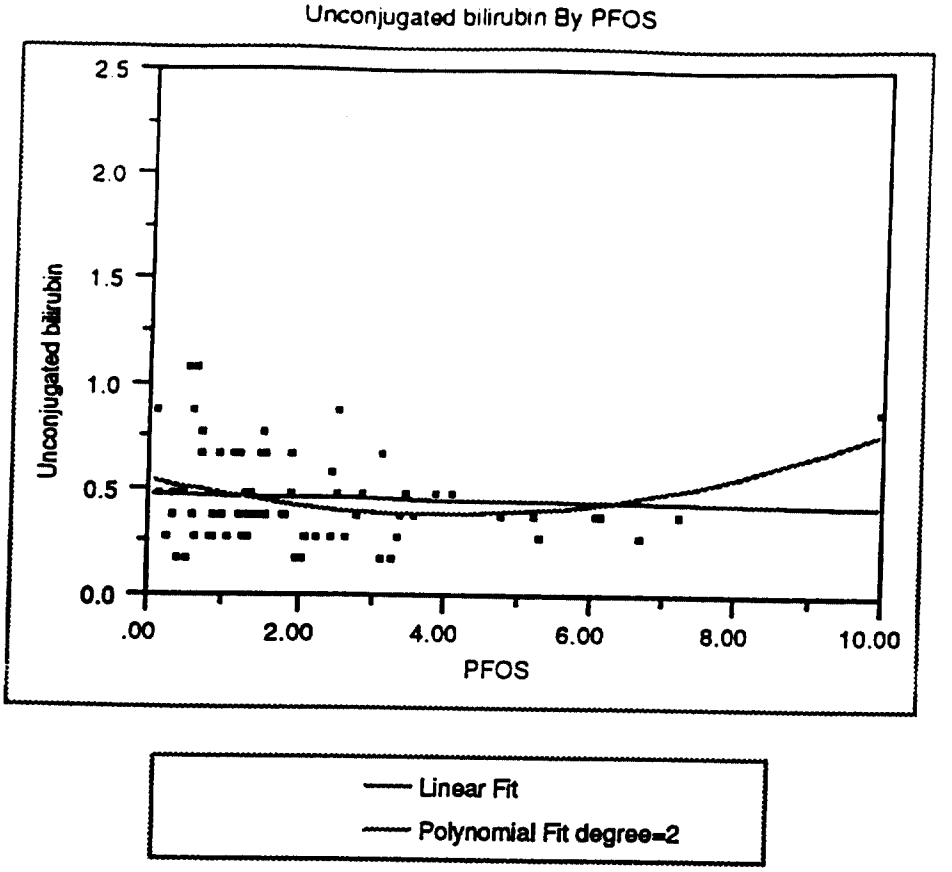
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.3385540	0.169277	1.5981
Error	61	6.4612897	0.105923	Prob>F
C Total	63	6.7998437		0.2106

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.7870832	0.088403	8.90	<.0001
PFOS	-0.192677	0.110395	-1.75	0.0860
PFOS^2	0.0394497	0.025386	1.55	0.1254

Scatter Plot of Unconjugated Bilirubin and PFOS, Decatur, 1997



Linear Fit

Unconjugated bilirubin = 0.47268 – 0.00489 PFOS

Summary of Fit

RSquare	0.001886
RSquare Adj	-0.01029
Root Mean Square Error	0.202702
Mean of Response	0.463095
Observations (or Sum Wgts)	84

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.0063673	0.006367	0.1550
Error	82	3.3692280	0.041088	Prob>F
C Total	83	3.3755952		0.6949

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.47268	0.032893	14.37	<.0001
PFOS	-0.004889	0.012419	-0.39	0.6949

Polynomial Fit degree=2

Unconjugated bilirubin = 0.5544 – 0.08508 PFOS + 0.01076 PFOS^2

Summary of Fit

RSquare	0.077372

RSquare Adj	0.054591
Root Mean Square Error	0.196086
Mean of Response	0.463095
Observations (or Sum Wgts)	84

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	0.2611750	0.130588	3.3963
Error	81	3.1144202	0.038450	Prob>F
C Total	83	3.3755952		0.0383

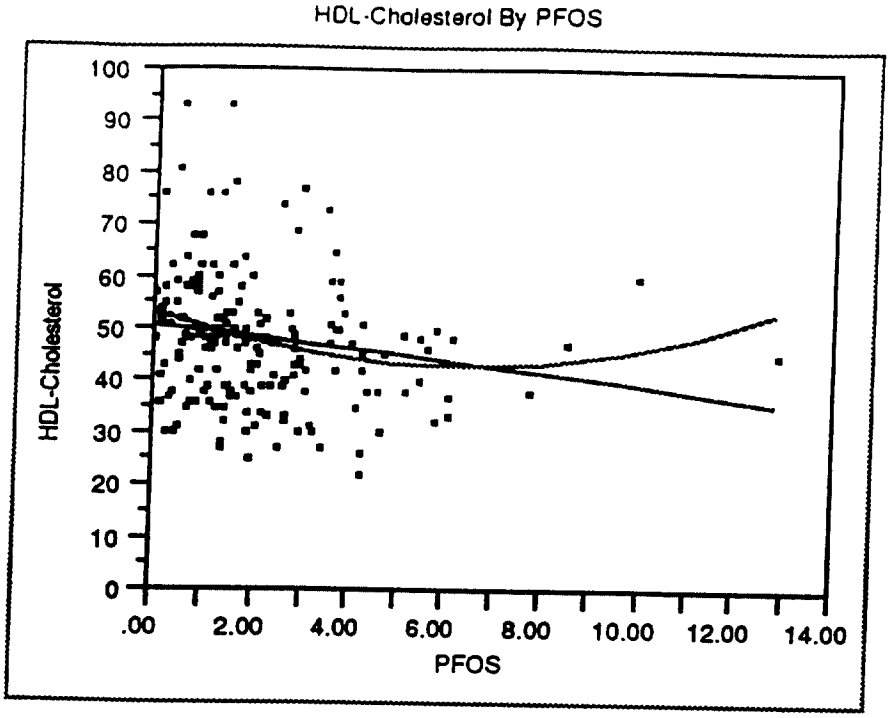
Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0.5544015	0.044947	12.33	<.0001
PFOS	-0.085075	0.033385	-2.55	0.0127
PFOS^2	0.0107606	0.00418	2.57	0.0119

APPENDIX C

HDL and PFOS Scatter Plots

Scatter Plot of HDL Cholesterol and PFOS, Both Locations Combined, 1995



Linear Fit

HDL-Cholesterol = 51.0197 – 1.17509 PFOS

Summary of Fit

RSquare	0.030337
RSquare Adj	0.0247
Root Mean Square Error	12.55611
Mean of Response	48.45977
Observations (or Sum Wgts)	174

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	848.392	848.392	5.3813
Error	172	27116.827	157.656	Prob>F
C Total	173	27965.218		0.0215

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	51.01971	1.457347	35.01	<.0001
PFOS	-1.17509	0.506557	-2.32	0.0215

