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ABSTRACT

Analytical methods have recently been developed, using high performance liquid chromatography/electrospray tandem mass spectrometry (HPLC-ESMSMS), that can be used to measure specific perfluoroinated chemicals in serum and liver samples. A recently completed six-month feeding study of perfluorooctanesulfonate (PFOS, $C_8F_{17}SO_3^-$) to cynomolgus monkeys reported liver to serum ratios at end of study that were approximately 1:1 in the low- (0.03 mg/kg/day) and mid- (0.15 mg/kg/day) dose groups. A non-linear response with a plateau in serum levels was reported for the high dose group (0.75 mg/kg/day). These primate data suggested that serum PFOS levels may serve as an adequate marker of liver burden at levels less than 100 ppm (parts per million, ug/mL). The purpose of this investigation was to determine whether the 1:1 liver to serum ratio reported in this primate study was mirrored in PFOS levels measured in non-occupationally exposed humans. Average serum levels (30 ng/mL) in humans have been measured at levels slightly less than three orders of magnitude lower than the average low-dose group serum PFOS level (20 ug/mL) in the primate study.

For the present study, all human sera and liver donor tissue were obtained through the International Institute for the Advancement of Medicine (IIAM). IIAM is a non-profit organization whose purpose is to facilitate the placement of non-transplantable human organs and tissues for biomedical research and education. Upon acceptable donor qualifications, IIAM obtained 5 ml of blood and 10 grams of liver and then froze the samples until shipment to the 3M Medical Department. A total of 31 donor samples were obtained over an 18 month time period.

All samples were analyzed for quantitative determination of four perfluorochemicals: PFOS; perfluorosulfonamide (PFOSA; $C_8F_{17}SO_2NH_2$); perfluorooctanoate (PFOA; $C_7F_{15}CO_2^-$); and perfluorohexanesulfonate (PFHS; $C_6F_{13}SO_3^-$). Sera and liver samples were extracted using an ion-pairing extraction procedure. The extracts were quantitatively assayed using HPLC-ESMSMS and evaluated versus an unextracted curve. Extensive matrix spike studies were performed to evaluate the precision and accuracy of the analysis. These matrix spike studies indicated that the data can be considered to be accurate to within one standard deviation of the average fortified sample recovery. For example, the average fortified sample recovery of PFOS from human sera was 89% (SD 21%). The average fortified sample recovery of PFOS from human liver was 78% (SD 24%).

A total of 31 donor samples (16 male, 15 female) were obtained over an 18 month time period. Average age of the male donors was 50 years (SD 15.6, range 5-69) and 45 years (SD 18.5, range 13-74) for the female donors. Causes of death were intracranial hemorrhage (n = 16, 52%), motor vehicle accident (n = 7, 23%), head trauma (n = 4, 13%), brain tumor (n = 2, 6%), drug overdose (N = 1, 3%) and respiratory arrest (n = 1, 3%).

Serum PFOS ranged from <6.1 (limit of quantitation, LOQ) to 58.3 ng/mL with a mean of 17.7 ng/mL (95% CI 13.0 - 22.5) for the average of the 24 donor samples analyzed. In the calculation of arithmetic means, any serum PFOS values that were determined to be <LOQ were assigned values midpoint between zero and the <LOQ. Liver PFOS ranged from <3.7 (LOQ) to 57.0 ng/g with a mean of 18.8 ng/g (95% CI 14.1 - 23.5) for the average of the 30 donor liver samples analyzed; likewise, any liver PFOS

values that were determined to be <LOQ were assigned values midpoint between zero and the <LOQ. Fifteen (50%) of the 30 donors had liver analyses <LOQ.

A ranked distribution of the average PFOS serum and liver data for each of the 23 paired samples showed good correlation (Spearman's Rho = 0.41, $p < .05$). In these 23 pairs, the mean liver to serum ratio was 1.3:1 (95% CI 0.9:1 - 1.7:1). Assuming the variation of the analytical error is one standard deviation, the mean liver:serum ratio ranged from a minimum of 0.8:1 (95% CI 0.5 - 1.0) to a maximum of 2.1:1 (95% CI 1.5 - 2.8). Although the study data were limited by the number of donors, it should be noted that the average serum PFOS levels determined in the present study were comparable to those reported elsewhere in nonoccupationally exposed human populations. The levels of PFOA, PFHS, and PFOSA were determined in the samples but we chose not to estimate liver:serum ratios for these analytes as 90% of the liver samples were determined to be <LOQ.

