

AR226 - 1353

FINAL REPORT
Epidemiology, 220-3W-05
Medical Department
3M Company
St. Paul, MN 55144

Date: June 17, 2003

Title: Descriptive Analysis of Serum Fluorochemical Concentrations from Decatur
Employee Participants of the 2002 Medical Surveillance Program

Protocol Number: N/A

IRB Approval: N/A

Principal Investigator:
Co-investigators:

Geary W. Olsen, D.V.M., Ph.D.
Jeffrey H. Mandel, M.D.

Study Director:

Jeffrey H. Mandel, M.D.

000070

ABSTRACT

In the Spring 2002, 54 3M Company Decatur (Alabama) employees voluntarily participated in the fluorochemical medical surveillance program. As part of this program, a blood sample was collected from each participating employee for determination of five serum fluorochemicals. These fluorochemicals were: perfluorooctanesulfonate (PFOS); N-ethyl perfluorooctanesulfonamidoacetate (PFOSAA); N-methyl perfluorooctanesulfonamidoacetate (M570); perfluorooctanoate (PFOA); and perfluorohexanesulfonate (PFHS). The serum PFOS concentrations ranged from 0.082 to 4.2580 ppm with an arithmetic mean of 1.621 ppm (95% CI 1.283 - 1.958) and a geometric mean of 1.008 ppm (95% CI 0.733 - 1.388). None of the employees tested had serum concentrations that exceeded the Biologic Limit Value of 5 ppm for PFOA [range 0.025 - 4.810 ppm; arithmetic mean = 1.497 ppm (95% CI 1.084-1.910); geometric mean = 0.713 ppm (95% CI 0.483-1.055)]. Comparison of the employees' 2002 serum fluorochemical concentrations with the most recent previous measurements suggested a decline in concentrations for PFOA, PFHS, PFOSAA and M570. A decline in serum PFOS concentrations was not observed. Cautious interpretation is warranted of any trend in serum concentrations because neither potential workplace exposure information or actual time since last test was incorporated in the analyses.

INTRODUCTION

In the Spring 2002, the fluorochemical medical surveillance program was offered to employees at the 3M Company Decatur (Alabama) chemical manufacturing plant. Results have been reported elsewhere for previous fluorochemical medical surveillance programs at the Decatur manufacturing plant (Olsen et al. 1999; 2001a; 2003a), as well as the 3M Antwerp (Belgium) fluorochemical manufacturing plant (Olsen et al. 1999; 2001b; 2003a) and the 3M Cottage Grove (Minnesota) fluorochemical manufacturing plant (Gilliland and Mandel 1996; Olsen et al. 1998; 2000; 2003b). There were fewer participants in the 2002 Decatur fluorochemical medical surveillance program than in previous examination years (1994, 1997, 2000) at this manufacturing site. This was likely due to the fact that the 2002 fluorochemical medical program was offered after the company's announcement to cease production of perfluorooctanesulfonyl fluoride (POSF)-related materials. This resulted in fewer production employees at the Decatur manufacturing site compared to previous years. The purpose of this study is to report the serum fluorochemical concentrations that were measured in 2002 and compare the participants' results with their most recent previous serum concentrations.

METHODS

The fluorochemical medical surveillance program is offered to employees at the Decatur manufacturing site on a periodic basis. Participation is voluntary. As part of the 2002 program, a blood sample was collected from each participating employee for determination of five serum fluorochemicals. These fluorochemicals were: perfluorooctanesulfonate (PFOS, $C_8F_{17}SO_3^-$); N-ethyl

000072

perfluorooctanesulfonamidoacetate (PFOSAA, $C_8F_{17}SO_2N(CH_2CH_3)CH_2COO^-$); N-methyl perfluorooctanesulfonamidoacetate (M570, $C_8F_{17}SO_2N(CH_3)CH_2COO^-$); perfluorooctanoate (PFOA, $C_7F_{15}COO^-$); and perfluorohexanesulfonate (PFHS, $C_6F_{13}SO_3^-$).

The five fluorochemicals were determined by high performance liquid chromatography electrospray tandem mass spectrometry methods (Hansen et al. 2001). Analyses were conducted at Tandem Labs (Salt Lake City, UT) using validated methods that have been detailed elsewhere (Tandem Labs 1999; 2001a; 2001b). Fluorochemical concentrations were measured in $\mu\text{g/mL}$ and reported as parts per million (ppm).

RESULTS

A total of 54 Decatur employees (41 males, 13 females) voluntarily participated in the 2002 fluorochemical medical surveillance program. Measures of central tendency for the five fluorochemicals are reported in Table 1. The serum PFOS concentrations ranged from 0.082 to 4.2580 ppm (Table 1) with a mean (arithmetic) of 1.621 ppm (95% CI 1.283 - 1.958). Because the concentrations were skewed (i.e., log normal distribution), a geometric mean was also calculated for PFOS (1.008 ppm, 95% CI 0.733 - 1.388).