Polynomial Fit degree=2

HDL-Cholesterol = 53.5286 – 3.30537 PFOS + 0.25758 PFOS^2

Summary of Fit

RSquare	0.053266
RSquare Adj	0.042193

Root Mean Square Error	12.443
Mean of Response	48.45977
Observations (or Sum Wgts)	174

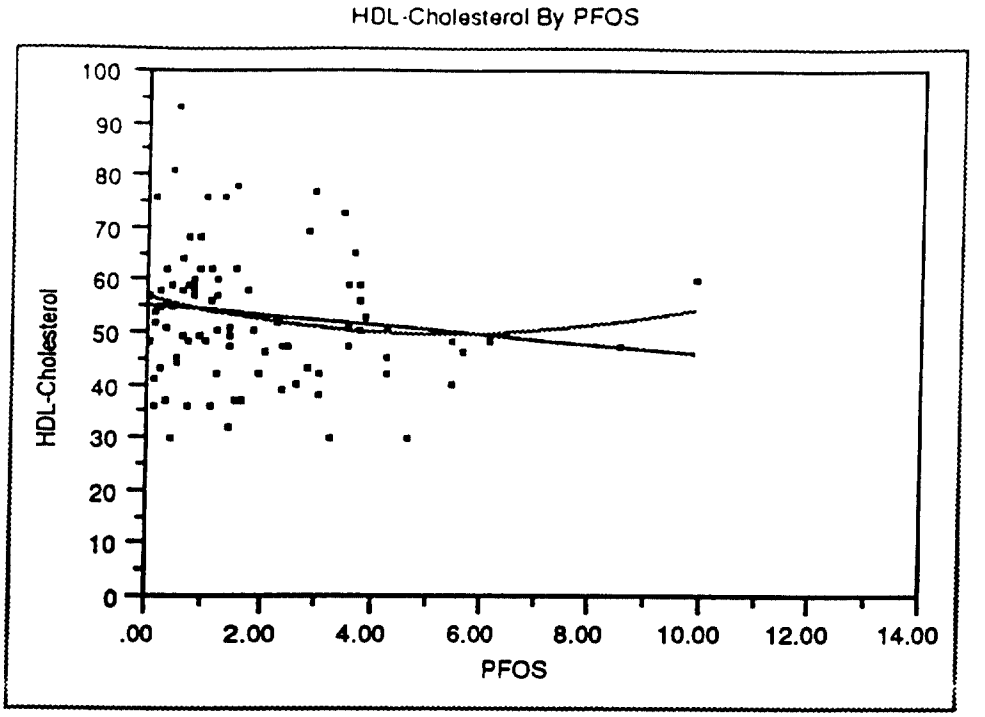
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	1489.605	744.802	4.8105
Error	171	26475.614	154.828	Prob>F
C Total	173	27965.218		0.0093

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	53.5286	1.898856	28.19	<.0001
PFOS	-3.305373	1.160937	-2.85	0.0050
PFOS^2	0.257576	0.12657	2.04	0.0434

Scatter Plot of HDL and PFOS, Antwerp, 1995



Linear Fit

HDL-Cholesterol = 55.2981 – 0.93355 PFOS

Summary of Fit

RSquare	0.019736
RSquare Adj	0.008337
Root Mean Square Error	12.32088
Mean of Response	53.5
Observations (or Sum Wgts)	88

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	262.842	262.842	1.7315
Error	86	13055.158	151.804	Prob>F
C Total	87	13318.000		0.1917

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	55.298149	1.895379	29.18	<.0001
PFOS	-0.933553	0.709469	-1.32	0.1917

Polynomial Fit degree=2

HDL-Cholesterol = 56.91 – 2.68656 PFOS + 0.24725 PFOS^2

Summary of Fit

RSquare	0.033054

RSquare Adj	0.010302
Root Mean Square Error	12.30867
Mean of Response	53.5
Observations (or Sum Wgts)	88

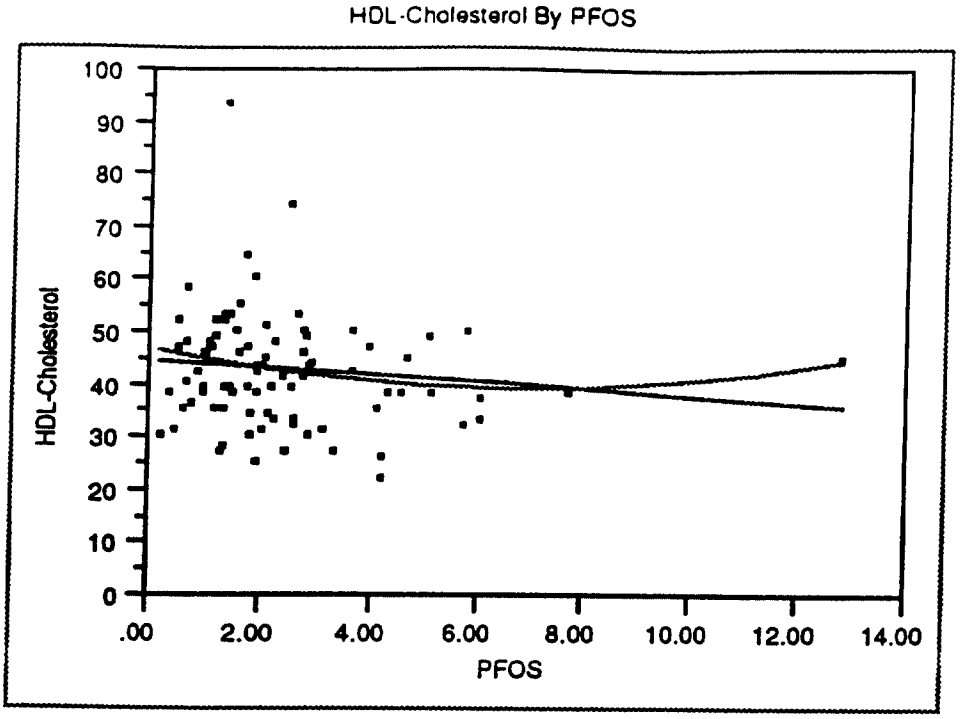
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	440.212	220.106	1.4528
Error	85	12877.788	151.503	Prob>F
C Total	87	13318.000		0.2397

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	56.910034	2.409276	23.62	<.0001
PFOS	-2.686556	1.768392	-1.52	0.1324
PFOS^2	0.2472466	0.228508	1.08	0.2823

Scatter Plot of HDL and PFOS, Decatur, 1995



Linear Fit

HDL-Cholesterol = 45.0317 – 0.7097 PFOS

Summary of Fit

RSquare	0.014998
RSquare Adj	0.003272
Root Mean Square Error	10.89577
Mean of Response	43.30233
Observations (or Sum Wgts)	86

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	151.843	151.843	1.2790
Error	84	9972.296	118.718	Prob>F
C Total	85	10124.140		0.2613

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	45.031672	1.928382	23.35	<.0001
PFOS	-0.709695	0.627527	-1.13	0.2613