In conclusion, our data, as well as the data from the six month primate study, would suggest that a liver:serum ratio that approximates 1:1 for the non-occupationally-exposed human population may be a reasonable assumption to use in a risk characterization assessment of PFOS. Assuming the variation of the analytical error is one standard deviation, the mean liver:serum ratio in our study would range from a minimum of 0.8:1 (95% CI 0.5 - 1.0) to a maximum of 2.1:1 (95% CI 1.5 - 2.8). We chose not to estimate mean liver:serum ratios for PFOSA, PFOA and PFHS because 90% of these liver sample analyses were <LOQ.

INTRODUCTION

Evidence that organic fluorine can be characterized as a component of human blood has existed for more than 30 years, although compound-specific characterization of the organic fluorine was not complete (Guy et al, 1974). Hansen et al (2001) have recently published an analytical method utilizing high performance liquid chromatography/electrospray tandem mass spectrometry (HPLC/ESMSMS) to measure specific perfluoroinated chemicals in human serum and animal serum and liver. Among 65 human serum samples purchased from biological supply companies, Hansen et al reported perfluorooctanesulfonate (PFOS) may be the primary contributor to the total organic fluorine levels in human sera. The average reported serum PFOS level was 28.4 ng/mL (SD 13.6, range 6.7-81.5 ng/mL). Lesser amounts of perfluorooctanoate (PFOA, mean = 6.4 ng/mL, SD = 4.8), perfluorohexanesulfonate (PFHS, mean = 6.6 ng/mL, SD = 5.1) and perfluorooctanesulfonamide (PFOSA, mean < 1.6 ng/mL) were also determined. Hansen et al calculated that the combined organic fluorine content of these four fluorochemicals approximated the total organic fluorine measured by Guy et al in the 1970's. Additional analyses of human serum from nonoccupationally exposed population samples (3M Company, 1999) has collaborated the serum PFOS findings reported by Hansen et al.

During their serum method development, Hansen et al (2001) also developed comparable methods for the analysis of fluorochemical levels in animal liver. PFOS has been demonstrated to primarily distribute into the liver (Johnson et al, 1979) and enter the enterohepatic circulation. The scope of work described by Hansen et al did not include the analysis of fluorochemicals in any human livers.

In a recently completed six-month feeding study of PFOS to cynomolgus monkeys, liver to serum ratios at end of study were reported to be approximately 1:1 in the low- (0.03 mg/kg/day) and mid- (0.15 mg/kg/day) dose groups (Seacat et al, 2001). A linear increase in serum PFOS was observed throughout the course of study for the low- and mid-dose groups. In the primate study, PFOS was measured with comparable analytical techniques to those described by Hansen et al (2001). End-of-study low- and mid-dose groups' serum PFOS levels averaged 15 and 75 ppm, respectively, and liver PFOS levels averaged 20 and 60 ppm, respectively. No toxicologically significant effects were observed in the low- and mid-dose groups. A non-linear response with a plateau in serum levels was reported for the high dose group (0.75 mg/kg/day); decreased cholesterol was the most sensitive clinical response, occurring only at serum PFOS levels > 100 ppm. End-of-study serum and liver levels for the high-dose group averaged 172 ppm and 334 ppm, respectively. These studies suggested that serum PFOS levels may serve as an adequate marker of liver burden at levels less than 100 ppm .

The purpose of this investigation was to determine whether the 1:1 liver to serum ratio observed in the primate study in the low- and mid-dose groups also occurrs in individual, non-occupationally exposed humans. Previous measurements by Hansen et al (2001) and others (3M Company 1999), have indicated that the average serum PFOS levels in nonoccupationally exposed populations may be approximately three orders of magnitude lower than the average low-dose serum PFOS level (20 ppm) measured in the six month primate study by Seacat et al.

