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3M

## Determination of Serum Fluorochemical Levels in Sumitomo 3M Employees

Ninety-four Sumitomo 3M employees participated in a voluntary, cross-sectional serum fluorochemical assessment. Three groups of employees were examined. Sagamihara Plant production employees (n = 32) were involved in the inspection and converting of finished goods. Sagamihara Plant management employees (n = 32) were involved in primarily non-production work activities. Tokyo Head Office employees (n = 32) are generally not occupationally-exposed to fluorochemicals. All but two of the 94 participants were male employees. Among the Sagamihara Plant production employees, the highest serum perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA) and perfluorohexanesulfonate (PFHS) levels were 0.628 ppm, 3.6 ppm and 0.117 ppm, respectively. Serum levels for the Sagamihara Plant Management and Tokyo Head Office were, on average, under 0.01 ppm (PFOS), 0.03 ppb (PFOA) and 0.025 ppm (PFHS)Serum levels of PFOS for Sagamihara Plant management and Tokyo Head Office employees were similar to levels seen in a small group of US 3M Center employees who were not occupationally exposed to PFOS. Serum PFOS levels of Sagamihara Plant production employees were below those of workers at the 3M Antwerp and Decatur plants.

# PROTOCOL

Occupational Medicine, 220-3W-05
Medical Department
3M Company
St. Paul, MN 55144

Date: 9 January 1999

Title: DETERMINATION OF SERUM FLUOROCHEMICAL LEVELS 3M SUMITOMO EMPLOYEES

Study Protocol Number: EPI-0008
Start Date:

IRB Approval
Exempt Expedited

Estimated Date of
Final Report:

IRB Approval Date: 1/20/99


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# PROTOCOL FOR SERUM FLUOROCHEMICAL DETERMINATION IN 3M SUMITOMO EMPLOYEES

ABSTRACT

3M manufactures products which contain chemical compounds, either as intentional components or residual impurities, that have as a parent molecule, perfluorooctane sulfonyl fluoride (POSF). These compounds may be expected to transform metabolically, to an undetermined degree, to PFOS as an end-stage metabolite. Another compound manufactured by 3M includes ammonium perfluorooctanoate (PFOA). These molecules enter a number of product applications (e.g., surfactants, food packaging additives, polymers).

3M Sumitomo in Japan processes many of these compounds into products for distribution and sale. Fluorochemical applications are also investigated in 3M Sumitomo laboratories.

The purpose of this study is to measure serum fluorochemical levels in selected employees of the 3M Sumitomo population. The specific fluorochemicals to be measured include perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS).

RESEARCH METHODS

Approximately 110 employees will be invited to participate in this non-randomized cross-sectional study; all subjects are volunteers. Thirty individuals are involved in the processing and formulation various forms of pure fluorochemicals into finished products for distribution throughout Asia. Approximately 20 individuals are actively involved in laboratory fluorochemical research. Approximately 60 managerial employees, considered non-occupationally exposed to fluorochemicals, will also be invited to participate.

Information concerning respondents' age, gender, and occupation will be obtained from 3M Sumitomo Human Resources for review with the serum fluorochemical results.

The study duration will be approximately three weeks. Written informed consent will be obtained from all study subjects in Japanese (Appendix A). Each subject will be involved for about 15 – 20 minutes and will donate two10 mL blood sample. Should any employee complications arise as a consequence of phlebotomy, physicians associated with 3M Sumitomo will treat them. .

Once the blood samples are obtained, they will be frozen in dry ice and sent by 3M Center in Saint Paul via Federal Express. At the 3M Center Medical Clinic, serum will be separated by centrifugation and sent to the 3M Environmental Laboratory for analysis. Standard electrospray HPLC MS/MS will be used to determine the fluorochemical content of all serum samples. Serum will be analyzed for the presence and amount of PFOA and PFOS. Results will be reported to the Principal Investigator in parts per billion (ppb). The Principal Investigator will inform 3M Sumitomo employees

of their PFOS and PFOA levels after results and a brief explanation are be translated into Japanese.