Polynomial Fit degree=2

HDL-Cholesterol = 47.1802 – 2.18908 PFOS + 0.15422 PFOS^2

Summary of Fit

RSquare	0.028286

RSquare Adj	0.004872
Root Mean Square Error	10.88702
Mean of Response	43.30233
Observations (or Sum Wgts)	86

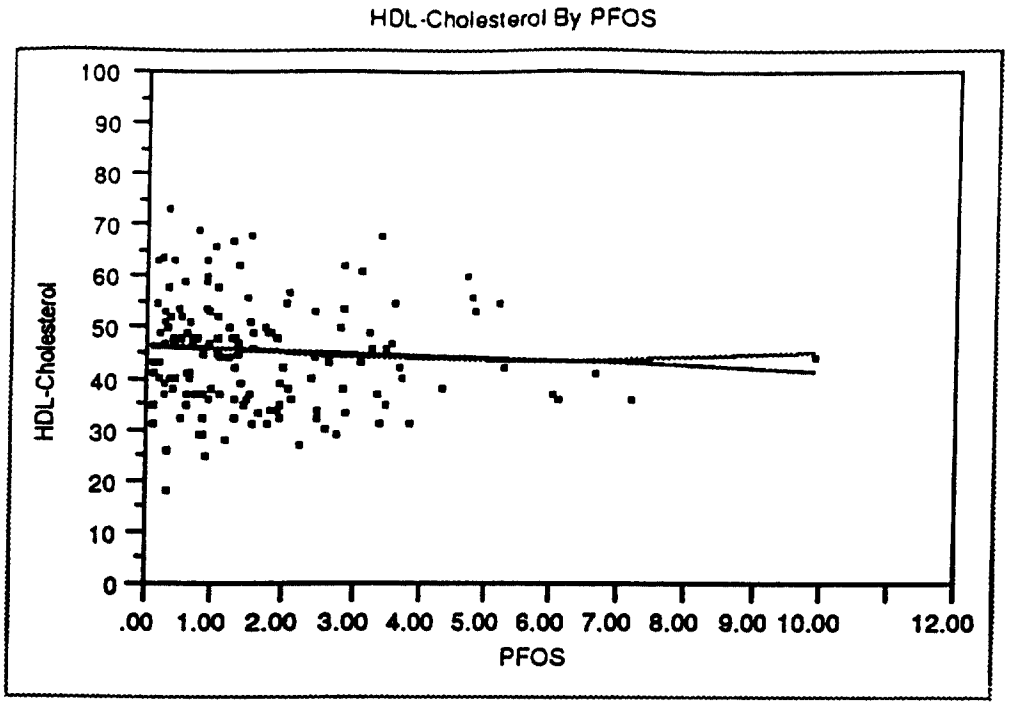
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	286.376	143.188	1.2081
Error	83	9837.764	118.527	Prob>F
C Total	85	10124.140		0.3040

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	47.180201	2.789208	16.92	<.0001
PFOS	-2.189082	1.523604	-1.44	0.1545
PFOS^2	0.1542222	0.144758	1.07	0.2898

Scatter Plot of HDL and PFOS, Both Locations Combined, 1997



Linear Fit

HDL-Cholesterol = 46.3275 – 0.45133 PFOS

Summary of Fit

RSquare	**0.004651**
RSquare Adj	-0.00212
Root Mean Square Error	10.57408
Mean of Response	45.53691
Observations (or Sum Wgts)	149

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	76.804	76.804	0.6869
Error	147	16436.243	111.811	Prob>F
C Total	148	16513.047		0.4086

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	46.327525	1.288559	35.95	<.0001
PFOS	-0.451333	0.544563	-0.83	0.4086

Polynomial Fit degree=2

HDL-Cholesterol = 46.8473 – 1.03203 PFOS + 0.08884 PFOS^2

Summary of Fit

RSquare	0.006173
RSquare Adj	-0.00744

Root Mean Square Error	10.60212
Mean of Response	45.53691
Observations (or Sum Wgts)	149

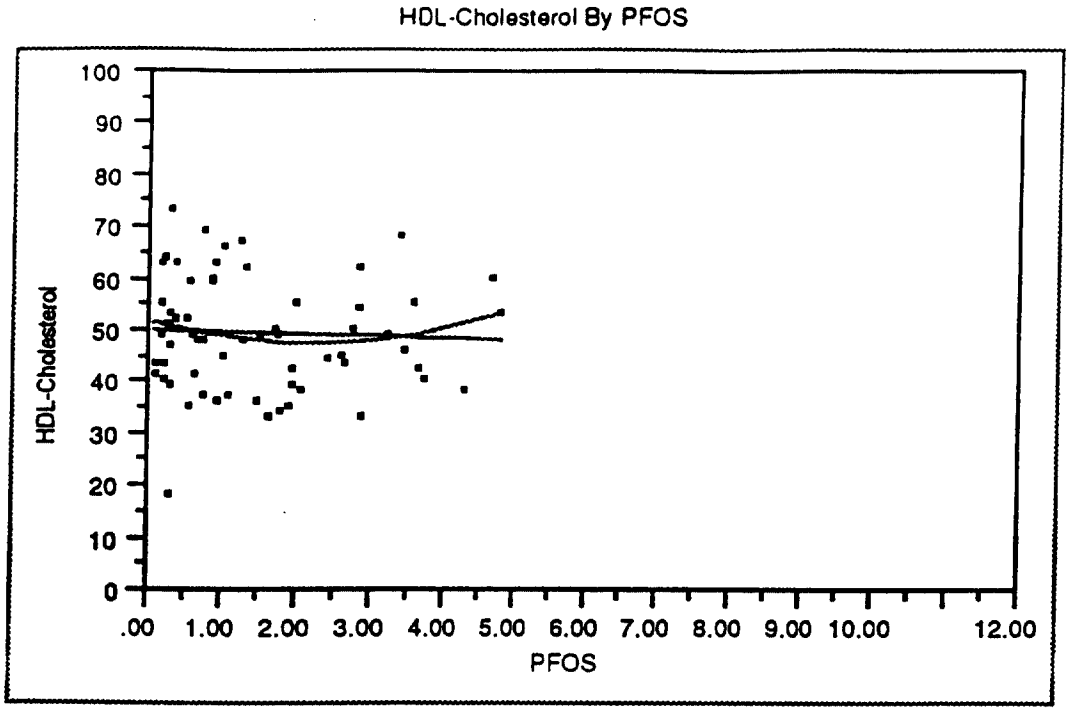
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	101.936	50.968	0.4534
Error	146	16411.111	112.405	Prob>F
C Total	148	16513.047		0.6363

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	46.847332	1.696367	27.62	<.0001
PFOS	-1.032032	1.343985	-0.77	0.4438
PFOS^2	0.0888404	0.187882	0.47	0.6370

Scatter Plot of HDL and PFOS, Antwerp, 1997



Linear Fit

HDL-Cholesterol = 50.2864 – 0.41131 PFOS

Summary of Fit

RSquare	0.00232
RSquare Adj	-0.01352
Root Mean Square Error	10.86492
Mean of Response	49.67692
Observations (or Sum Wgts)	65