METHODS

Procurement of Human Tissue

All human sera and liver donor tissue were obtained through the International Institute for the Advancement of Medicine (IIAM). IIAM is a non-profit organization whose purpose is to facilitate the placement of non-transplantable human organs and tissues for biomedical research and education (Bode 1997). IIAM is a division of the Pennsylvania Regional Tissue and Transplant Bank. This is an inspected and accredited program which meets or exceeds all of the Food and Drug Administration (FDA) and America Association of Tissue Banks (AATB) standards. IIAM works with a network of organ procurement organizations and tissue banks throughout the United States from which tissues are received from postmortem donors. IIAM abides by U.S. legislation governing the consent process for organ and tissue donation in accordance with the Uniform Anatomical Gift Act and Title III of the National Organ Transplant Act. IIAM ensures and guarantees donor confidentiality per Title 45, Part 46 of the U.S. Code of Federal Regulations. All donors were tested for HIV-1 and HIV-2 antibodies, hepatitis B surface antigen, hepatitis C antibody, HTLV-1 antibody, syphilis, and hepatitis B core antibody (IgG plus IgM). In addition, one or more of the following tests were sometimes done: CMV antibody, hepatitis B surface antibody, hepatitis B core IgM and HIV p24 antigen. Results that suggested the donor was infectious precluded the distribution of the tissue. The Medical Department at the 3M Company completed an agreement with IIAM for human biological material for research use which included a letter of approval from the 3M Institutional Review Board. Upon acceptable donor qualifications, IIAM

obtained 5 ml of blood and 10 grams of liver and then froze the samples until shipment to the 3M Medical Department.

Analysis of Samples

All samples were analyzed for quantitative determination of four perfluorochemicals: PFOS ($C_8F_{17}SO_3^-$), PFOSA ($C_8F_{17}SO_2NH_2$), PFOA ($C_7F_{15}CO_2^-$) and PFHS ($C_6F_{13}SO_3^-$). Sera and liver samples were extracted using an ion-pairing extraction procedure, as detailed by Hansen et al (2001). The extracts were quantitatively assayed using HPLC-ESMSMS and evaluated versus an unextracted curve. The difficulties presented by background levels of fluorochemical in samples of "blank" test matrix were circumvented by utilizing rabbit sera as a surrogate matrix for extraction blanks. The linear range was determined by analyzing duplicate curves over a wide range (approx. 0.005-1.00 ug/mL). Each sample was extracted and analyzed in duplicate.

Extensive matrix spike studies were performed to evaluate the precision and accuracy of the analysis. Thirty one matrix spikes were prepared in human sera and 41 spikes were prepared in human liver. Spikes were prepared to approximate the levels of PFOS determined in the samples. It is not possible to verify true recovery of endogenous analyte from tissues without radiolabeled reference material. The only measurement of accuracy available, matrix spike studies, indicated that the data can be considered to be accurate to within one standard deviation of the average fortified sample recovery. For PFOS, the average fortified sample recovery in human sera was 89% (SD 21%). The average fortified sample recovery of PFOS from human liver was 78% (SD 24%). For the remaining analytes, PFOSA, PFHS and PFOA the average fortified sample recovery

in human sera were 86% (SD 30%), 55% (SD 26%) and 89% (SD 33%), respectively. Likewise, the average fortified sample recovery in human liver for these three analytes were 83% (SD 20%), 42% (SD 30%) and 67% (SD 30%), respectively. Results for sera are reported as ng/mL and for liver as ng/g.

RESULTS

Serum and/or liver samples were obtained from 31 donors over an 18 month time period (Table 1). Both serum and liver tissue were harvested from 23 donors; 7 donors contributed liver tissue only and 1 donor contributed serum only. Average age was 50 years (SD 15.6, range 5-69) for male donors (n = 16) and 45 years (SD 18.5, range 13-74) for female donors (n = 15). Causes of death as provided by IIAM were intracranial hemorrhage (n = 16, 52%), motor vehicle accident (n = 7, 23%), head trauma (n = 4, 13%), brain tumor (n = 2, 6%), drug overdose (N = 1, 3%) and respiratory arrest (n = 1, 3%).