The Principal Investigator will forward the results to the appropriate Co-investigator for statistical analysis. Descriptive statistics performed will include group mean fluorochemical level and standard deviation of the mean, and range of serum fluorochemical levels. Correlation and regression analyses will be performed utilizing information obtained concerning age, gender, and occupation.

RESULTS

A formal report of the research findings, including data analysis, will be submitted to the 3M Medical Director and Institutional Review Board at the conclusion of the study. The protocol will be amended only with approval of the 3M Institutional Review Board.

APPENDIX A – CONSENT FORM

## CONSENT FORM FOR COLLECTION OF BLOOD FOR SERUM FLUOROCHEMICAL LEVEL DETERMINATION

### INTRODUCTION

You and your colleagues are involved in fluorochemical production, research, or management at 3M Sumitomo. You are invited to participate in a research study being conducted by 3M Corporate Occupational Medicine regarding fluorochemicals. Your participation would involve donating two red-topped test tubes of blood. Your blood will only be tested for the amount PFOA, PFOS, and its precursors it contains; it will not be used to test for any other substances or disease. Please review this consent form carefully and be sure your questions are answered before you make a decision to participate. A 3M Sumitomo representative will be available to provide you with additional information at the time of your blood donation.

### PURPOSE OF STUDY

The purpose of the study is to determine the presence and amount of perfluorooctanoic acid (PFOA), perfluorooctane sulfonate, and its precursors in your serum.

### STUDY PROCEDURES

Your blood will be drawn with one needle stick and require two test tubes. This will be a one-time blood donation.

### POTENTIAL RISKS/BENEFITS

The risks of venipuncture include pain on needle insertion, bleeding under the skin, discoloration from bleeding under the skin, and discomfort from blood clotting (hematoma) if bleeding under the skin occurs.

### BENEFITS

There will be no direct benefit from your participation in this study. However, the information gained from this study will further help us understand human exposures to fluorochemicals. Your individual results as well as the overall results will be communicated to you only. Your individual results will be considered confidential information and will not be disclosed to anyone outside the 3M Medical Department without your written consent.

### COMPENSATION

No financial compensation will be forthcoming as a result of participating in this study. If you suffer injury or a medical condition that appears to be the result of participating in this study, you will be referred to another health care professional at no cost to you. In the event of a research related injury, compensation will be determined on a case by case basis by 3M.

CONFIDENTIALITY

The overall results collected in this study may be used in publications or public presentation. Your name will not be revealed in any publication or other documents intended for publication examination. Your individual results will be communicated to you only. Your individual results will be considered confidential information and will not be disclosed to anyone outside the 3M Medical Department without your written consent.

SUBJECT RIGHTS/AVAILABILITY OF INFORMATION

If you have any questions about the study now, or later, or in the event of a research related injury or emergency, contact Dr. Jeffrey Mandel (651-733-8670) or Jean Burris, R.N. (651-737-7867). For answers to questions about your rights in regard to this research, you may contact Dr. Larry Zobel, Chair, 3M Institutional Review Board at 651-733-5181.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Participation in this study is voluntary. Refusal to participate will involve no penalty of loss of benefits to which you are otherwise entitled. You are free to refuse to participate for any reason. The investigator may stop your participation in this study should it be determined that continued participation may be detrimental to your health.

SUBJECT CONSENT

By signing the consent form, I certify that I am at least 18 years old. I confirm that I have read this consent form, and that I have been given adequate opportunity to ask any questions I may have about this consent form or the study. I also confirm that I understand the scope of my participation in this study, and that all of my questions have been answered to my satisfaction. I am signing this consent form voluntarily, and I desire to participate in the study. I understand that I will receive a copy of this signed consent form. I understand that I will not receive any financial compensation for participating in this study.