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	17.2928	17.293	0.1465
Error	63	7436.9226	118.046	Prob>F
C Total	64	7454.2154		0.7032

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	50.286404	2.086111	24.11	<.0001
PFOS	-0.41131	1.074642	-0.38	0.7032

Polynomial Fit degree=2

HDL-Cholesterol = 52.4254 – 4.16781 PFOS + 0.90954 PFOS^2

Summary of Fit

RSquare	0.020968
RSquare Adj	-0.01061

Root Mean Square Error	10.84934
Mean of Response	49.67692
Observations (or Sum Wgts)	65

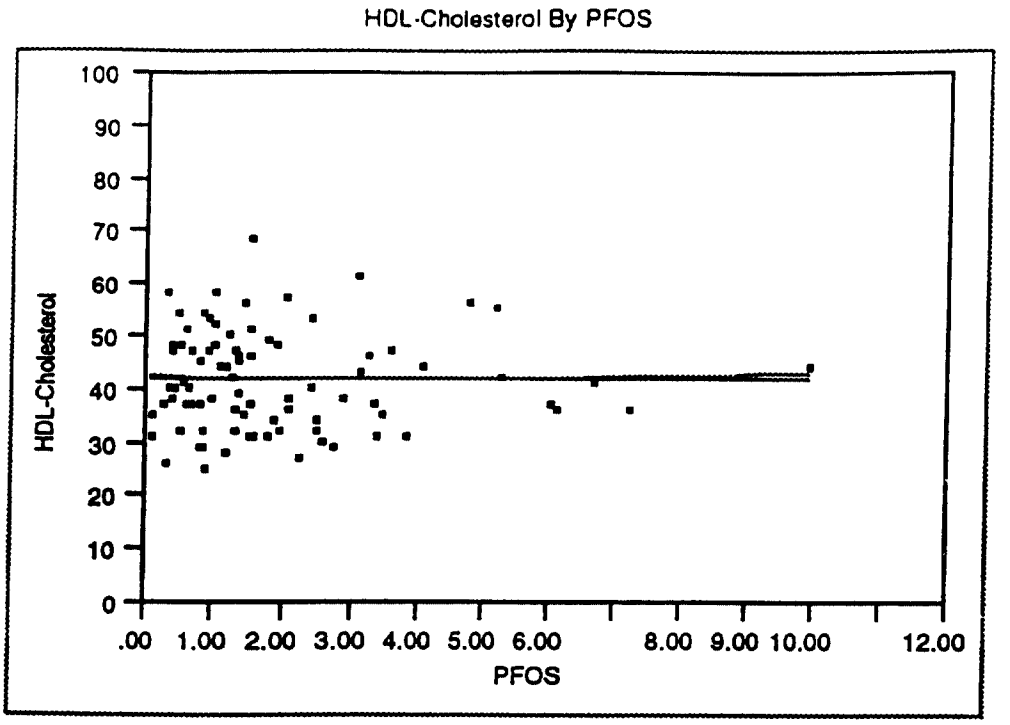
Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	156.3026	78.151	0.6639
Error	62	7297.9128	117.708	Prob>F
C Total	64	7454.2154		0.5184

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	52.425357	2.865909	18.29	<.0001
PFOS	-4.167812	3.619456	-1.15	0.2539
PFOS^2	0.9095417	0.836957	1.09	0.2814

Scatter Plot of HDL and PFOS, Decatur, 1995



Linear Fit

HDL-Cholesterol = 42.3281 + 0.00268 PFOS

Summary of Fit

RSquare	2.712e-7
RSquare Adj	-0.01219
Root Mean Square Error	9.293759
Mean of Response	42.33333
Observations (or Sum Wgts)	84

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	1	0.0019	0.0019	0.0000
Error	82	7082.6647	86.3740	Prob>F
C Total	83	7082.6667		0.9962

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	42.328069	1.508131	28.07	<.0001
PFOS	0.002685	0.569385	0.00	0.9962

Polynomial Fit degree=2

HDL-Cholesterol = 42.5348 – 0.20021 PFOS + 0.02723 PFOS^2

Summary of Fit

RSquare	0.000231

001238

RSquare Adj	-0.02446
Root Mean Square Error	9.349875
Mean of Response	42.33333
Observations (or Sum Wgts)	84

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	2	1.6333	0.8166	0.0093
Error	81	7081.0334	87.4202	Prob>F
C Total	83	7082.6667		0.9907

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	42.534847	2.143189	19.85	<.0001
PFOS	-0.20021	1.591892	-0.13	0.9002
PFOS^2	0.0272273	0.199313	0.14	0.8917

Serum Perfluorooctane Sulfonate and Hepatic and Lipid Clinical Chemistry Tests in Fluorochemical Production Employees

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The 3M Company manufactures fluorochemicals, which have as a precursor perfluorooctane sulfonyl fluoride ($C_8F_{17}SO_2F$). These compounds may be expected to transform metabolically, to an undetermined degree, to perfluorooctane sulfonate (PFOS, $C_8F_{17}SO_3^-$) as an end-stage metabolite. Subchronic studies in rats and primates indicate a potential for cumulative toxicity with PFOS with the primary effect related to metabolic wasting with hypolipidemia as a consistent finding. Biennial medical surveillance has been offered to the company's fluorochemical production workers located in Decatur, Alabama, and Antwerp, Belgium. In 1995, the mean serum PFOS level, as measured by high-performance liquid chromatography mass spectrometry, for 178 male employees was 2.19 parts per million (ppm; range, 0.00 to 12.83 ppm), and in 1997, for 149 male employees, it was 1.75 ppm (0.10 to 9.93 ppm). Our analyses suggest that among these production employees, there were no substantial changes in serum hepatic enzymes, cholesterol, or lipoproteins associated with PFOS levels less than 6 ppm. It was not possible to derive inferences from the few employees who had serum PFOS levels ≥ 6 ppm. These results may be due to the lower levels of serum PFOS measured among these production employees, compared to those suspected to cause effects in laboratory animals.

The 3M Company manufactures products that contain fluorochemicals, either as intentional components or residual impurities, that have as a precursor molecule perfluorooctane sulfonyl fluoride ($C_8F_{17}SO_2F$). Workplace exposure may occur by inhalation, ingestion, and dermal routes. These fluorochemicals may transform metabolically, to an undetermined degree, to perfluorooctane sulfonate (PFOS; $C_8F_{17}SO_3^-$) as an end-stage metabolite.[1] Potassium perfluorooctane sulfonate ($C_8F_{17}SO_3^-K^+$) is itself a surfactant used as a wetting and foaming agent in industrial and commercial processes.