Serum and liver results for PFOS are provided in Table 2. Serum PFOS levels determined to be less than the limit of quantitation (<LOQ) were assigned a value midpoint between zero and the LOQ. Mean serum PFOS level was 17.7 ng/mL (95% CI 13.0-22.5; range <6.1 - 58.3 ng/mL) for the average of the 24 serum donors' samples analyzed. The geometric mean for serum PFOS was 14.7 ng/mL (95% CI 11.1 - 19.4). Similarly, PFOS liver samples that were determined to be <LOQ were assigned a value midpoint between zero and the LOQ. Fifteen (50%) of the 30 liver donors had liver PFOS results at <LOQ. The mean liver PFOS was 18.8 ng/g (95% CI 14.1 - 23.5; range <3.7 - 57.0 ng/g) for the average of the 30 liver donors' samples analyzed. The geometric

mean for liver PFOS was 15.2 ng/g (95% CI 11.9 - 19.6). Mean PFOS levels between male and female donors for serum (male = 18.2 ng/mL; female = 17.2 ng/mL) or liver (male = 19.2 ng/g; female = 18.4 ng/g) were similar. No associations were observed between measured PFOS levels and age (data not shown).

A ranked distribution of the average PFOS serum and liver data for each of the 23 paired samples (sera and liver from the same individual) showed good correlation (Spearman's Rho = 0.41, $p < .05$). The mean liver to serum ratio was 1.3:1 (95% CI 0.9-1.7; range 0.2 - 3.7) for these 23 pairs. There was no significant difference between genders. Of the 13 male donors with paired samples, the mean liver:serum ratio was 1.3:1 (95% CI 0.8:1 - 1.9:1). Their mean serum and liver levels were 18.2 ng/mL (95% CI 10.2 - 26.2) and 20.8 ng/g (95% CI 11.4 - 30.1), respectively. Of the 10 female donors with paired samples, their mean liver:serum ratio was 1.3:1 (95% CI 0.6:1 - 2.0:1). Their mean serum and liver levels were 16.9 ng/mL (95% CI 10.0 - 23.7) and 16.3 ng/g (95% CI 9.3 - 23.2), respectively.

In order to study the maximum liver:serum ratio for PFOS, the average values were adjusted to accommodate the upper (liver) and lower (sera) quantitative limits described by the analytical accuracy (Table 3). As stated previously, the stated accuracy for PFOS determination in sera was 89+/-21% and 78+/-28% in liver. Assuming a one standard deviation increase in liver and one standard deviation decrease in serum, the liver:serum ratio became 2.1:1 (95% CI 1.5:1 - 2.8:1). In order to examine the lower limits of the liver:serum ratio the average liver PFOS levels were decreased by one standard deviation deviation and the sera PFOS levels were increased by one standard deviation which resulted in a liver:serum ratio of 0.8:1 (95% CI 0.5:1 - 1.0:1). [Note:

Assuming a two standard deviation increase in liver PFOS levels and a two standard deviation decrease in sera PFOS levels resulted in a maximum liver:serum ratio of 3.4:1 (95% CI 2.3:1 - 4.4:1). Likewise, a two standard deviation decrease in liver PFOS levels and a two standard deviation increase in sera PFOS levels resulted in a minimum liver:serum ratio of 0.5:1 (95% CI 0.3 - 0.6).

Provided in Tables 4 through 6 are the serum and liver values for the 31 donors for PFOSA, PFOA and PFHS, respectively. Unlike the results of PFOS determination where liver samples from 15 of the donors were determined to contain PFOS above the LOQ in at least one of the duplicate measurements, values greater than the LOQ for PFOSA, PFOA, and PFHS were sparse. A larger number of values less than the LOQ for PFOSA, PFOA, and PFHS were also determined in the analysis of sera samples. Serum values ranged from <LOQ (<1.3) to 22.1 ng/mL for PFOSA , < LOQ (<3.0) to 7.0 ng/mL for PFOA and < LOQ (<1.2) to 5.9 ng/mL for PFHS. Again, assuming the midpoint value between zero and the LOQ serum value for <LOQ samples, the mean serum PFOSA level was 4.5 ng/mL (95% CI 2.6 - 6.5). The geometric mean for serum PFOSA was 3.0 ng/mL (95% CI 2.0 - 4.4). The mean serum PFOA level was 3.1 ng/mL (95% CI 1.9 - 4.3) with a geometric mean of 2.5 ng/mL (95% CI 1.9 - 3.2). The mean serum PFHS level was 2.4 ng/mL (95% CI 1.7 - 3.0) with a geometric mean of 1.8 ng/mL (95% CI 1.3 - 2.6). We did not provide any liver/serum ratios in Tables 3 through 5 because more than 90% of the individual liver samples were determined to be <LOQ.