_____ _____

Signature Date

_____

Printed Name

_____

Witness

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

Date: September 3, 1999

Title: Determination of Serum Fluorochemical Levels in Sumitomo 3M Employees

Study Start Date: March, 1999

IRB Approval Date: January 20, 1999


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## Introduction

3M manufactures products, which contain chemical compounds, either as intentional components or as manufacturing residuals, which, have as a parent molecule, perfluorooctane sulfonyl fluoride (POSF). These compounds may be expected to transform metabolically, to an undetermined degree, to PFOS as an end-stage metabolite. Another compound manufactured by 3M includes ammonium perfluorooctanoate (POAA). These compounds enter a number of product applications (e.g., surfactants, polymers, and food packaging additives).

Sumitomo 3M in Japan processes many of these compounds into products such as fire protection products and surface protection products for distribution and sale. Other potential fluorochemical applications are also investigated in Sumitomo 3M laboratories.

## Purpose

The purpose of this investigation was to estimate potential fluorochemical exposure to Sumitomo 3M employees, using the serum component of blood as an exposure measure.

## Methods

94 Sumitomo 3M employees participated in a voluntary, cross-sectional, fluorochemical serum measurement. It is assumed that serum fluorochemicals measured represent occupational exposures, although we have not included fluorochemical air measurements from the Sagamihara plant in this assessment. Employees ranged in age from 31-67. These employees came from three job exposure groups as described in a personal communication with S. Yamana. These groups were defined as: Sagamihara Plant production employees (n=32) involved in the inspection and converting of finished goods. These workers were also involved with compounding, using chemicals made from POSF, and formulation of products containing additional fluorochemicals. The next group included Sagamihara Plant management employees (n=32) working primarily at the same site as the Sagamihara Plant production employees. There was no regular handling of fluorochemicals in their usual work capacities. The last group included management employees from the Tokyo Head Office who are generally not

occupationally exposed to fluorochemicals (n=30). All but two of the 94 participants were male employees.

Each study participant donated two 10 cc tubes of blood. Blood was collected between March 17 and 19, 1999. The blood was centrifuged twice for 15 minutes at 3000 RPM immediately after drawing to obtain serum. The serum was shipped frozen to the 3M Medical Clinic in St. Paul, Minnesota where it was distributed to the appropriate laboratories for analysis. Following analyses, individuals were notified of their results by confidential letter.

**Laboratory Analysis**

Individual serum was analyzed for seven fluorochemical compounds using high-pressure liquid chromatography electrospray tandem mass spectrometry measurement (LC/MS/MS). Northwest Bioanalytical (NWB) Salt Lake City, Utah analyzed five of the fluorochemical compounds. They analyzed the serum for perfluorooctane sulfonate (PFOS), perfluorooctane sulfonamide (PFOSA), n-ethyl perfluorooctanesulfonamido acetate (PFOSAA), perfluorooctanoate (POAA), and perfluorohexane sulfonate (PFHS). NWB conducts all studies within the guidelines of the US FDA Good Laboratory Practice, the OECD Principles of Good Laboratory Practice and the Japanese MHW Good Laboratory Practice Standard Ordinance for Nonclinical Laboratory Studies on the Safety of Drugs (Ordinance No. 21, PAB Notification No. 424). The 3M Environmental Technology and Services Laboratory analyzed the serum for perfluorooctanesulfonamido acetate (M556) and n-methyl perfluorooctane sulfonamido acetate (M570).

Northwest Bioanalytical's validated LC/MS/MS provided a lower limit of quantitation (LLOQ) in parts per million (ppm) of 0.0314 (PFOS), 0.001 (PFOSA), 0.00223 (PFOSAA), 0.00527 (POAA), and 0.00261 (PFHS).

3M Environmental Technology & Services Laboratory provided a lower limit of quantitation (LLOQ) in parts per million (ppm) for M556 that ranged from 0.01-0.025 ppm, and M570 that ranged from 0.01-0.05 ppm.

Data Analysis

Data were analyzed using standard statistical software programs. Comparisons of arithmetic means was done using student's t test. A statistically significant difference in one of the means was set at p = .05 or less.