Presented in Table 2 are results for the 30 Decatur employees who participated in both the 2000 and 2002 fluorochemical medical surveillance programs. The arithmetic mean differences are based on subtracting the employees' 2000 serum fluorochemical concentrations from their respective 2002 serum fluorochemical concentrations. There was no statistically significant ($p < .05$) mean difference between serum PFOS

concentrations for these 30 employees. On the other hand, the mean serum fluorochemical concentrations significantly ($p < .05$) decreased for PFOA, PFHS, PFOSAA and M570 in this two year interval (Table 2). Figures 1 through 5 provide a paired comparison of the 30 employees' 2000 and 2002 serum fluorochemical concentrations. It should be noted that employees labeled #14 and #18 (see x axis) in Figure 1 are the same as employees #4 and #16 in Figure 2, respectively. Because of the long serum elimination half-life of PFOS and PFOA (Burris et al. 2002), we suspect that the 2000 serum concentrations of these two employees might have been in error (biased upwards).

Presented in Table 3 are the mean differences in serum PFOS and PFOA concentrations for 44 employee participants of the 2002 fluorochemical medical surveillance program in relation to their most recent previous serum fluorochemical measurements (i.e., prior to the 2002 fluorochemical medical surveillance program). The previously most recent measurements for these 44 employees ranged between blood samples collected between 1997 and 2001. Mean serum PFOS concentrations did not decrease for these 44 employees whereas mean serum PFOA concentrations significantly ($p < .05$) decreased. Data are not presented for PFHS, PFOSAA and M570 because they were not measured in the 1997 fluorochemical surveillance program which was the most recent previous measurement for some employees.

Presented in Table 4 are the mean differences in serum PFOS and PFOA concentrations for the 11 employee participants in the 2002 fluorochemical medical surveillance program who also participated in the PFOA Biologic Limit Value (BLV) program in 2001 (after completion of the 2000 fluorochemical medical surveillance

program). The purpose for the PFOA BLV program is explained, in detail, elsewhere (3M Company 2001). Basically, 3M established the BLV (5 ppm serum PFOA) to represent the best estimate of a level of a chemical substance or its metabolite in a biological fluid that if present, even on a chronic basis, would not be expected to pose, or correlate with, a significant risk of adverse health effects to the worker(s). By establishing this BLV at 5 ppm for PFOA, the exposure guideline committee at 3M did not intend to imply that serum levels of PFOA greater than the BLV immediately impose a significant risk of adverse health effects. However, if an employee's serum PFOA level either meets or exceeds the BLV, it should be understood that corrective actions (which may include temporary removal from the immediate work area) may need to be applied, on a case-by-case basis, at the direction of 3M Corporate Occupational Medicine. The PFOA BLV program was directed at those workers engaged in the production of PFOA which, in Decatur, occurred in 1999 and continued into 2001. None of the 11 employees who were tested in 2001 under the direction of the BLV program had serum PFOA concentrations that exceeded the BLV (5 ppm) in either 2001 or 2002 (Table 4). There was no statistically significant decrease in serum PFOA concentrations among the 11 employees tested in the initial BLV analysis for Decatur in 2001 in relation to serum PFOA concentrations reported in their 2002 fluorochemical medical surveillance examinations (Table 4). None of the remaining 43 participating employees exceeded the BLV for PFOA in 2002 (Table 1).

DISCUSSION

The employee participants of the 2002 Decatur fluorochemical medical surveillance program had a distribution of serum PFOS concentrations comparable to the results obtained from prior serum fluorochemical assessments. These previously collected data were obtained from fluorochemical surveillance programs conducted at Decatur in 1994, 1997 or 2000 (Olsen et al. 1999, 2001, 2003a) or with a random sample of production employees in 1998 (Olsen et al. 2003c). Likewise, the distributions of serum PFOA, PFHS, PFOSAA and M570 concentrations were similar to prior assessments (Olsen et al. 2003a; 2003b; 2003c). Analysis of the 54 employees' 2002 results suggests, overall, there has been a modest decline in the serum concentrations of PFOA, PFHS, PFOSAA and M570 since the 2000 fluorochemical medical surveillance program. The mean serum PFOS concentration did not decline in this two year time period. Because potential exposure to POSF-related materials occurred during 2000 and 2001, it is not possible to determine whether the decline in PFOA, PFHS, PFOSAA and M570 is the result of serum elimination, reduced opportunity for potential workplace exposure or both. On the other hand, serum PFOS concentrations did not decrease. This observation may be a function of poor serum elimination (Burris et al. 2002) and/or opportunity for potential workplace exposure to POSF-related materials through 2001. An ongoing study is examining the serum half-life of elimination for PFOS, PFOA and PFHS among 27 retirees followed for 5 years at the Decatur and Cottage Grove manufacturing sites. Results from this investigation should be available in 2004. Presently, the estimated serum half-lives of elimination for PFOS and PFOA are 8.7

000076

years (SD = 6.1) and 4.4 years (SD = 3.5), respectively (Burris et al. 2002). These estimates, however, are based on only 9 of these retirees followed for 18 months.