DISCUSSION

The purpose of this study was to estimate a mean liver:serum ratio in human donors from a nonoccupationally exposed population. Our data indicated that at non-occupationally exposed population serum levels (approximately 30 ng/mL), the mean liver:serum ratio for PFOS was 1.3:1 (95% CI 0.9 - 1.7) which is similar to the 1:1 ratio reported by Seacat et al (2001) in the low- and mid- dose groups in their six month primate study. Serum PFOS levels measured at the end of this primate study were considerably greater for the low- and mid-dose groups (average 20 and 75 ug/mL, respectively) than what has been determined in sera samples from nonoccupationally exposed human populations. Further refinement of this ratio for humans is unlikely without more precise analytical techniques that can consistently measure PFOS at lower levels as well as the other fluorochemical analytes that were measured this study. Although the study data were limited by the number of donors (raising the question about the representiveness of the sample set), it should be noted that the average serum PFOS levels determined in the present study were comparable to those reported elsewhere (Hansen et al, 2001; 3M Company, 1999).

In summary, our study data, as well as the results from the recently completed six month primate study (Seacat et al, 2001), suggest that a liver:serum ratio of 1:1 for the nonoccupationally exposed human population may be a reasonable approximation to use in a risk characterization process for PFOS. Assuming the variation of the analytical error is one standard deviation, the mean liver:serum ratio in our study would range from a minimum of 0.8:1 (95% CI 0.5 - 1.0) to a maximum of 2.1:1 (95% CI 1.5 - 2.8). We

chose not to estimate mean liver:serum ratios for PFOSA, PFOA and PFHS because 90% of these liver sample analyses were <LOQ.

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Table 1

Demographic and Cause of Death Distribution of 31 Human Donors

Individual	Gender	Race	Age	Cause of Death	Tissue Available	
					Serum	Liver
M1	Male	White	5	MVA	No	Yes
M2	Male	White	34	Brain tumor	Yes	Yes
M3	Male	Hispanic	38	MVA	Yes	Yes
M4	Male	Black	41	Head trauma	Yes	Yes
M5	Male	White	43	MVA**	Yes	Yes
M6	Male	Hispanic	46	ICH	Yes	Yes
M7	Male	White	52	Head trauma	Yes	Yes
M8	Male	White	55	ICH	Yes	Yes
M9	Male	White	56	MVA	Yes	Yes
M10	Male	White	56	Head trauma	Yes	Yes
M11	Male	Hispanic	57	ICH	Yes	Yes
M12	Male	White	58	ICH	No	Yes
M13	Male	Asian	60	ICH	No	Yes
M14	Male	White	64	ICH*	Yes	Yes
M15	Male	White	64	ICH	Yes	Yes

Table 1 (continued)

M16	Male	White	69	ICH	Yes	Yes
F1	Female	White	13	Brain tumor	No	Yes
F2	Female	White	18	MVA	No	Yes
F3	Female	White	26	Drug overdose	Yes	Yes
F4	Female	White	30	Respiratory arrest	Yes	Yes
F5	Female	White	37	ICH	Yes	Yes
F6	Female	White	38	MVA	No	Yes
F7	Female	White	42	ICH	Yes	No
F8	Female	Unknown	44	ICH	Yes	Yes
F9	Female	White	47	ICH	Yes	Yes
F10	Female	White	51	MVA	Yes	Yes
F11	Female	White	58	ICH	Yes	Yes
F12	Female	White	60	ICH	Yes	Yes
F13	Female	White	66	ICH	Yes	Yes
F14	Female	White	70	Head trauma	Yes	Yes
F15	Female	White	74	ICH	No	Yes