PFOS is known to concentrate primarily in the liver and, to a 10-fold lesser extent, in the plasma of rats.[2] There appears to be significant enterohepatic circulation of PFOS with both urinary and fecal excretion.[2,3] Cholestyramine decreased the retention of radiolabeled PFOS in the liver and plasma and increased its elimination via feces.[3] Subchronic studies in rats and primates suggest there is cumulative toxicity with PFOS.[4-7] Lowered serum total cholesterol levels appear to be an early consistent finding, with cumulative toxicity resulting in metabolic wasting and ultimately death. Although the mechanism of toxicity in laboratory animals is not fully understood, it may be due to an effect on fatty acid transport and metabolism, membrane function, peroxisome proliferation, and/or mitochondrial bioenergetics.[8-11]

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Voluntary biennial medical surveillance of fluorochemical production employees has been routinely performed since the late 1970s at 3M's Decatur, Alabama, and Antwerp, Belgium, locations. Total serum organic fluorine levels were analyzed until the mid-1990s when serum PFOS determination, quantifiable by high-performance liquid chromatography mass spectrometry, became available. The purpose of this study was to provide a cross-sectional analysis of the medical surveillance data in relation to the employees' serum PFOS levels.

Methods

Fluorochemical Production

Fluorochemical production began in Decatur in 1961 and Antwerp in 1976. In general, perfluorinated chemicals are produced via an electrochemical process: a solution of organic substrate is electrolyzed in anhydrous hydrogen fluoride at a low voltage.[12] The products of this electrolysis cell reaction are highly fluorinated compounds, with the end-product defined by the starting material. Potential for workplace exposure to those fluorochemicals that metabolize to PFOS can occur in the electrochemical cell, the reactor, mixing, drumming, and packaging areas, as well as in the plant's quality assurance and research and development laboratories.

Subject Selection

Voluntary fluorochemical medical surveillance examinations are offered biennially to approximately 200 Antwerp and 300 Decatur production employees. In 1995, a total of 178 male employees (Antwerp: $n = 88$; Decatur: $n = 90$) participated in the medical surveillance examinations. In 1997, 149 male employees (Antwerp: $n = 65$; Decatur: $n = 84$) participated. (There were too few female employees to include in the data analysis.) Sixty-one employees participated in both years. This reduction was due to a large turnover of employees at both plant locations during 1996 and 1997. The surveillance consisted of a medical questionnaire; measurement of height, weight, and blood pressure; standard clinical chemistry and hematology tests; and determination of serum PFOS levels.

PFOS Analysis

In 1995, the analysis for serum PFOS was conducted by 3M's Environmental Laboratory in St. Paul, Minnesota. The method used tetrabutylammonium to ion-pair with PFOS in serum.[13] The ion-pairs were then extracted with ethyl acetate. The abstraction product was then analyzed using high-performance liquid chromatography–thermospray mass spectrometry. In 1997, the serum samples were analyzed by liquid chromatography/mass spectrometry, using selected ion monitoring in the negative-ion mode.[14,15]

Laboratory Analyses

For both time periods and plant locations, United Laboratory Services (St. Paul, MN) performed the standard hematological and serum chemistry tests. These included the following: alkaline phosphatase (IU/L), gamma glutamyl transferase (IU/L), aspartate aminotransferase (IU/L), alanine aminotransferase (IU/L), total and direct bilirubin (mg/dL), cholesterol (mg/dL), low-density protein (mg/dL), high-density cholesterol (HDL; mg/dL) and triglycerides (mg/dL). Clinical chemistry, hematology, and serum PFOS determinations were performed on overnight fasted blood samples.

Data Analysis

Descriptive, simple, and stratified analyses, analyses of variance, and ordinary multivariable regression were used to evaluate associations between PFOS and each hematological and clinical chemistry test. Age, body mass index (BMI; kg/m^2), current alcohol consumption (drinks per day), and cigarette use (cigarettes smoked per day) were potential confounding factors that were considered in the analyses. For stratified analyses, employees were divided into four PFOS categories (0 to <1 ppm, 1 to <3 ppm, 3 to <6 ppm, and ≥6 ppm) to determine whether an effect could be detected at the highest serum PFOS levels. Other categorical levels were used that provided similar results. For multivariable regression analyses, serum PFOS and the potential confounders of age, BMI, alcohol use, and cigarette use were examined as continuous and categorical explanatory variables in the models. Multivariable regression models were fitted, with PFOS analyzed as a continuous variable, using linear as well as non-linear transformations in order to maximize the possibility of finding associations between PFOS and the dependent variable of interest. Natural log transformations of the dependent variables were performed, when necessary, to normalize variables and to enhance model fit. Traditional stepwise selection procedures were also utilized (selection in and out of model was set at $P = 0.1$), as well as taking into account other covariates that may be on the biologic pathway of effect.[16] We did not examine changes in measured PFOS between the two time periods because the estimated half-life of PFOS in the serum is believed to range between 1000 and 1500 days (J. H. Mandel, MD, unpublished data based on 4 years of serum measurements of three retirees, 1998). Study results were analyzed using the SAS System.[17]

Results

The distribution of employees, by serum PFOS exposure categorization, is presented in Table 1. Whereas 20% of the Decatur employees had exposures at ≥3 ppm for both years, this proportion in Antwerp declined from 25% in 1995 to 13% in 1997. For both years, 95% of the employees' serum PFOS levels were below 6 ppm. There were no PFOS measurements ≥6 ppm in Antwerp in 1997.

TABLE 1
Distribution of Employees, by Year, Location, and Perfluorooctane Sulfonate (PFOS) Exposure Level (in parts per million [ppm])

	1995 Data						1997 Data					
	All Employees		Antwerp		Decatur		All Employees		Antwerp		Decatur	
PFOS	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
0 to <1 ppm	45	25	34	39	11	12	60	40	31	48	29	35
1 to <3 ppm	91	51	32	36	59	66	63	43	25	38	38	45
3 to <6 ppm	35	20	19	22	16	18	21	14	9	14	12	14
≥6 ppm	7	4	3	3	4	4	5	3	0	0	5	6
Total	178	100	88	100	90	100	149	100	65	100	84	100

TABLE 2
Mean Values of PFOS, Demographic, Serum Chemistry, and Hematologic Parameters for Antwerp and Decatur, 1995 and 1997 Examinations[a]

	1995 Data		1997 Data	
Variable	Antwerp	Decatur	Antwerp	Decatur
PFOS, ppm	1.93	2.44	1.48	1.96
Age, years	37***	45	33***	44
BMI, kg/m^2	23.9***	29.2	23.5***	30.0
Cigarettes, no. per day	4.7*	7.9	5.5	6.6
Alcohol, drinks per day	1.3***	0.2	1.1***	0.1
Alk Phos, IU/L	75***	97	70***	87
GGT, IU/L	41	48	26*	36
AST, IU/L	26*	29	27	26
ALT, IU/L	44	47	31	34
T. bilirubin, mg/dL	0.86***	0.58	0.80***	0.58
D. bilirubin, mg/dL	0.22	0.21	0.15***	0.12
Cholesterol, mg/dL	214	218	206	215
LDL, mg/dL	138	136	134	137
HDL, mg/dL	54***	43	50***	42
Triglycerides, mg/dL	115***	187	111***	192

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.
[a] BMI, body mass index; Alk Phos, alkaline phosphatase; GGT, gamma glutamyl transferase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T., total; D., direct; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

The mean values for PFOS, demographic, and liver and lipid test results, by location, are presented in Table 2. The Antwerp male employee population was significantly younger than that at Decatur, had lower BMIs, and had higher self-reported daily consumption of alcohol. In addition, their clinical profiles were different for several tests. For both time periods, the Antwerp employees had lower mean alkaline phosphatase and triglyceride values and higher total bilirubin and HDL values.