There are several limitations to the analyses presented in this report. The results arise from a small subset of employees who voluntarily participated in the 2002 Decatur fluorochemical medical surveillance program. The number of employees in the 2002 fluorochemical medical surveillance program is only 20 percent of those who participated in the 2000 fluorochemical medical surveillance program (n = 263). Attrition of employees due to production cessation of POSF-related materials occurred between 2000 and 2002. Unlike 2000, no employee interview data were collected in 2002 to provide an estimate of exposure to POSF-related production areas for these workers. Therefore, it was not possible to associate serum fluorochemical concentrations to potential workplace exposures in the 2000-2002 time period. Actual time was not taken into account in the comparison of the most recent prior test results compared to the 2002 serum fluorochemical measurements. Knowledge regarding the serum elimination half-life of these fluorochemicals remains sparse. More precise estimates of the serum elimination half-lives of PFOS, PFOA and PFHS are forthcoming from a separate study designed to analyze the half-lives from 27 retirees of the 3M Decatur and Cottage Grove manufacturing sites. Because of these limitations, there needs to be cautious interpretation of any time trend analysis of the serum fluorochemical concentrations of the 54 Decatur employees who participated in the 2002 fluorochemical medical surveillance program.

We conclude that the serum fluorochemical concentrations of the 54 employees who voluntarily participated in the 2002 Decatur fluorochemical medical surveillance

program did not increase to any substantial extent since the 2000 fluorochemical medical surveillance program. For a number of employees, their serum PFOA, PFHS, PFOSAA and M570 serum concentrations appeared to have decreased. None of the employees tested had serum PFOA concentrations that exceeded the PFOA BLV of 5 ppm.

Cautious interpretation is warranted of any time trend in serum concentrations because neither potential workplace exposure information or actual time since last test was not incorporated in the analyses.

000078

REFERENCES

- Burris JM, Lundberg JK, Olsen G, Simpson C, Mandel J. 2002. Determination of serum half-lives of several fluorochemicals. St. Paul (MN):3M Company. U.S. Environmental Protection Agency docket AR-226-1086.
- Gilliland FD, Mandel JS. 1996. Serum perfluorooctanoic acid and hepatic enzymes, lipoproteins, and cholesterol: a study of occupationally exposed men. *Am J Ind Med* 29:560-568.
- Hansen KJ, Clemen LA, Ellefson ME, Johnson HO. 2001. Compound-specific, quantitative characterization of organic fluorochemicals in biological matrices. *Environ Sci Technol* 35:766-770.
- Olsen GW, Gilliland FD, Burlew MM, Burris JM, Mandel JS, Mandel JH. 1998. An epidemiologic investigation of reproductive hormones in men with occupational exposure to perfluorooctanoic acid. *J Occup Environ Med* 40:614-621.
- Olsen GW, Burris JM, Mandel JH, Zobel LR. 1999. Serum perfluorooctane sulfonate and hepatic and lipid clinical chemistry tests in fluorochemical production employees. *J Occup Environ Med* 41:799-806.
- Olsen GW, Burris JM, Burlew MM, Mandel JH. 2000. Plasma cholecystokinin and hepatic enzymes, cholesterol and lipoproteins in ammonium perfluorooctanoate production workers. *Drug Chem Toxicol* 23:603-620.
- Olsen GW, Logan PW, Simpson CA, Burris JM, Burelw MM, Lundberg JK, Mandel JH. 2001a. Descriptive summary of serum fluorochemical levels among employee participants of the year 2000 Decatur fluorochemical medical surveillance program. St. Paul (MN):3M Company. U.S. Environmental Protection Agency docket AR-226-1030a020a.
- Olsen GW, Schmickler MN, Tierens JM, Logan PW, Burris JM, Burlew MM, Lundberg JK, Mandel JH. 2001b. Descriptive summary of serum fluorochemical levels among employee participants of the year 2000 Antwerp fluorochemical medical surveillance program. St. Paul (MN):3M Company. U.S. Environmental Protection Agency docket AR-226-1030a020b.
- Olsen GW, Burris JM, Burlew MM, Mandel JH. 2003a. Epidemiologic assessment of worker serum perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations and medical surveillance examinations. *J Occup Environ Med* 45:260-270.

000079

Olsen GW, Butenhoff JL, Mandel JH. 2003b. Assessment of lipid, hepatic and thyroid function in relation to an occupational biologic limit value for perfluorooctanoate. St. Paul (MN):3M Company. U.S. Environmental Protection Agency docket AR-226.

Olsen GW, Logan PW, Hansen KJ, Simpson CA, Burris JM, Burlew MM, Vorarath PP, Venkateswarlu P, Schumpert JC, Mandel JH. 2003c. An occupational exposure assessment of a perfluorooctanesulfonyl fluoride production site. Biomonitoring. Am Ind Hyg Assoc J. (in press).