*ICH = Intracranial hemorrhage
**MVA = Motor vehicle accident

Table 2

PFOS Serum, Liver and Liver Serum Ratios for 31 Human Donors

Individual	Serum (ng/ml) Analysis	Serum (ng/ml) Mean	Liver (ng/g) Analysis	Liver (ng/g) Mean	Liver/Serum Ratio
M1	No serum	-	<LOQ (18.4) <LOQ (18.4)	<LOQ (18.4)	-
M2	13.9 13.2	13.6	<LOQ (4.5) 4.5	<4.5	<0.3:1
M3	9.8 10.8	10.3	<LOQ (18.4) <LOQ (18.4)	<LOQ (18.4)	<1.8:1
M4	15.6 16.4	16.0	13.4 18.0	15.7	1.0:1
M5	15.5 16.5	16.0	36.4 43.6	40.0	2.5:1
M6	20.4 18.6	19.5	<LOQ (18.4) <LOQ (18.4)	<LOQ (18.4)	<1.0:1
M7	9.4 9.5	9.5	<LOQ (36.8) <LOQ (36.8)	<LOQ (36.8	<3.9:1
M8	7.4 7.7	7.6	22.7 20.7	21.7	2.9:1
M9	25.3 24.5	24.9	14.6 16.2	15.4	0.6:1
M10	14.5 13.9	14.2	12.4 10.4	11.4	0.8:1

Table 2 (continued)

M11	11.9 13.9	12.9	<LOQ (18.4) <LOQ (18.4)	<LOQ (18.4)	<1.4:1
M12	No serum	-	18.9 18.5	18.7	-
M13	No serum	-	<LOQ (18.4) <LOQ (18.4)	<LOQ (18.4)	-
M14	58.3 55.7	57.0	47.0 41.4	44.2	<0.8:1
M15	29.4 25.9	27.6	57.0 50.6	53.8	1.9:1
M16	8.1 6.9	7.5	<LOQ (36.8) <LOQ (36.8)	<LOQ (36.8)	<4.9:1
F1	No serum	-	<LOQ (36.8) <LOQ (36.8)	<LOQ (36.8)	-
F2	No serum	-	17.2 16.9	17.1	-
F3	14.2 14.3	14.2	<LOQ (32.6) <LOQ (32.6)	<LOQ (32.6)	<2.3:1
F4	31.2 28.5	29.8	<LOQ (32.6) <LOQ (32.6)	<LOQ (32.6)	<1.1:1
F5	19.3 20.1	19.7	<LOQ (7.3) <LOQ (7.3)	<LOQ (7.3)	<0.4:1
F6	No serum	-	23.6 <LOQ (18.4)	-	-

Table 2 (continued)

F7	20.5 20.7	20.6	No liver	-	-
F8	22.9 26.5	24.7	26.5 20.9	23.7	<1.0:1
F9	3.0 2.4	2.7	<LOQ (18.4) <LOQ (7.3)	<LOQ (18.4)	<6.8:1
F10	<LOQ (6.1) 6.9	<6.9	<LOQ (36.8) <LOQ (36.8)	<LOQ (36.8)	<5.3:1
F11	26.0 16.6	21.3	25.2 28.9	27.0	1.3:1
F12	8.2 6.5	7.4	<LOQ (18.4) <LOQ (18.4)	<LOQ (18.4)	<2.5:1
F13	15.8 15.3	15.6	<LOQ (16.3) <LOQ (16.3)	<LOQ (16.3)	<1.1:1
F14	24.5 32.2	28.4	39.3 27.8	33.5	<1.2:1
F15	No serum	-	42.2 42.7	42.5	-

Table 3

Liver [PFOS]:Serum [PFOS] Ratio Analysis

Limit Described	Alterations	Liver [PFOS]:Serum [PFOS] Ratio	95% C.I. of Ratio
Average	None	1.3:1	0.9:1 - 1.7:1
Lower Limit I	Liver PFOS decreased 1 SD* Serum PFOS increased 1 SD**	0.8:1	0.5:1 - 1.0:1
Upper Limit I	Liver PFOS increased 1 SD Serum PFOS decreased 1 SD	2.1:1	1.5:1 - 2.8:1
Lower Limit II	Liver PFOS decreased 2 SD Serum PFOS increased 2 SD	0.5:1	0.3:1 - 0.6:1
Upper Limit II	Liver PFOS increased 2 SD Serum PFOS decreased 2 SD	3.4:1	2.3:1 - 4.4:1