Table 3 lists the mean, median, standard deviation, and range of the covariates and hepatic enzymes, cholesterol, and lipoproteins by four levels of PFOS categorization (0 to <1, 1 to <3, 3 to <6, and ≥6 ppm) for the combined populations for each surveillance year. (Hematology and other clinical chemistry data were unremarkable and are not shown.) Several observations are noteworthy. First, the mean for the ≥6 ppm PFOS category was one order of magnitude higher than the lowest PFOS category (0 to <1 ppm) for both years. Also, the means of the four PFOS categories were significantly different from each other. Second, there was only one variable, total bilirubin, that had significant ($P < 0.05$) F tests for differences in means in both years of analysis. Stratification by plant location and surveillance year did not result in significant findings for total bilirubin or direct bilirubin (Table 4). Third, mean serum cholesterol levels remained constant (1995) or increased (1997) with higher PFOS category levels, although the HDL mean values trended lower among those employees with the highest PFOS categorizations. Stratification by plant location and surveillance year did not result in significantly different mean cholesterol or HDL values by PFOS categories (Table 5). Finally, it should be noted that employees in the highest PFOS category were older and had higher BMIs than did employees in the lowest PFOS category. Furthermore, in 1997, the employees with ≥6 ppm serum PFOS levels were only from Decatur (Table 1); thus the analyses may be confounded because Decatur employees were generally older and heavier than Antwerp employees. For example, in 1997 the mean HDL level for the ≥6 ppm group was 40 mg/dL (Table 3). However, this mean value was solely from Decatur employees.

Linear and nonlinear relationships between PFOS and the dependent variables of interest, taking into account the potential confounding affects of age, BMI, alcohol, and cigarettes, resulted in many analyses. Total bilirubin showed a significant

TABLE 3
Mean, Median, Standard Deviation (SD) of Mean and Range of PFOS, by Demographic and Serum Chemistries for Antwerp and Decatur Employees Combined, for 1995 (n = 178) and 1997 (n = 147)

	1995 Data				1997 Data			
PFOS* (ppm)	Mean	Median	SD	Range	Mean	Median	SD	Range
PFOS, ppm								
0 to <1	0.49[1]	0.50	0.27	0.00 to 0.90	0.52[1]	0.52	0.27	0.10 to 0.97
1 to <3	1.82[1]	1.77	0.58	1.00 to 2.91	1.78[1]	1.64	0.56	1.02 to 2.89
3 to <6	4.12[1]	3.97	0.81	3.00 to 5.80	3.87[1]	3.59	0.70	3.09 to 5.30
≥6	8.17[1]	7.73	2.52	6.06 to 12.83	7.20[1]	6.68	1.59	6.05 to 9.3
	F value = 321.9, $P < 0.0001$				F value = 367.6, $P < 0.0001$			
Age, years								
0 to <1	37	36	8	21 to 58	36	34	11	21 to 62
1 to <3	42[2]	41	9	25 to 60	42[2]	41	9	24 to 63
3 to <6	40	40	7	26 to 55	41	42	5	32 to 54
≥6	45	43	7	37 to 56	42	45	9	29 to 52
	F value = 3.7, P = 0.02				F value = 5.1, P = 0.002			
Alcohol, drinks per day								
0 to <1	0.8	0.6	0.9	0 to 3.6	0.5	0.1	0.8	0 to 4.3
1 to <3	0.5	0.1	0.7	0 to 3.6	0.5	0.1	0.8	0 to 5.0
3 to <6	1.2	0.3	1.9	0 to 6.0	1.0	0.1	1.8	0 to 7.1
≥6	0.7	0.0	1.1	0 to 2.9	0.2	0.1	0.2	0.1 to 0.8
	F value = 4.0, P = 0.009				F value = 1.8, P = 0.15			
BMI, kg/m^2								
0 to <1	25.5	24.8	4.2	17.9 to 38.7	26.0	24.9	4.9	20.1 to 41.7
1 to <3	27.7	26.3	5.8	19.6 to 60.7	27.7	26.4	5.7	18.1 to 48.5
3 to <6	24.9[3]	25.0	3.8	17.9 to 32.5	27.3	27.9	4.4	19.1 to 36.0
≥6	27.7	29.4	4.2	20.6 to 33.0	30.8	29.7	4.0	26.1 to 36.2
	F value = 3.7, P = 0.02				F value = 2.1, P = 0.10			
Cigarettes, no. per day								
0 to <1	2.6	0.0	6.4	0.0 to 25.0	4.7	0.0	9.4	0 to 40
1 to <3	6.8	0.0	11.3	0.0 to 40.0	8.2	0.0	11.3	0 to 40
3 to <6	10.6	8.0	12.4	0.0 to 40.0	4.1	0.0	8.3	0 to 30
≥6	0.4	0.0	1.1	0.0 to 3.0	6.0	0.0	13.4	0 to 30
	F value = 4.8, P = 0.003				F value = 1.5, P = 0.23			
Alkaline phosphatase, IU/L								
0 to <1	80	78	22	31 to 158	77	73	17	49 to 132
1 to <3	89	89	27	49 to 191	83	79	23	41 to 163
3 to <6	86	85	21	32 to 124	76	74	22	29 to 120
≥6	88	85	24	63 to 136	88	84	18	65 to 114
	F value = 1.3, P = 0.28				F value = 1.2, P = 0.32			
GGT, U/L								
0 to <1	43	31	28	16 to 155	28	22	20	10 to 142
1 to <3	47	36	39	2 to 293	36	25	33	10 to 179
3 to <6	40	39	15	21 to 80	28	27	14	13 to 71
≥6	43	33	18	28 to 79	33	37	12	17 to 48
	F value = 0.5, P = 0.71				F value = 1.1, P = 0.34			
AST, U/L								
0 to <1	27	25	13	15 to 96	27	25	7	13 to 53
1 to <3	29	26	12	14 to 90	26	25	7	15 to 56
3 to <6	25	24	5	13 to 37	25	23	7	14 to 43
≥6	33	33	6	26 to 43	29	28	3	26 to 34
	F value = 1.8, P = 0.14				F value = 0.5, P = 0.67			
ALT, IU/L								
0 to <1	48	43	20	27 to 118	31	30	11	13 to 60
1 to <3	46	42	21	18 to 183	33	29	16	10 to 89
3 to <6	42	41	7	30 to 59	34	31	18	14 to 82
≥6	51	49	17	29 to 82	41	45	10	25 to 49
	F value = 1.0, P = 0.38				F value = 0.9, P = 0.46			
T. bilirubin, mg/dL								
0 to <1	0.88	0.70	0.50	0.40 to 2.90	0.77	0.60	0.40	0.30 to 2.30
1 to <3	0.66[2]	0.60	0.30	0.20 to 1.50	0.61[2]	0.60	0.21	0.30 to 1.30
3 to <6	0.64[2]	0.60	0.28	0.20 to 1.40	0.63	0.50	0.31	0.40 to 1.30
≥6	0.76	0.70	0.23	0.50 to 1.20	0.58	0.50	0.24	0.40 to 1.00
	F value = 4.4, P = 0.005				F value = 2.9, P = 0.04			

TABLE 3
Continued.