Tandem Labs. 1999. Assay validation report. Quantitative determination of PFOS, PFOSA, PFOSAA, N-MeFOSE-OH, N-EtFOSE, POAA, and PFHS in human serum by LC/MS/MS. Study No. NWBS98-082, Report No. NWBR99-005. NWT Inc., Salt Lake City, UT., U.S. Environmental Protection Agency docket AR-226-1208.

Tandem Labs. 2001a. Quantitative determination of PFOS, PFOSA, PFOSAA, POAA, PFHS, M556 and M570 in human serum by LC/MS/MS. Assay revalidation report. Study No. NWBS00-040, Report No. NWBR00-108. NWT Inc., Salt Lake City, UT., U.S. Environmental Protection Agency docket AR-226-1209.

Tandem Labs. 2001b. Quantitative determination of PFOS, PFOSA, PFOSAA, POAA, PFHS, M556 and M570 in human serum by LC/MS/MS. Assay revalidation addendum report. Study No. NWBS00-040, Report No. NWBR00-122. NWT Inc., Salt Lake City, UT., US Environmental Protection Agency docket AR-226-1210.

3M Company. 2001. Documentation of an Occupational Biological Limit Value (BLV) for Perfluorooctanoate [CF₃(CF₂)₆CO₂]. St. Paul (MN):3M Company. U.S. Environmental Protection Agency docket AR-226.

000080

**Table 1: Measures of Central Tendency for Five Serum Fluorochemical Concentrations
for 54 Decatur Employee Participants of the 2002 Medical Fluorochemical Surveillance Program**

<u>Statistic</u>	<u>PFOS</u>	<u>PFOA</u>	<u>PFHS</u>	<u>PFOSAA</u>	<u>M570</u>
Range	0.082-4.580	0.025-4.810	0.007-0.943	0.002-0.074	0.002-0.432
Mean	1.621	1.497	0.285	0.013	0.061
95% C.I.	1.283-1.958	1.084-1.910	0.210-0.359	0.009-0.017	0.037-0.085
Geometric mean (G.M.)	1.008	0.713	0.147	0.008	0.026
95% C.I. of G.M.	0.733-1.388	0.483-1.055	0.101-0.214	0.006-0.011	0.018-0.038

000081

Table 2: Differences in Serum Fluorochemical Concentrations Between 2002 and 2000 Fluorochemical Medical Surveillance Programs for 30 Decatur Employee Participants in 2002

Statistic	<u>PFOs</u>	<u>PFOA</u>	<u>PFHs</u>	<u>PFOSAA</u>	<u>M570</u>
Range of difference	(-1.649)-1.069	(-3.905)-0.091	(-1.018)-0.059	(-0.172)-0.021	(-0.906)-(-0.007)
Mean difference	0.195	-0.544	-0.062	-0.039	-0.178
95% C.I.	(-0.031)-0.422	(-0.904)-0.184	(-0.132)-0.009	(-0.058)-(-0.021)	(-0.270)-(-0.085)
p value	.96	.002	.04	<.0001	.0002

000062

Table 3: Differences in Serum PFOS and PFOA Concentrations Between 2002 Fluorochemical Medical Surveillance Results and the Previous Most Recent Measurements (1997-2001) for 44 Decatur Employee Participants in 2002

<u>Statistic</u>	<u>PFOS</u>	<u>PFOA</u>
Range of difference	(-1.649)-1.069	(-3.905)-1.260
Mean difference	0.212	-0.274
95% C.I.	0.031-0.392	(-0.560)-0.011
p value	.99	.03