*Liver [PFOS] SD = 24%
**Serum [PFOS] SD = 21%

Table 4

PFOSA Serum and Liver Analyses for 31 Human Donors

	Serum (ng/ml)		Liver (ng/g)	
Individual	Analysis	Mean	Analysis	Mean
M1	No serum	-	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M2	<LOQ (1.3) <LOQ (1.3)	<LOQ (1.3)	<LOQ (7.5) <LOQ (7.5)	<LOQ (7.5)
M3	2.0 3.4	2.7	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M4	9.9 9.3	9.6	<LOQ (7.6) <LOQ (7.6)	<LOQ (7.6)
M5	<LOQ (1.3) <LOQ (1.3)	<LOQ (1.3)	<LOQ (7.5) <LOQ (7.5)	<LOQ (7.5)
M6	6.4 5.9	6.1	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M7	<LOQ (3.1) <LOQ (3.1)	<LOQ (3.1)	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M8	4.4 9.2	6.8	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M9	<LOQ (3.3) <LOQ (3.3)	<LOQ (3.3)	<LOQ (7.9) <LOQ (7.9)	<LOQ (7.9)
M10	12.8 13.0	12.9	<LOQ (7.5) <LOQ (7.5)	<LOQ (17.5)

Table 4 (continued)

M11	5.1 5.1	5.1	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M12	No serum	-	<LOQ (19.6) <LOQ (19.6)	<LOQ (19.6)
M13	No serum	-	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
M14	3.6 3.8	3.7	<LOQ (7.5) <LOQ (7.5)	<LOQ (7.5)
M15	2.9 3.5	3.2	<LOQ (19.6) <LOQ (19.6)	<LOQ (19.6)
M16	<LOQ (3.1) <LOQ (3.1)	<LOQ (3.1)	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
F1	No serum	-	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
F2	No serum	-	<LOQ (19.6) <LOQ (19.6)	<LOQ (19.6)
F3	<LOQ (1.3) 1.3	<1.3	<LOQ (7.9) <LOQ (7.9)	<LOQ (7.9)
F4	2.2 2.0	2.1	<LOQ (7.9) <LOQ (7.9)	<LOQ (7.9)
F5	<LOQ (1.3) <LOQ (1.3)	<LOQ (1.3)	<LOQ (7.5) <LOQ (7.5)	<LOQ (7.5)
F6	No serum	-	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)

Table 4 (continued)

F7	2.5 3.1	2.8	No liver	-
F8	7.9 12.1	10.0	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
F9	1.6 1.5	1.5	6.3 <LOQ (7.5)	<LOQ (7.5)
F10	<LOQ (3.1) <LOQ (3.1)	<LOQ (3.1)	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
F11	7.5 5.5	6.5	<LOQ (19.6) <LOQ (19.6)	<LOQ (19.6)
F12	5.0 4.0	4.5	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
F13	<LOQ (3.3) <LOQ (3.3)	<LOQ (3.3)	<LOQ (7.9) <LOQ (7.9)	<LOQ (7.9)
F14	17.8 22.1	20.0	<LOQ (18.8) <LOQ (18.8)	<LOQ (18.8)
F15	No serum	-	<LOQ (19.6) <LOQ (19.6)	<LOQ (19.6)

Table 5

PFOA Serum and Liver Analyses for 31 Human Donors

	Serum (ng/ml)		Liver (ng/g)	
Individual	Analysis	Mean	Analysis	Mean
M1	No serum	-	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M2	2.1 2.0	2.1	<LOQ (5.4) 2.5	<LOQ (5.4)
M3	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M4	15.6 13.8	14.7	50.0 43.8	46.9
M5	<LOQ (6.0) <LOQ (6.0)	<LOQ (6.0)	<LOQ (35.9) <LOQ (35.9)	<LOQ (35.9)
M6	6.7 5.5	6.1	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M7	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M8	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M9	3.3 3.1	3.2	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
M10	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)