PFOS* (ppm)	1995 Data Mean	Median	SD	Range	1997 Data Mean	Median	SD	Range
D. bilirubin, mg/dL								
0 to <1	0.22	0.20	0.05	0.02 to 0.40	0.15	0.10	0.07	0.10 to 0.40
1 to <3	0.21	0.20	0.06	0.10 to 0.40	0.12[2]	0.10	0.04	0.10 to 0.20
3 to <6	0.21	0.20	0.04	0.20 to 0.30	0.12	0.10	0.04	0.10 to 0.20
≥6	0.20	0.20	0.02	0.10 to 0.30	0.10	0.10	0.00	0.10 to 0.10
	F value = 0.6, *P* = 0.58				*F* value = 3.5, *P* = 0.02			
Cholesterol, mg/dL								
0 to <1	219	215	47	100 to 340	198	197	40	110 to 280
1 to <3	216	213	43	118 to 315	216	219	42	116 to 365
3 to <6	214	214	35	128 to 278	229[2]	224	29	192 to 321
≥6	213	221	36	160 to 251	229	238	26	186 to 250
	F value = 0.1, *P* = 0.96				*F* value = 4.3, *P* = 0.006			
LDL, mg/dL								
0 to <1	140	137	43	29 to 261	124	128	34	50 to 205
1 to <3	134	134	40	44 to 234	141	134	38	61 to 290
3 to <6	137	135	34	65 to 190	148[2]	142	24	111 to 196
≥6	142	136	32	95 to 178	145	156	26	103 to 164
	F value = 0.2, *P* = 0.87				*F* value = 3.7, *P* = 0.01			
HDL, mg/dL								
0 to <1	53	53	13	31 to 94	46	48	11	19 to 74
1 to <3	48	47	13	26 to 94	44	45	10	28 to 69
3 to <6	45	46	11	23 to 74	48	47	10	32 to 69
≥6	45	46	9	34 to 61	40	38	4	37 to 45
	F value = 2.9, *P* = 0.04				*F* value = 1.1, *P* = 0.34			
Triglycerides, mg/dL								
0 to <1	129	96	98	41 to 622	148	107	162	38 to 1209
1 to <3	161	133	107	41 to 651	156	122	108	44 to 534
3 to <6	158	142	88	34 to 413	166	158	92	45 to 394
≥6	132	151	45	64 to 187	220	191	83	149 to 352
	F value = 1.1, *P* = 0.35				*F* value = 0.5, *P* = 0.67			

* See Table 1 for sample size by year.
[1] Mean is significantly different ($P < 0.05$, Bonferroni (Dunn) test) from the mean of the other PFOS categories.
[2] Mean is significantly different ($P < 0.05$, Bonferroni (Dunn) test) from the mean of 0 to <1 ppm PFOS category.
[3] Mean is significantly different ($P < 0.05$, Bonferroni (Dunn) test) from the mean of 1 to <3 ppm PFOS category.

quadratic association with PFOS for Decatur employees. That is, total bilirubin levels initially declined but subsequently increased with increasing PFOS levels. This association was not observed in the Antwerp employee population, which had higher total bilirubin levels. In 1997, serum cholesterol levels were positively associated (linearly) with serum PFOS, after adjustment for potential confounding factors among Decatur employees (data not shown). This association was not observed with serum PFOS and cholesterol in 1995 among Decatur employees or in either time period with the Antwerp employees. Stratification of the data by plant (Table 5) and multivariable analyses (data not shown) showed no consistent associations between PFOS and HDL. For both plants combined, HDL levels were significantly negatively associated (linearly) with PFOS in 1995, after adjustment for possible confounding factors, but this was not observed in 1997.

Discussion

We conducted two cross-sectional analyses of surveillance data to examine the associations between serum PFOS levels and several hematological and clinical chemistry tests in male fluorochemical production employees. For both years, 95% of the measured serum PFOS levels were below 6 ppm. Because the Antwerp and Decatur employees were dissimilar by age, BMIs, and self-reported alcohol use, we conducted combined as well as separate analyses by plant location. These three demographic factors explain, at least partially, why the Antwerp employees had lower mean serum triglycerides and higher HDL levels than the Decatur employees.[18–22]

Clinical hepatic enzyme tests were not associated with the employees' serum PFOS levels. This was an important question to address because PFOS has been reported (1) to be a peroxisome proliferator in rats[8,10]; (2) to result in increased plasma liver transaminase tests in a

TABLE 4
Mean, Median (Med), Standard Deviation (SD) of Mean and Range of PFOS, and Total and Direct Bilirubin Levels, by Year and Plant Location

	Antwerp				Decatur			
PFOS* (ppm)	Mean	Med	SD	Range	Mean	Med	SD	Range
1995 Data								
T. bilirubin, mg/dL								
0 to <1	0.96	0.80	0.55	0.40 to 2.90	0.65	0.60	0.16	0.40 to 0.90
1 to <3	0.83	0.80	0.26	0.40 to 1.30	0.57	0.50	0.28	0.20 to 1.50
3 to <6	0.75	0.70	0.30	0.30 to 1.40	0.51	0.50	0.18	0.20 to 1.00
≥6	0.93	0.90	0.25	0.70 to 1.20	0.63	0.65	0.10	0.50 to 0.70
	F value = 1.2, P = 0.31				F value = 0.7, P = 0.54			
D. bilirubin, mg/dL								
0 to <1	0.23	0.20	0.06	0.20 to 0.40	0.20	0.20	0.00	0.20 to 0.20
1 to <3	0.22	0.20	0.04	0.20 to 0.30	0.20	0.20	0.06	0.10 to 0.40
3 to <6	0.21	0.20	0.03	0.20 to 0.30	0.20	0.20	0.04	0.20 to 0.30
≥6	0.20	0.20	0.00	0.20 to 0.20	0.20	0.20	0.08	0.10 to 0.30
	F value = 0.7, P = 0.55				F value = 0.4, P = 0.74			
1997 Data								
T. bilirubin, mg/dL								
0 to <1	0.90	0.80	0.46	0.40 to 2.30	0.63	0.60	0.30	0.30 to 1.40
1 to <3	0.68	0.70	0.23	0.30 to 1.30	0.56	0.50	0.18	0.30 to 1.00
3 to <6	0.79	0.70	0.40	0.30 to 1.30	0.51	0.50	0.16	0.30 to 0.90
≥6	—	—	—	—	0.58	0.50	0.24	0.40 to 1.00
	F value = 2.3, P = 0.11				F value = 1.0, P = 0.41			
D. bilirubin, mg/dL								
0 to <1	0.16	0.20	0.08	0.10 to 0.40	0.13	0.10	0.06	0.10 to 0.30
1 to <3	0.13	0.10	0.05	0.10 to 0.20	0.11	0.10	0.03	0.10 to 0.20
3 to <6	0.14	0.10	0.05	0.10 to 0.20	0.11	0.10	0.03	0.10 to 0.20
≥6	—	—	—	—	0.10	0.10	0.00	0.10 to 0.10
	F value = 2.2, P = 0.12				F value = 1.3, P = 0.28			

