Corporate Health Physics
Corporate Occupational Medicine
Corporate Product Responsibility
Corporate Toxicology
3M Medical Department

3M Center, 220-2E-02
PO Box 33220
St. Paul, MN 55133-3220
651 733 1110

3M

Identification of Fluorochemicals in Sera of Children in the United States

The objective of this study is to determine in a sample of children their sera levels of perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), perfluorohexanesulfonate, N-ethyl perfluorooctanesulfonamidoacetate (PFOSAA), N-methyl perfluorooctanesulfonamidoacetate (M570), perfluorooctanesulfonamidoacetate (M556), and perfluorooctanesulfonamide (PFOSA). In cooperation with the University of Minnesota Department of Pediatrics, samples will be obtained that represent sera from 1,131 children (ages 2 to 12 years) from 23 states in the United States. The sera were collected as part of a large clinical trial regarding group A streptococcal infections. A total of 599 samples will be tested. Sera levels will be compared to the childrens' age, gender and state of residence. The timeline for study completion, estimated at January 1, 2001, is entirely dependent upon a validated analytical method to analyze 0.1 ml of human serum for these fluorochemicals with a lower limit of quantitation of $\leq$ 10 ppb based on high performance liquid chromatography electrospray tandem mass spectrometry methods.

Corporate Occupational Medicine Section/Epidemiology Unit
Proposal
March 16, 2000

Title: Identification of Fluorochemicals in Sera of Children in the United States

Purpose: Evidence that organic compounds containing the element fluorine chemically bonded to carbon can be found in human blood was reported in the literature more than 30 years ago. Average serum perfluorooctanesulfonate (PFOS) levels may be within the 20 to 60 ppb range in the general population. This is primarily based on pooled serum samples; thus it is difficult to ascribe findings to any specific demographic group. The purpose of this study is to determine the level of several fluorochemicals from the sera of children (2 - 12 years of age) in the United States.

Significance: Determination of the serum concentrations of selected fluorochemicals will provide for a more specific understanding of the distribution of these compounds in children. These data should be helpful in the risk characterization process.

Objectives: The objective of this study is to determine in a sample of children their sera levels of perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), perfluorohexanesulfonate, N-ethyl perfluorooctanesulfonamidoacetate (PFOSAA), N-methyl perfluorooctanesulfonamidoacetate (M570), perfluorooctanesulfonamidoacetate (M556), and perfluorooctanesulfonamide (PFOSA).

Protocol: The Department of Pediatrics at the University of Minnesota Medical School has stored sera from 1,131 children (ages 2 to 12 years) from 23 states in the United States. The sera were collected as part of a large clinical trial regarding group A streptococccal infections. [See Pediatrics 1998;101:86-88.] Sera were obtained between January 1994 and March 1995. These children presented with signs and symptoms of acute-onset pharyngitis. All of the 1,131 children had positive throat cultures at the initial visit. Sera have been kept frozen at -20°C. At 3M's request, the Department of Pediatrics has agreed to provide 3M up to 0.1 ml per individual. An initial pilot sample was conducted to determine whether the presence or absence of fluorochemicals can be determined with 0.1 ml serum. These findings suggested that method validation should proceed. Because we are uncertain of the population distribution, it is possible to calculate sample size based on tolerance limits which are independent of the form of the distribution. However, the tolerance limits will be wider than a parametric distribution (Natrella MG. Experimental Statistics New York:Wiley & Sons, 1966). For example, the largest observation in a sample of 45 individuals of a given age and gender will be an upper limit on 95% of that specific population with confidence level 0.90. In this particular study, the sample size will be limited by the number of samples, especially in the youngest age ranges. On the other hand, the use of bootstrap methods will allow for some smoothing of data thereby increasing the precision of tolerance limits and reducing the sample size requirements (personal communication, Dr. Timothy Church, biostatistician, Univ of MN). Therefore, the following samples are proposed to be analyzed in this study:

Age Group	Total N	Total Sampled (%)
2	27	27 (100)
3	51	51 (100)
4	81	81 (100)
5	122	100 (82)
6	146	80 (55)
7	161	60 (37)
8	131	40 (31)
9	135	40 (30)
10	109	40 (37)
11	87	40 (46)
12	81	40 (49)
Total	1131	599 (53)

For those ages where the sample size is less than 100%, we will obtain equal percentages by gender. Age (birth date was not collected), gender and state of residence for each sample will be provided.

Fluorochemicals to be analyzed are PFOS, PFOA, PFHS, PFOSAA, M570, M556 and PFOSA. Prior to this study proceeding, there must be a validated method to analyze for these fluorochemicals in 0.1 ml of human serum using high performance liquid chromatography electrospray tandem mass spectrometry methods. The validated analytical method should have a lower limit of quantitation of $\leq$ 10 ppb. This validated procedure will be performed by Northwest Bioanalytical with technical assistance from the 3M Environmental Laboratory.

PI/location/cost: Geary Olsen will be the principal investigator on this project. Dr. Timothy Church (Associate Professor, University of Minnesota Division of Occupational and Environmental Health) will serve as the biostatistician. Jean Burris, Dr. Kris Hansen, Dr. Jeff Mandel and Dr. Larry Zobel will serve as 3M co-investigators. Total estimated cost of the study is $250,000.

Timeline: The timeline for study completion is entirely dependent upon a validated analytical method to analyze 0.1 ml of human serum for these fluorochemicals with an LLOQ of $\leq$ 10 ppb. If such a method is validated by June 2000, then it is estimated that the sample analyses will be completed by late summer. Statistical analyses of the data should then be completed by October 1st with a draft final report written by November 15, 2000. Review and approval may take an additional 45 days. Therefore, a final report is estimated to be available by January 1, 2001. A final report will be delayed should the validation of the analytical method take longer than expected.