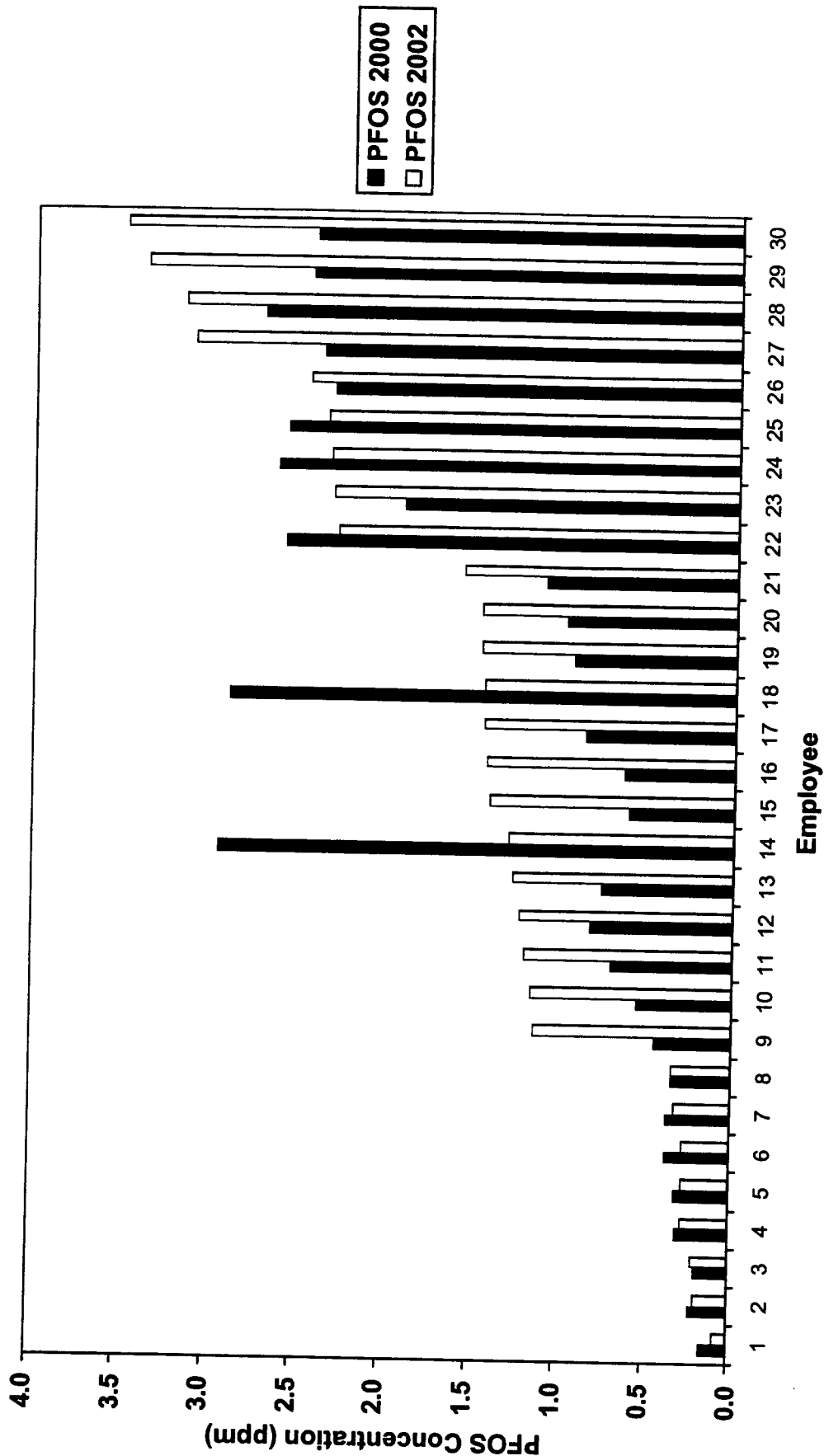
000083

Table 4: Differences in Serum PFOS and PFOA Concentrations Between 2002 Fluorochemical Medical Surveillance Results for 11 Employees and their Previous Biologic Limit Value (BLV) Results in 2001

<u>Statistic</u>	<u>PFOS</u>	<u>PFOA</u>
Range of difference	(-1.250)-0.989	(-0.590)-0.990
Mean difference	0.175	0.267
95% C.I.	(-0.240)-0.590	(-0.095)-(0.629)
t-ratio	0.94	1.64
p value	.82	.93

