

3M "CONFIDENTIAL"

CHRONOLOGY - FLUOROCHEMICALS IN BLOOD

AUG 28 1977

August 22, 1975 - Initiating event. J.D. LaZerte receives phone call from W.S. Guy. W.S. Guy, D.R. Taves, and W.S. Brey Jr. are to present a paper at the Chicago A.C. & S. meeting entitled "Characteristics and Concentration of Organic Fluorocompounds Found in Human Tissues". W.S. Guy was attempting to locate the source of the organic fluorocompound and thought that SCOTCHGARD might be the source. J.D. LaZerte advises Guy not to speculate.

August 25, 1975 - At the request of Commercial Chemicals Division Central Research sends B.W. Nippolt to the Chicago ACS Meeting to hear the paper by Guy, Taves and Brey. A copy of the ^{19}F NMR spectrum of the fluorocompound isolated from human blood is shown.

September 17, 1975 - At a joint CRL-CCD meeting B.W. Nippolt presents data from the Chicago ASC paper of Guy, Taves and Brey. A copy of the ^{19}F spectrum of the fluorocompound isolated from human blood is shown.

September 21, 1975 - Commercial Chemicals Division Laboratory begins submitting ten samples of perfluorocarboxylic and perfluorosulfonic acid derivatives to Central Research Analytical for ^{19}F NMR analysis in an attempt to identify the material found by Guy and Taves in human blood.

September 22, 1975 - Taves calls J.D. LaZerte to see if 3M will further analyze sample of fluorocompound isolated from human blood and is given a qualified "yes". Further requests that we open contents of FDA (FC-807) petition to him and is given an unqualified no. Taves indicates "strong and continuing" interest in finding source of fluorocompound.

October 7, 1975 - Central Research Analytical submits research proposal to determine quantity and character of organic fluorine in human blood with an estimated project duration of 5 months and estimated cost of \$12,000.

October 21, 1975 - Research proposal accepted by Commercial Chemicals Division.

November 6, 1975 - Of the ten samples submitted on September 21, 1975, Central Research reports that the ^{19}F NMR analysis shows that the spectrum of $\text{C}_8\text{F}_{17}\text{SO}_3\text{H}$ or its salts matches that presented by Guy and Taves.

$\text{C}_8\text{F}_{17}\text{SO}_3\text{H}$ - LD ₅₀ (Oral)	Less than 630 mg/Kg - Toxic
$\text{C}_8\text{F}_{17}\text{SO}_3\text{K}$ - LD ₅₀ (Oral)	About 1250 mg/Kg - Moderately Toxic

December 16, 1975 - J.D. LaZerte, H.E. Freier and J.E. Long visit Guy and Taves at University of Rochester. Agreement is reached that 3M will attempt to isolate and identify fluorochemicals in blood.

February 17, 1976 - Central Research Analytical completes development of accurate analytical method for determining ppb quantities of organic fluorine in human blood. Method is tested on sample of pooled serum from American Red Cross.

April 14, 1976 - Central Reserach Analytical completes analysis of four blood samples from Commercial Chemical Division personnel. Laboratory personnel exposed to fluorochemicals have up to 100 times "normal" amounts of organically bound fluorine in their blood.

May 4, 1976 - Taves calls D.F. Hagen of CRL and requests help in developing a chromatographic method for analyzing perfluoro-octanoic acid. He requests that we analyze some of his perfluorooctanoic acid.

May 13, 1976 - H.E. Freier calls Taves. Agrees to analyze their sample by gas chromatography.

June 29, 1976 - Central Research Analytical completes analysis of nine blood samples including three from Chemolite. Chemolite personnel exposed to fluorochemicals have up to 1000 times "normal" amounts of organically bound fluorine in their blood. Results from previously exposed laboratory personnel indicate that organically based fluorine remains in the blood for an indefinite period.

July 19, 1976 - 3M Medical Department initiates program to study blood chemistry of persons exposed to fluorochemicals.

August 23, 1976 - Central Research Analytical completes analysis of nine blood samples including eight from Cordova. Cordova personnel exposed to fluorochemicals have up to 50 times "normal" amounts of organically bound fluorine in their blood.

August 26, 1976 - Central Research Analytical isolates and characterizes fluorochemical from blood of Chemolite supervisor. The fluorochemical is identified as $C_7F_{15}CO_2H$ or one of its salts by G.C. and ^{19}F NMR.

September 9, 1976 - Central Research Analytical completes analysis of the blood of mice which were fed FC-807 at 1000 and 3000 ppm for 30 days. The mice which were fed FC-807 had roughly 4000 times as much organically bound fluorine in their blood as "nonexposed" mice.

September 17, 1976 - Central Research Analytical characterizes the fluorochemical metabolite from the mouse feeding studies as $C_8F_{17}SO_3H$ or one of its salts. Characterization by ^{19}F NMR.

September 20, 1976 - H.E. Freier calls Taves to keep him informed of our interest. Gave Taves results of CRL analysis of the $C_7F_{15}CO_2H$ which Taves sent. Taves is also told:

1. We are using a modified Wickbold method for fluorine analysis.
2. We have analyzed pooled Red Cross plasma and found organic fluorine levels comparable to those in the literature.
3. We have not yet begun to isolate fluorochemicals in pooled Red Cross plasma.