**Results**

PFOS

Table 1 summarizes the serum PFOS, POAA and PFHS values for the Sumitomo 3M employees. Twenty-four PFOS values were reported below the lower limit of quantitation (0.0314 ppm). Twelve (38%) of 32 Sagamihara plant management employees had values less than the lower limit of quantitation (<LLOQ). The range of PFOS for the remaining 20 employees in this group was 0.032-0.057 ppm. Descriptive statistics and t-tests were calculated using the LLOQ value (0.0314 ppm) for those individuals who had values below the LLOQ

Forty percent of the Tokyo Head Office employees had PFOS values <LLOQ. The range of measurable PFOS was 0.033-0.0967 ppm for the remaining employees. The remaining statistics were calculated using the LLOQ value (0.0314 ppm). PFOS was quantifiable in all 32 Sagamihara Production employees. The arithmetic mean value was 0.135 ppm (range: 0.0475-0.628 ppm) which was significantly different ($p<0.05$) than the mean PFOS value for employees in both the Tokyo Head Office and Sagamihara Plant managers group.

POAA

As per Table 1 the lower limit of quantitation for POAA was 0.00527 ppm. Three of the 94 employees had a POAA value reported less than the lower limit of quantitation. One of these employees was from the Sagamihara Plant management and two were from the Tokyo Head Office. The midpoint between zero and the LLOQ was utilized in calculating the statistics for POAA. The mean POAA value for the Sagamihara Production employees was 0.201 ppm that was significantly different ($p<0.05$) than the mean POAA values for the Tokyo Head Office and Sagamihara Plant managers group.

PFHS

As per Table 1 fourteen percent of employees had PFHS values reported <LLOQ (0.00261 ppm). Ten were employees from the Sagamihara plant management group and three were from the Tokyo Head Office. The midpoint between zero and the LLOQ (0.0013 ppm) was utilized to calculate the univariate statistics for the Sagamihara plant management group. The arithmetic mean value for this group was 0.00626 ppm with a range of 0.0027-0.0241 ppm. Again, the arithmetic mean PFHS (0.020 ppm) for the Sagamihara Production employees was significantly different than the other exposure groups ($p<0.05$).

PFOSAA, PFOSA

We chose not to statistically analyze PFOSAA and PFOSA because of the large number of employees who had serum values reported below the lower limit of quantitation. Eighty-four percent of all Sumitomo 3M employees had PFOSAA values reported below the lower limit of quantitation (0.00223 ppm). Fifteen of 94 employees had a PFOSAA value reported between 0.00247 and 0.0133 ppm.

The lower limit of quantitation for PFOSA is 0.001 ppm. Four of the 94 employees had a detectable level of PFOSA. These values ranged from 0.00241-0.0068 ppm.

M556, M570

We chose not to statistically analyze M556 and M570 because of the large number of employees who had serum values reported below the lower limit of quantitation. Only one Sumitomo 3M employee had a quantifiable level of M556 (0.0032 ppm).

Ninety-three percent of all employees had M570 values reported below the lower limit of quantitation. The average M570 value for the seven employees with quantifiable levels of M570 was 0.007 ppm. The range was 0.00311-0.0144 ppm.

**Discussion**

Ninety-four Sumitomo 3M employees participated in a voluntary, cross-sectional serum fluorochemical assessment. Thirty-two employees were identified as Sagamihara Plant production employees involved in the inspection and converting of finished goods, doing some compounding, using chemicals made from POSF, and doing some formulation of products containing other fluorochemicals. Thirty-two employees were described as Sagamihara Plant management employees who work primarily at the same site as the Sagamihara Plant production employees. Finally, 30 management employees from the Tokyo Head Office who are not usually exposed to manufactured fluorochemicals participated in the assessment.

Employees described as having the highest exposure to POSF chemistry had PFOS levels three times higher than employees in both the Sagamihara plant management group and the Tokyo Head Office. The mean serum PFOS level for plant production employees was 0.135 ppm (range: 0.0475-0.628 ppm) compared to mean PFOS values of 0.0403 ppm (range: 0.0319-0.0566 ppm) for Sagamihara Plant management employees and mean PFOS of 0.0523 ppm (range 0.033-0.0967 ppm) for Tokyo Head Office employees.