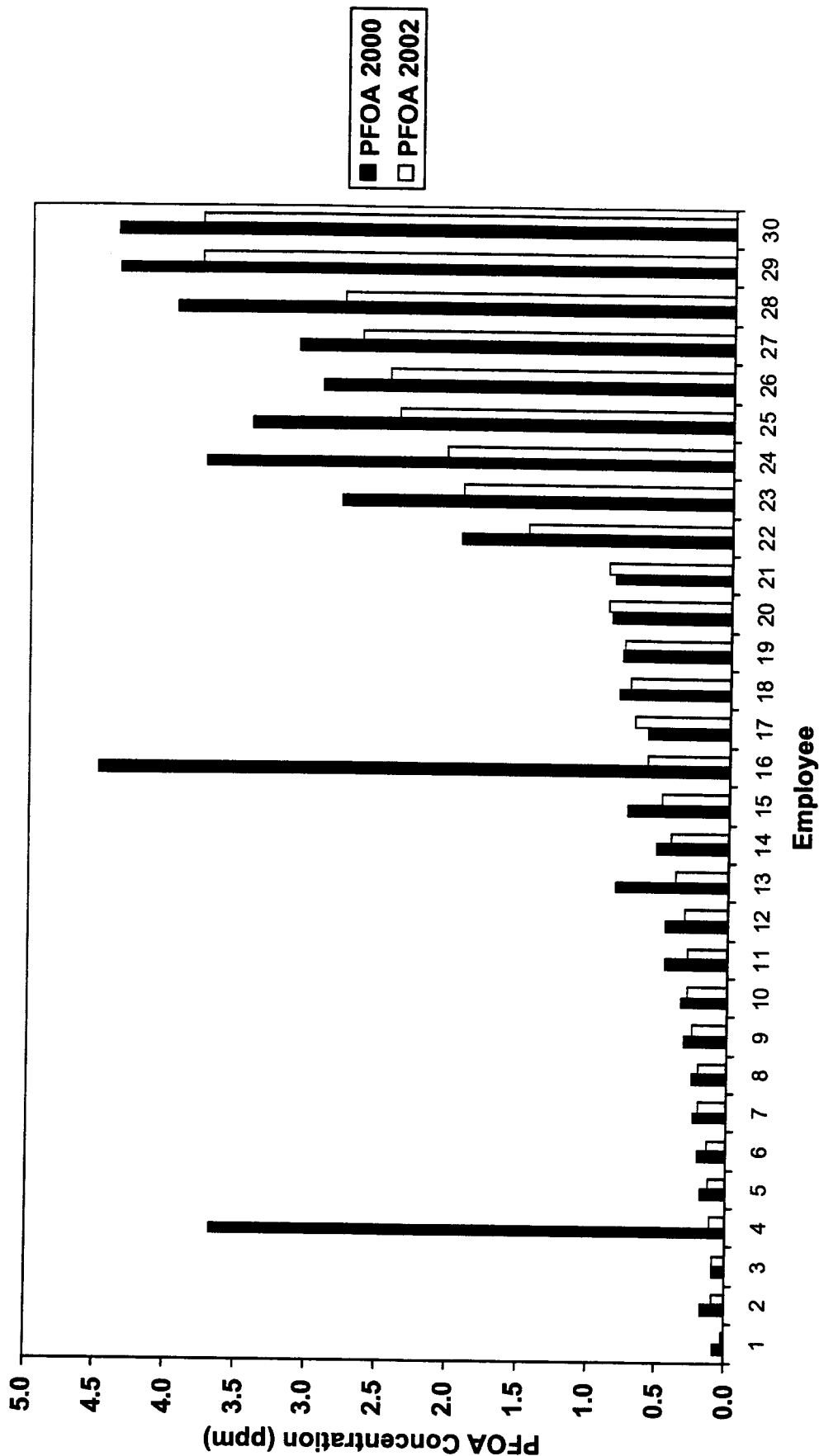
000054

**Figure 1. Comparison of PFOS Concentrations,
in Ascending 2002 PFOS Concentration Order, for 30 Decatur Employees
Who Participated in the 2000 and 2002 Fluorochemical Medical Surveillance Programs**



