Interim Report #1
Epidemiology, 220-3W-05
Medical Department
3M Company
St. Paul, MN 55144

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Title: Determination of Serum Half-Lives of Several Fluorochemicals

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Principal Investigator:	Jean M. Burris, RN, MPH[1]
Co-investigators:	Geary Olsen, DVM, PhD[1] Cathy Simpson, RN[2] Jeffrey Mandel, MD, MPH[1]
Study Director:	Jeffrey Mandel, MD, MPH[1]
Study Sponsor:	Corporate Occupational Medicine Department 3M Company 220-3W-05 Saint Paul, MN 55144

1. Occupational Medicine, Medical Department, 3M Company, 220-3W-05, St. Paul, MN 55114
2. 3M Decatur Specialty Adhesives and Chemicals Plant, P.O. Box 2206, Decatur, AL 35609-2206

ABSTRACT

Previous estimates regarding the human serum half-life of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) ranged between 1000-1500 days and 365-530 days respectively [Olsen et al., 1999; Ubel et al., 1980]. These estimates were based on very few subjects. We are currently in the process of collecting data from 27 retired, fluorochemical production employees in an effort to more completely estimate the half-life of PFOS and PFOA along with five other fluorochemical analytes. To date, preliminary analyses from three serum collection periods utilizing a one compartment model suggests that the serum half-life of PFOS in these retirees is likely to be four-fold lower than the range of 1000-1500 days that was previously suggested. The serum half-life of PFOA in these retirees appears to be approximately one year, which is comparable to the estimate suggested by Ubel et al [1980]. Because of the lower limit of quantitation assayed for the other fluorochemical analytes, we believe additional collection periods are necessary before serum half-life calculations can be determined. There are several limitations to the current report, the most important being the paucity of data available to date and the range of the serum levels measured (PFOS range 0.2-2.0ppm; PFOA 0.1-3.1 ppm). We anticipate completing two additional serum collection cycles before December 2000. Additional data should allow a better assessment of fluorochemical half-lives of all participants in this study.

INTRODUCTION

Although it has been reported that the serum half-life of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) in humans may range between 1000-1500 days and 365-530 days respectively [Olsen et al., 1999; Ubel et al., 1980], such estimations have been based on very few subjects. The purpose of this study is to determine the serum half-life from a group of Decatur and Cottage Grove retirees for the following fluorochemicals: PFOS, PFOA, perfluorohexanesulfonate (PFHS), N-ethyl perfluorooctanesulfonamidoacetate (PFOSAA), N-methyl perfluorooctanesulfonamdoacetate (M570), perfluorooctanesulfonamide (PFOSA). and perfluorooctanesulfonamidoacetate (M556).

METHODS

Twenty-four Decatur retirees and three Cottage Grove retirees have voluntarily participated in multiple serum sample collection cycles for fluorochemical analysis. The majority of the twenty-seven participants are male, only two are female. All participants are long-term 3M employees. They have worked an average of 28 years in either the Decatur or Cottage Grove chemical division. The average age of the participant at the time of the first collection is 60 years (range: 55-74). The mean number of months from retirement to the start of the study is 30 months (range: 5-130 months).

To date, there have been three Decatur collection periods: November 1998, June 1999 and November 1999. Cottage Grove retirees have participated in two collection periods: June 1999 and November/December 1999. The next serum sampling is scheduled for May 2000. Participants have received letters informing them of their

individual fluorochemical results as data have become available from the laboratory. Each participant completes a brief medical history questionnaire containing information about current medications, and disease diagnosis. Responses have been keyed into a SAS dataset and analyzed by JMP software.

High-performance liquid chromatography mass spectrometry/mass spectrometry has been utilized to analyze all serum samples (NWB,1999). All samples were analyzed by Northwest Bioanalytical Laboratory, Salt Lake City, Utah with the exception of the M556 and M570 from November 1998. The 3M Environmental Technology and Services Laboratory analyzed these samples.

Half-lives were calculated assuming a one compartment model. A log-linear relationship was used to estimate the serum fluorochemical elimination half-life in participating retirees. In this log linear relationship, the slope of the line is related to the elimination constant ($-k_{el}$) via the equation: Slope = $-k_{el}(2.303)$. Once the elimination constant is calculated, the half-life is determined using the relationship: $t_{1/2} = 0.693/k_{el}$ (Medinsky & Klassen, 1996).