Table 5 (continued)

M11	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M12	No serum	-	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
M13	No serum	-	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
M14	7.0 <LOQ (6.0)	<7.0	<LOQ (35.9) <LOQ (35.9)	<LOQ (35.9)
M15	5.6 4.9	5.3	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
M16	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F1	No serum	-	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F2	No serum	-	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
F3	<LOQ (3.1) <LOQ (3.1)	<LOQ (3.1)	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
F4	<LOQ (3.1) <LOQ (3.1)	<LOQ (3.1)	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
F5	3.0 <LOQ (3.0)	<3.0	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F6	No serum	-	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)

Table 5 (continued)

F7	3.4 <LOQ (3.0)	<3.4	No liver	-
F8	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F9	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (35.9) <LOQ (17.9)	<LOQ (35.9)
F10	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F11	3.8 2.5	3.1	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
F12	<LOQ (3.0) <LOQ (3.0)	<LOQ (3.0)	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F13	3.5 4.0	3.7	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)
F14	5.1 5.9	5.5	<LOQ (17.9) <LOQ (17.9)	<LOQ (17.9)
F15	No serum	-	<LOQ (18.7) <LOQ (18.7)	<LOQ (18.7)

Table 6

PFHS Serum and Liver Analyses for 31 Human Donors

	Serum (ng/ml)		Liver (ng/g)	
Individual	Analysis	Mean	Analysis	Mean
M1	No serum	-	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M2	4.1 4.0	4.1	<LOQ (3.4) 1.4	<LOQ (3.4)
M3	2.5 3.0	2.8	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M4	<LOQ (5.7) <LOQ (5.7)	<LOQ (5.7)	Not analyzed	-
M5	3.1 2.6	2.9	<LOQ (3.4) <LOQ (3.4)	<LOQ (3.4)
M6	0.8 0.6	0.7	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M7	4.9 4.8	4.8	<LOQ (18.5) <LOQ (18.5)	<LOQ (18.5)
M8	0.4 0.4	0.4	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M9	3.2 3.4	3.3	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M10	<LOQ (1.2) <LOQ (1.2)	<LOQ (1.2)	<LOQ (7.4) <LOQ (7.4)	<LOQ (7.4)

Table 6 (continued)

M11	3.7 3.6	3.7	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M12	No serum	-	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M13	No serum	-	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
M14	3.7 3.3	3.5	<LOQ (3.4) <LOQ (3.4)	<LOQ (3.4)
M15	5.9 5.3	5.6	7.5 8.9	8.2
M16	<LOQ (3.1) <LOQ (3.1)	<LOQ (3.1)	<LOQ (18.5) <LOQ (18.5)	<LOQ (18.5)
F1	No serum	-	<LOQ (18.5) <LOQ (18.5)	<LOQ (18.5)
F2	No serum	-	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
F3	1.4 1.5	1.5	<LOQ (7.4) <LOQ (7.4)	<LOQ (7.4)
F4	2.0 1.8	1.9	<LOQ (7.4) <LOQ (7.4)	<LOQ (7.4)
F5	<LOQ (1.2) <LOQ (1.2)	<LOQ (1.2)	<LOQ (7.4) <LOQ (7.4)	<LOQ (7.4)
F6	No serum	-	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)

Table 6 (continued)

F7	1.1 1.3	1.2	No liver	-
F8	3.0 3.2	3.1	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
F9	<LOQ (1.2) <LOQ (1.2)	<LOQ (1.2)	5.6 <LOQ (7.4)	<LOQ (7.4)
F10	4.7 4.7	4.7	<LOQ (18.5) <LOQ (18.5)	<LOQ (18.5)
F11	2.0 1.3	1.6	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
F12	0.5 0.4	0.5	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
F13	2.1 2.4	2.3	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
F14	2.3 3.0	2.7	<LOQ (3.7) <LOQ (3.7)	<LOQ (3.7)
F15	No serum	-	<LOQ (3.4) <LOQ (3.4)	<LOQ (3.4)