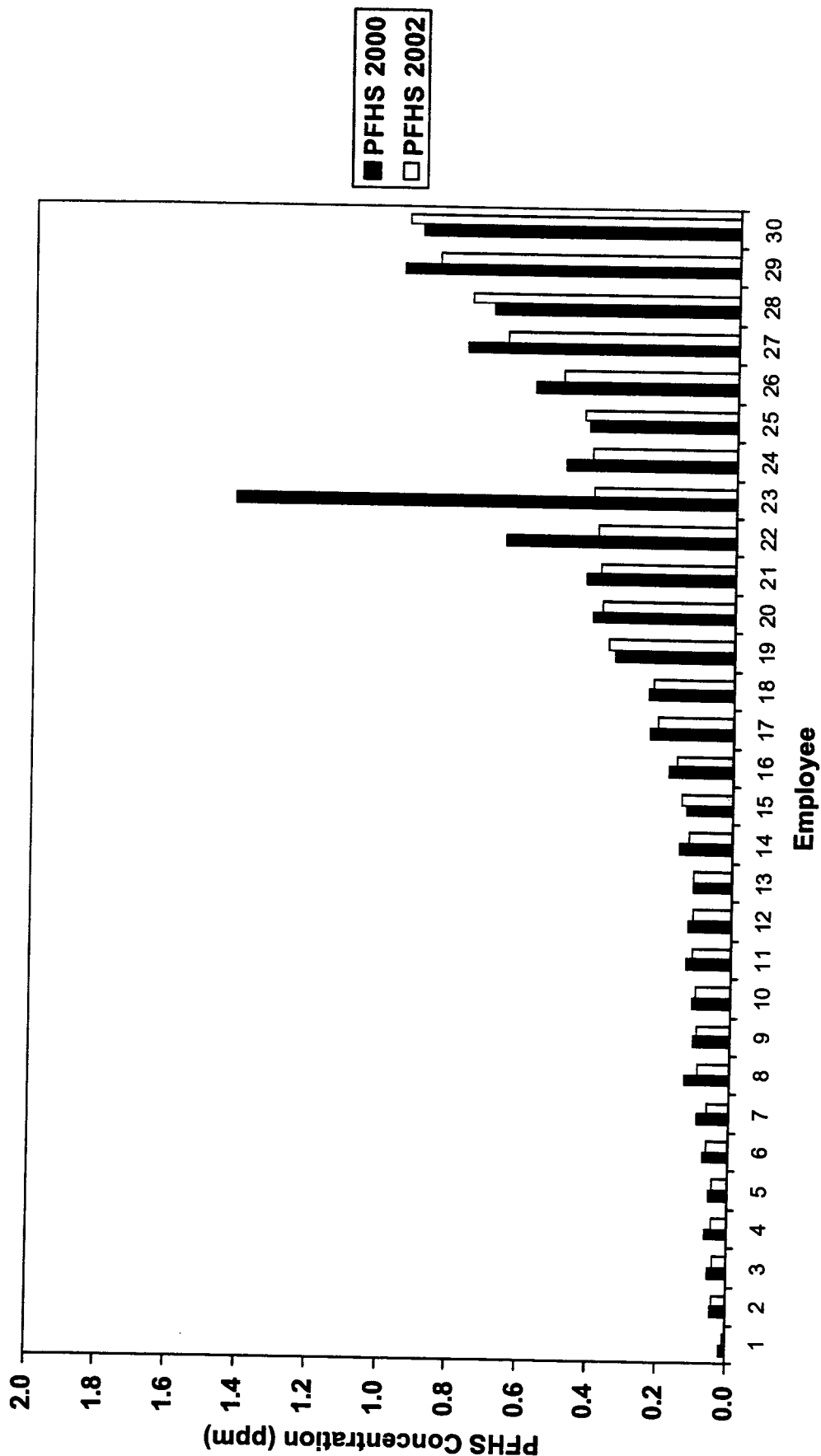
580000

**Figure 2. Comparison of PFOA Concentrations,
in Ascending 2002 PFOA Concentration Order, for 30 Decatur Employees
Who Participated in the 2000 and 2002 Fluorochemical Medical Surveillance Programs**



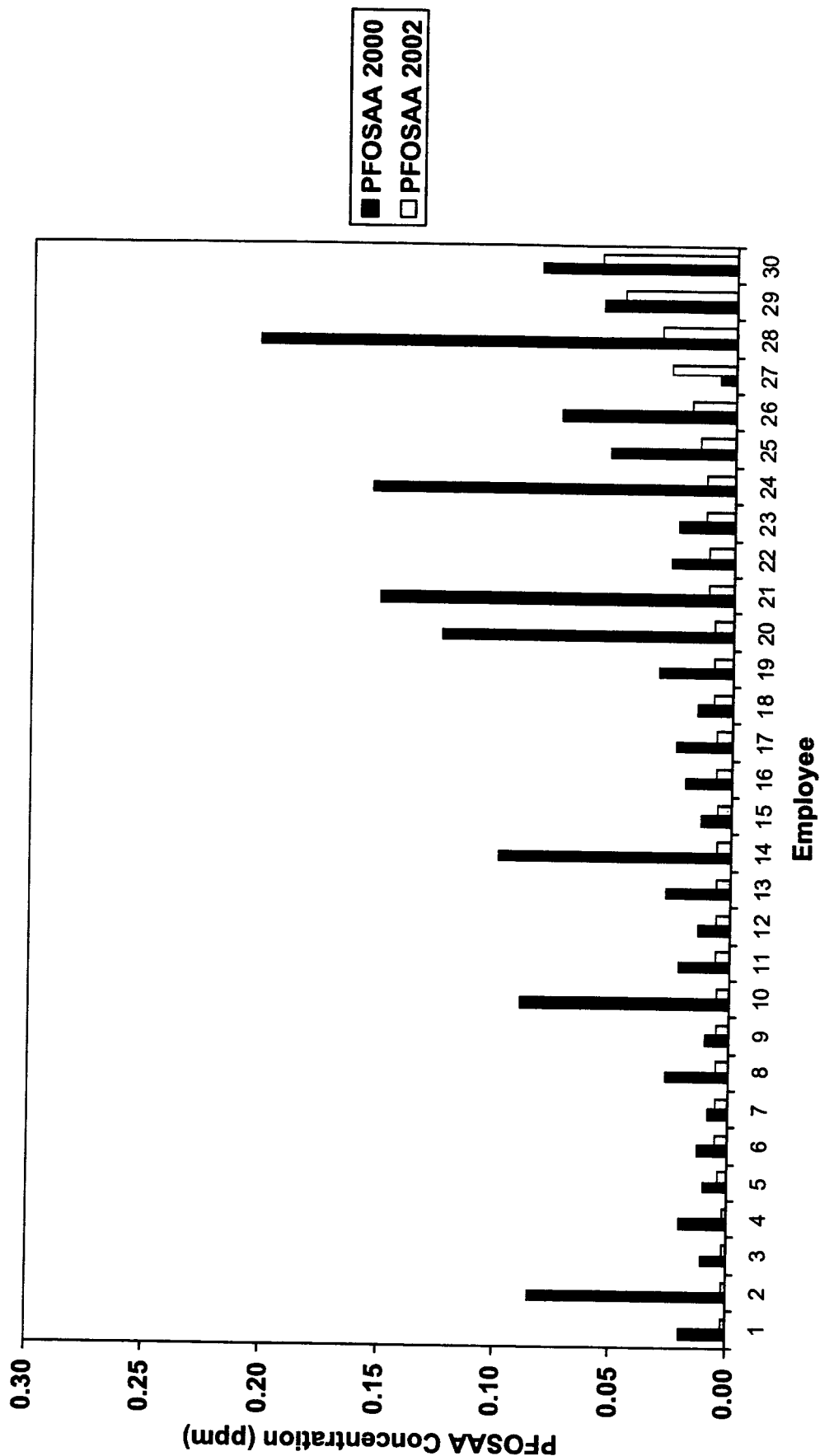
980000

**Figure 3. Comparison of PFHS Concentrations,
in Ascending 2002 PFHS Concentration Order, for 30 Decatur Employees
Who Participated in the 2000 and 2002 Fluorochemical Medical Surveillance Programs**