RESULTS

A total of 24 participants provided serum samples for each collection period. A half-life was calculated for each of these individuals for PFOS and PFOA. Except for PFHS, half-lives for the other fluorochemicals were not calculated as the majority was below the limit of quantitation by the third collection. Because the assay measurement of PFHS was inconsistent (e.g., many subsequently collected samples were at higher levels

than initial samples), the calculation of the PFHS half-life was deferred until further blood collections occur.

Table 1 presents the mean, median, range and 95% confidence interval of the half-lives calculated for those retirees (n=18 for PFOS, n=20 for PFOA) who were judged to have a good fit ($r^2 \geq 0.6$) for a linear one compartmental model for PFOS and PFOA. At this time we have not included the other participants in these analyses for two reasons: 1) lack of three data points for some subjects; and 2) lack of fit of model (i.e., $r^2 < 0.6$). The latter was often due to the fact that the second measurement was higher than the first. At this time we are uncertain whether this may be due to subsequent exposure, biological variation or assay error and/or variation. [Note: We are scheduled to collect two more data points by December 2000. By that time we anticipate including all participants in the analysis.]

The range of serum PFOS measured was 0.2 - 2.0 ppm (Table 1). The range of serum PFOA measured was 0.1 - 3.1 ppm. All PFOS serum half-life calculations were of male retirees. Two of the 20 PFOA serum half-life calculations were of female retirees.

As can be seen from Table 1, the median serum half life of PFOS was 270 days (range 139-640) for the 18 male retirees whose log linear regression model had an $r^2 \geq 0.6$. The median serum half life of PFOA was 344 days for the 20 male and female retirees whose log linear regression model had an $r^2 \geq 0.6$. Restricting the models to $r^2 \geq 0.8$ did not substantially change the half-life calculations for PFOS or PFOA. It should be noted that the highest PFOA half-life calculations were from the two female retirees: 654 and 1308 days. Neither age nor the number of months retired was associated with the serum half-life calculations for PFOS or PFOA.

DISCUSSION

The results from this first interim analysis suggest that the serum half-life of PFOS in humans is likely to be four-fold lower than the range of 1000-1500 days that was initially suggested [Olsen et al., 1999]. The serum half-life of PFOA in humans appears to be approximately one year, which is comparable to the estimate suggested by Ubel et al [1980]. Additional collection cycles will further refine these half-life estimates and take into account the retirees who were excluded in this interim report due to lack of fit of the one compartment model. This, of course, assumes a one-compartment model is appropriate at the low ppm serum levels measured in this group of retirees.

Our results from this preliminary interim analysis should be interpreted cautiously due to the paucity of data available to date. The fourth data point is scheduled to be collected and analyzed by mid-summer. There are several additional limitations to these interim data. To date, Cottage Grove retirees have participated in only two serum collection cycles. Three of the twenty-four Decatur retirees have indicated at each serum collection cycle that they have worked in a consulting capacity in the 3M Decatur plant at some point during the intervening six months. However, their log linear regression models were considered to be of reasonably good fit (i.e., r^2 for PFOS $\geq .80$; r^2 for PFOA $\geq .57$). Four of the seven fluorochemical analytes (PFOSAA, PFOSA, M556 and M570) measured below the lower limit of quantitation for more than 80% of the samples prohibiting a reasonable half-life calculation. At this time we are uncertain why many subsequent PFHS serum levels were higher than the first measurement. With additional data we hope to define half-lives in these compounds although if levels remain below the LLOQ this may not be feasible.

The next collection period will occur in May 2000 with anticipated results due back from Northwest Bioanalytical by mid-summer. Additional data should allow a better assessment of the half-lives of all retirees. The next interim report should be available by August 2000.

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Table 1

Half-Life Summary Data In Days For Those Retirees With Three Collection Periods Whose Log Linear Models Had $R^2 > 0.6$

	N	Mean	Median	Range	95% CI of Mean
PFOS					
$R^2 \geq 0.6$	18	303	270	139-640	228-378
$R^2 \geq 0.8$	16	303	259	139-640	217-388
PFOA					
$R^2 \geq 0.6$	20	389	344	109-1308	269-509
$R^2 \geq 0.8$	13	395	324	109-1308	204-585