* See Table 1 for sample sizes by year.

subchronic rat study[4]; and (3) to increase serum aspartate aminotransferase and lower alkaline phosphatase levels in a subchronic rhesus monkey study.[5]

There appears to be significant enterohepatic circulation of PFOS with both urinary and fecal excretion in the rat.[2,3] Although we observed a quadratic relation between PFOS and total bilirubin in our multivariable analyses with the Decatur employee population, interpretation of these data is difficult, given the narrow range of PFOS serum levels associated with the total bilirubin values. Interestingly, the Antwerp employees' total bilirubin levels were significantly higher than the Decatur employees' levels. We suspect there may be a greater prevalence of Gilbert's syndrome[20,23] among the Antwerp employees. In 1995, 15 (17%) Antwerp employees had total bilirubin values ≥1.2 mg/dL, compared with three (3%) Decatur employees. Comparable percentages also existed in 1997. We are uncertain whether post-collection factors, including hemolysis, light, and heat, could have contributed to the differences in total bilirubin levels between the Antwerp and Decatur employees.[18] Unfortunately, total bilirubin was not analyzed in two subchronic rhesus monkey studies, which resulted in death of all animals in the 4.5 mg/kg/day PFOS dose group or higher.[5,6] Ongoing toxicology studies in rats and primates should provide additional perspectives regarding any biological effect between PFOS and bilirubin levels.

Our data do not suggest a reduction in total serum cholesterol with PFOS at the serum levels measured among these production employees. PFOS is a peroxisome proliferator in the rat, and hypolipidemia has been consistently observed in subchronic rat and primate toxicology studies.[5–8,10] Rhesus monkeys that had been administered PFOS at 4.5 mg/kg/day had mean serum cholesterol values that decreased from 183 mg/dL to 99 mg/dL within 30 days.[5] Rhesus monkeys administered 1.5 mg/kg/day had mean cholesterol levels that decreased from 195 mg/dL to 111 mg/dL within 90 days. A no-observable-effect level was seen for the 0.5 mg/kg dose group at 90 days. Serum PFOS measurements were not determined in these rhesus monkeys. However, data from a recent cynomolgus monkey dose-range-finding study suggested that hypolipidemia may be initially associated with serum PFOS levels in the range of 100 to 200 ppm.[7] Haughom and Spydevold suggested that the hypolipidemic effect of PFOS may be due to reduced liver activity of hydroxymethyl glutaric acid-CoA reductase and acyl-CoA cholesterol acyltransferase, with enhanced fatty acid oxidation in the liver.[9] Nabbefeld et al observed that PFOS has a high affinity for the fatty acid carrier proteins albumin and L-fatty acid–binding

TABLE 5
Mean, Median (Med), Standard Deviation (SD) of Mean and Range of PFOS, and Total and HDL Cholesterol, by Year and Plant Location

	Antwerp				Decatur			
PFOS* (ppm)	Mean	Med	SD	Range	Mean	Med	SD	Range
1995 Data								
Cholesterol, mg/dL								
0 to <1	220	219	50	100 to 340	215	208	39	154 to 276
1 to <3	206	211	49	118 to 315	221	218	39	132 to 300
3 to <6	217	215	30	178 to 266	209	213	42	128 to 278
≥6	223	221	16	208 to 240	206	206	47	160 to 251
	F value = 0.6, P = 0.61				F value = 0.5, P = 0.69			
HDL, mg/dL								
0 to <1	56	57	13	31 to 94	43	41	9	31 to 59
1 to <3	53	51	13	33 to 79	45	44	12	26 to 94
3 to <6	50	49	11	31 to 74	39	39	9	23 to 51
≥6	53	49	7	48 to 61	39	39	5	34 to 46
	F value = 1.1, P = 0.35				F value = 1.4, P = 0.25			
1997 Data								
Cholesterol, mg/dL								
0 to <1	193	190	41	110 to 277	204	208	38	145 to 277
1 to <3	213	205	48	116 to 365	218	226	39	152 to 290
3 to <6	228	223	38	192 to 321	230	230	23	197 to 280
≥6	—	—	—	—	229	238	26	186 to 250
	F value = 2.9, P = 0.07				F value = 2.0, P = 0.13			
HDL, mg/dL								
0 to <1	51	50	12	19 to 74	42	41	9	26 to 59
1 to <3	48	46	10	34 to 68	42	41	10	28 to 69
3 to <6	51	50	10	39 to 69	45	45	10	32 to 62
≥6	—	—	—	—	40	38	4	37 to 45
	F value = 0.8, P = 0.47				F value = 0.5, P = 0.67			

* See Table 1 for sample sizes by year.

protein in vivo. This could potentially alter fatty acid transport, biochemistry, and metabolism, which conceivably could then lead to a decrease in cholesterol esterification and metabolic wasting.[11]

Several methodological issues should be considered in evaluating the results from our study. First, the cross-sectional design does not allow for a direct analysis of the temporality of an association. Second, the voluntary participation rates in the fluorochemical medical surveillance were not ideal among the eligible fluorochemical production employees. Third, the serum levels of PFOS that were measured may be below the no-effect level in laboratory animals. Fourth, PFOS concentrates primarily in the liver of laboratory animals. Serum measurements of PFOS may not adequately reflect body burden. Fifth, the two cross-sectional analyses cannot be viewed as independent populations. Sixty-one employees were studied in both years. This was due, in part, to a large turnover of employees at both plants between examinations. Sixth, there could be measurement error in important confounding variables. Analysis of the data of the 61 subjects who participated in both years showed that there was excellent correlation for the confounding factors of BMI (r = .92, P = 0.0001), self-reported aspects of alcohol consumption (r = .88, P = 0.0001), and cigarette smoking (r = .79, P = 0.0001). As expected, these 61 employees' serum PFOS levels for the 2 years were highly correlated (r = .92, P = 0.0001). Their results did not differ from those of the entire study population. Finally, the quality of medical surveillance data, prior to its use for studying an a priori hypothesis, can often be evaluated by whether known positive associations are observed. In this regard, we did observe various expected associations, such as cigarette smoking and elevated white blood cell counts and large BMIs, associated with elevated liver transaminase levels.[24,25]

In summary, our findings suggest that among these Antwerp and Decatur male fluorochemical production employees, there were no substantial changes in serum hepatic enzymes, cholesterol, or lipoproteins associated with PFOS levels less than 6 ppm. It is not possible to derive inferences from the few employees with serum levels ≥6 ppm. Limitations of this study include its cross-sectional design, the low voluntary participation rates among the employees, and the lower levels of serum PFOS measured among these employees, compared with those suspected to cause effects in laboratory animals.

Acknowledgment

The authors gratefully acknowledge the assistance of Michele Burlew.

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