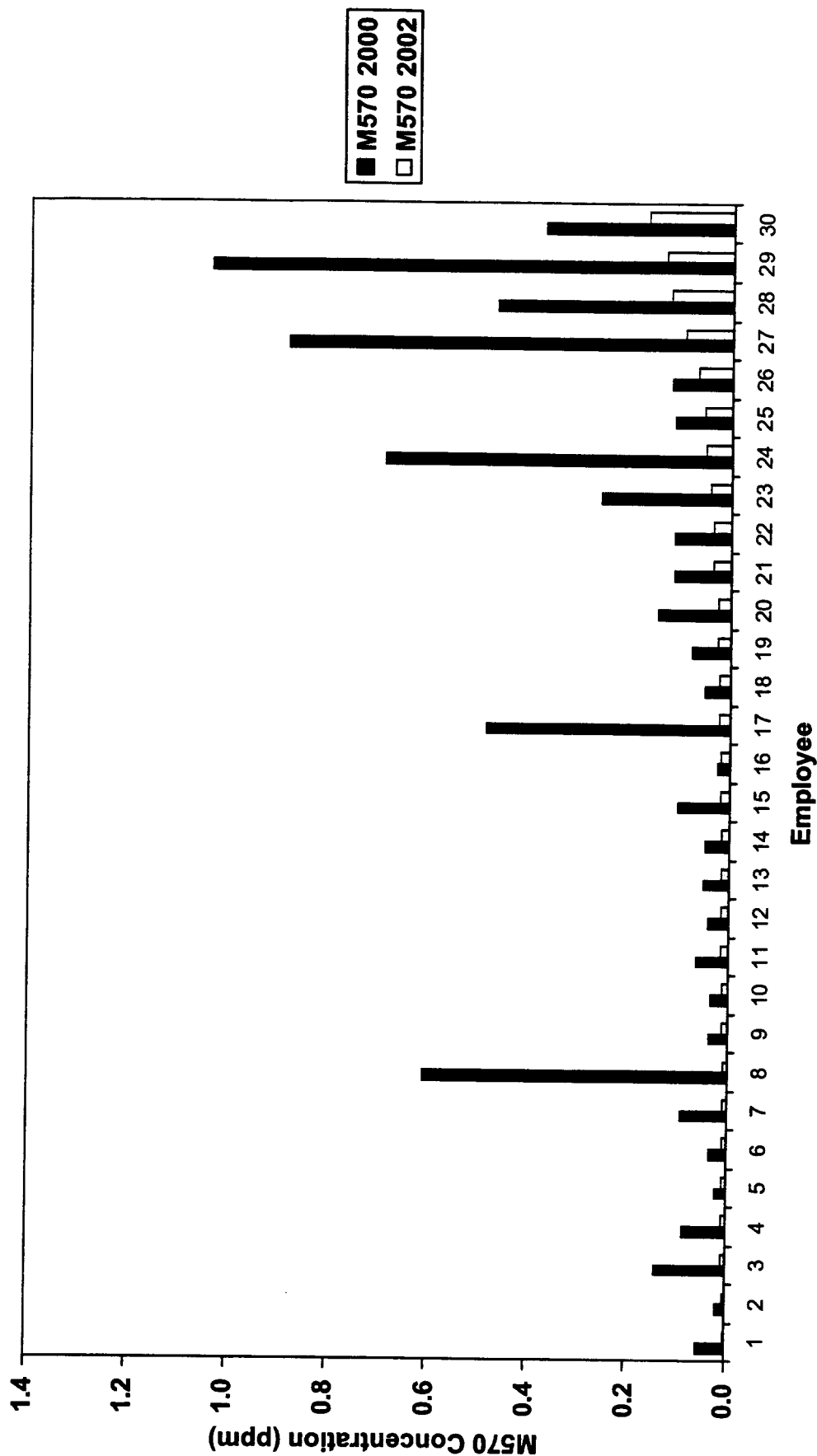
780000

**Figure 4. Comparison of PFOSAA Concentrations,
in Ascending 2002 PFOSAA Concentration Order, for 30 Decatur Employees
Who Participated in the 2000 and 2002 Fluorochemical Medical Surveillance Programs**



880000

**Figure 5. Comparison of M570 Concentrations,
in Ascending 2002 M570 Concentration Order, for 30 Decatur Employees
Who Participated in the 2000 and 2002 Fluorochemical Medical Surveillance Programs**



680000