Serum fluorochemical levels in Sumitomo 3M employees can be compared to serum levels recently measured in 3M employees occupationally exposed to fluorochemicals in facilities outside of Japan (Table 2). Serum fluorochemical levels were measured in employees at 3M Decatur Alabama as part of an on going medical monitoring program in 1997. Since 1980 the Decatur plant is the primary location of the production of certain fluorochemicals that may ultimately be measured in the serum as PFOS. Arithmetic mean serum PFOS levels in 1997 were 1.96 ppm (range 0.10-9.93 ppm).[1] Outside the United States 3M manufactures PFOS related materials at its Antwerp, Belgium facility. Arithmetic mean serum PFOS levels in Antwerp employees in 1997 were 1.5 ppm (range: 0.1-4.8 ppm).[1]

In 1998 31 3M Center employees in St. Paul, Minnesota were tested for serum PFOS. All were corporate staff or division managers. None had worked in fluorochemical

production. Employees ranged in age from 37-62 years. Arithmetic mean PFOS was 0.047 ppm (range: 0.028-0.096 ppm). Both the arithmetic mean and range for this group are similar to the arithmetic mean and range PFOS of the Sagamihara Plant management (mean=0.0403; range=0.0319-0.0566) and Tokyo Head Office (mean=0.0523; range=0.033-0.0967).

**Conclusion**

Ninety-four Sumitomo 3M employees participated in a voluntary, cross-sectional serum fluorochemical assessment. Serum levels were highest for Sagamihara Production employees. This is the same group where there is potential for greater occupational fluorochemical exposure, although industrial hygiene measurements were not part of this assessment. Serum levels of PFOS for Sagamihara Plant management and Tokyo Head Office employees were similar to levels seen in a small group of US 3M Center employees who were not occupationally exposed to PFOS. PFOS levels are well below levels found in workers at plant sites where POSF chemistries are produced (Decatur, Antwerp). None of these levels would be expected to be associated with health problems based on our current understanding of these compounds.

Table 1

**Serum Fluorochemical Levels in Sumitomo 3M Employees**

| | | PFOS (ppm) LLOQ=0.0314 | POAA (ppm) LLOQ=0.00527 | PFHS (ppm) LLOQ=0.00261 |
|---|---|---|---|---|
| **Sagamihara Plant Production Employees N=32** | Mean | 0.135 | 0.201 | 0.020 |
| | Median | 0.0919 | 0.0496 | 0.010 |
| | Std Dev | 0.131 | 0.6265 | 0.0283 |
| | Range | 0.0475-0.628 | 0.0189-3.600 | 0.00287-0.117 |
| **Sagamihara Plant Management N=32** | Mean | 0.0403 | 0.0117 | 0.00626 |
| | Median | 0.0385 | 0.0096 | 0.0047 |
| | Std Dev | 0.0071 | 0.0095 | 0.0054 |
| | Range | 0.0319-0.0566 | 0.00264-0.059 | 0.0027-0.0241 |
| **Tokyo Head Office N=30** | Mean | 0.0523 | 0.0126 | 0.0048 |
| | Median | 0.046 | 0.01195 | 0.0038 |
| | Std Dev | 0.0191 | 0.00618 | 0.003 |
| | Range | 0.033-0.0967 | 0.00264-0.029 | 0.0013-0.016 |

Table 2

**Mean Serum PFOS Levels**

| | 3M Center 1998 N=31 | Decatur 1997 N=84 | Antwerp 1997 N=65 | Sagamihara Production N=32 | Sagamihara Plant Mgmt N=32 | Tokyo Head Office N=30 |
|---|---|---|---|---|---|---|
| Mean PFOS (ppm) | 0.047 | 1.96 | 1.48 | 0.135 | 0.0403 | 0.0523 |

## REFERENCES

Olsen GW, Burris JM, Mandel JH, Zobel LR. Serum perfluorooctane sulfonate and hepatic and lipid clinical chemistry tests in fluorochemical production employees. J Occup Env Med (1999, in press).