October 8, 1976 - Central Research Analytical completes analysis of thirteen blood samples including seven from Decatur. Decatur personnel exposed to fluorochemicals have up to 300 times "normal" levels of organically bound fluorine in their blood. Other samples show:

1. Rats exposed to FC-70 do not have FC-70 in their blood.
2. Individuals exposed to fluorochemicals over twenty years ago and not exposed since, have "normal" organically bound fluorine levels.

October 18, 1976 - Central Research Analytical isolates and characterizes fluorochemical from blood of Decatur cell operator. The fluorochemical is identified as $C_8F_{17}SO_3H$ or one of its salts by ^{19}F NMR.

October 20, 1976 - H. E. Freier calls Taves to report results on analysis of $C_7F_{15}CO_2H$ sample supplied by Taves.

October 28, 1976 - Dr. Leon Singer requests sample of $C_7F_{15}CO_2H$ from 3M. Singer believes he can improve on Tave's method of analysis.

November 8, 1976 - 3M sends 25 g $C_7F_{15}CO_2H$ to Dr. Leon Singer

November 17, 1976 - Central Research Analytical completes analysis of six blood samples from Chemolite personnel exposed to fluorochemicals and again finds up to 1000 times "normal" levels of organic fluorine. Further analysis of one individual's blood showed both $C_7F_{15}CO_2H$ and $C_8F_{17}SO_3H$ to be present.

Blood samples are sent to General Activation Analysis to see if Neutron Activation Analysis can be used for determining organically bound fluorine.

December 1, 1976 - Industrial Hygiene begins medical examination of Chemolite personnel including those exposed to fluorochemicals. Examination includes blood, urine and enzyme analysis as well as a partial physical examination.

January, 1977 - J. E. Long arranges to supply Central Research Analytical with blood and liver samples from rats exposed to FC-43 vapors.

January 14, 1977 - Central Research Analytical is unable to detect FC-43 in the blood of rats exposed to FC-43, but finds that organically bound fluorine is present in the blood of exposed rats at seven times the level of a control.

January 15, 1977 - Industrial Hygiene completes medical examinations of Chemolite personnel. Those exposed to fluorochemicals show no medical abnormalities which can be attributed to fluorochemical exposure.

January 20, 1977 - Attempted analysis for organically bound fluorine in blood by General Activation Analysis using photon activation is unsuccessful.

January 27, 1977 - Central Research Analytical completes method for determining organically bound fluorine in whole blood. Blood samples from American Red Cross donors have "normal" plasma levels of organic fluoride.

February 3, 1977 - Central Research Analytical completes work on livers of rats exposed to FC-43. Gas chromatography shows FC-43 to be present at approximately 2ppm. Total organic fluorine level is 8.7 ppm in exposed rats as compared to 7.8 ppm in the control.

January 4, 1977 - Central Research Analytical completes work on blood and livers of rats fed 3000 and 10,000 ppm FC-807 for 30 days. Rats fed at 3000 ppm show an organic fluorine level of 75 ppm in blood while those fed at 10,000 ppm show a level of 125 ppm. (Control = 0.03 ppm.)

Analysis of the livers of the rats fed at the 10,000 ppm level show an organic fluorine level of 500 ppm (Control = 1 ppm).

February 14, 1977 - Central Research Analytical begins a concentrated effort to characterize $C_8F_{15}SO_3H$ derivatives in the 10 ppb range using the Gas Chromatography.

April 12, 1977 - J. D. LaZerte reviews status of organic fluorochemicals in blood with J. V. Erwin and P. H. Schertler of Personal Care Products. Decision made to determine amount of organically bound fluorine in blood of individuals who use Skaid Brand Repellents.

May 5, 1977 - Central Research Analytical completes analysis of blood from 3 employees at High Point, North Carolina. Organically bound fluorine level is on the high side of "normal".

June 9, 1977 - Central Research Analytical completes analysis of blood from three employees who use Skaid Brand Repellents. All blood samples contain organically bound fluorine at higher than "normal" levels. One sample is ten times "normal".

June 15, 1977 - J. D. LaZerte reviews status of organic fluorochemicals in blood with J. A. Muhlenpoh and R.W.H. Chang of Home Health Care Products. Muhlenpoh and Chang review plans for use of fluorochemicals in plague and carrier prevention.

July 6, 1977 - J. E. Long submits tentative schedule for chronic toxicity/carcinogenity study on FC-807 metabolite, FC-143 and Ethyl POSE Alcohol.

July 29, 1977 - July issue of "Fluoride" contains special report on AAAS Fluoride Symposium held on February 25, 1977. Guy and Taves again report finding $C_7F_{15}CO_2H$ in pooled plasma and attribute its presence to industrial products such as SCOTCHGARD and ZEPHEL.

August 3, 1977 - Toxicology proposes four studies to be carried out with SCOTCHGARD and FLUORAD type products. Purpose of studies is to determine if these materials can enter the blood in significant quantities.