

Subject: MEETING MINUTES -  
MEETING WITH J.R. MITCHELL

April 26, 1979

THOSE PRESENT:

M.T. Case - 218-2  
F.D. Griffith - 220-2E  
L.C. Krogh - 223-6SE  
J.D. LaZerte - 236-1  
J.R. Mitchell - Baylor School of Medicine  
R.A. Nelson - 218-3  
R.E. Ober - 218-2  
J.A. Pendergrass - 220-2E  
R.A. Prokop - 236-2B  
F.A. Ubel - 220-2E

Those present met on April 13, 1979 at the Host International Hotel in Houston Texas to review recent results which are relevant to the Fluorochemicals in Blood program and to discuss future plans.

R.A. Prokop began the meeting by giving background on preparation of 3M fluorochemicals. He reviewed the preparation of perfluorooctanesulfonyl fluoride, perfluorooctanoyl fluoride, inert fluids, FC-95, FC-143 and FC-807. (Slides attached)

J.R. Mitchell expressed concern that residual  $C_7F_{15}COF$  might be present in FC-143. He was concerned that  $C_7F_{15}COF$  might be excellent acylating agent and thus a potential carcinogen. He was told that since  $C_7F_{15}COF$  is treated vigorously with excess base, it was highly unlikely that even trace amounts would be present in FC-143.

J.A. Pendergrass reviewed data on workplace concentrations of various fluorochemicals in Alabama and Minnesota plants. (See attached slides and Meeting Minutes of meeting with H.C. Hodge, 4/12/79).

**Exhibit  
2722**

State of Minnesota v. 3M Co.,  
Court File No. 27-CV-10-28862

F.A. Ubel reviewed recent developments in the areas of serum organic fluorine levels, human health and epidemiology as they relate to the fluorochemicals in blood program. (See attached slides and Meeting Minutes of meeting with H.C. Hodge, 4/12/79).

J.R. Mitchell had the following questions and comments:

1. Wives of employees having high serum organic fluorine levels should be examined for the presence of organic fluorine in their serum.
2. Have you looked for target organ problems in your epidemiology study? (Answer-yes, we found nothing.)
3. Why are there so many (apparent) alcoholics in packaging? Is there a correlation between serum organic fluorine levels, alcohol and occupation? Is this being done in the epidemiology study? (Answer-no.)
4. You should get more information on length of employment and type of exposure to a specific chemical. Fat and liver biopsies are important. Indications of exposure can be obtained from serum organic fluorine levels.
5. You should determine the saturation level of human albumen with fluorochemicals. Human metabolism and distribution in the body are important. We must know the amount of organic fluorine in the fat and liver. It is possible that certain fluorochemicals are only in the blood. This information combined with analysis for serum organic fluorine levels gives better information than classical animal studies.
6. It would be medically acceptable to do a liver biopsy on employees who are exposed to fluorochemicals and are also alcoholics. Fat biopsy poses no problem. It would not be advisable to do liver biopsies on employees who are not alcoholics.

7. If there turns out to be health problems due to organic fluorochemicals in blood, the fluorochemicals could possibly be removed by haemoperfusion, plasma perfusion or plasma phoresis.

A comment was made that it would be beneficial to our understanding of fluorochemical distribution if tissue samples were available from a deceased individual who had worked with fluorochemicals. J.R. Mitchell agreed.

R.A. Nelson reviewed results of 90 day subacute toxicity studies using FC-95, FC-143 and FM-3422 (See attached slides and Meeting Minutes with H.C. Hodge of 4/12/79). J.R. Mitchell made the following comments:

1. The effects of fluoride ion on haematopoietic effects and liver toxicity should be investigated.
2. The slides from the I.R.D.C. study relating to liver toxicity should be obtained and reviewed to better define the liver changes.
3. Some of the symptoms in animals from these 90 day studies are similar to those observed with carcinogens.

M.T. Case agreed to get slides from all 90 day studies at I.R.D.C. and re-examine them.

M.T. Case summarized briefly the proposed study on FC-807 including the reasons for proceeding with the studies and the selected dose levels for the in-utero study. J.R. Mitchell made the following comments:

1. At present you have no definite evidence that FC-807 has entered man. Animal studies may be irrelevant.
2. Results are obtainable on FC-807 in humans. Analytical work can be done on virgin persons. Exposure can be studied.

3. You should get more information (in man) to properly design animal studies. Dose levels must be set and the proper animal species chosen which as a metabolic pathway comparable to man.

J.R. Mitchell was asked if he recommended any mutagenicity tests other than the Ames. He replied that he did not.

R.E. Ober questioned whether the amount of FC-807 actually transferred to food should be looked at. J.R. Mitchell considered this to be a good approach.

R.E. Ober questioned whether distribution of FC-807 should be looked at in animals before man. J.R. Mitchell replied that animals should not be studied in place of man if man is available.

R.E. Ober questioned whether it would be desirable to try to remove fluorochemicals from man by means of resins. J.R. Mitchell was uncertain as to this approach. It would depend on how fast the resin would remove the fluorochemicals. There could be problems.

J.R. Mitchell then summarized the meeting in the form of a slide as follows:

SUMMARY BY J.R. MITCHELL

- I. People at Risk
  1. 3M Employees
  2. Subcontractor Employees
  3. Public Health
  4. Environmental (fish, fowl, etc.)
- II. Legal Issues
  1. TSCA Sec. 8(e)
    - ? All criterial must be filled
  2. Human Injury

III. Clinical (Human) Studies

1.  $R_f$  disposition and distribution
2. Metabolites in tissue and urine
3. Intervention of Haemoperfusion or plasma phoresis (removal by) cholestamine type resins - others?
4. Epidemiology
  - a. Of assay and family
  - b. Other sources in USA
5. Epidemiology Review by Categories
  - a. Compound
  - b. Time Level
  - c. Dose
  - d. Organ System

IV. Animal Studies

1. Pharmacokinetic
2. Toxic Effects
  - a. Acute
  - b. Effect of  $F^-$

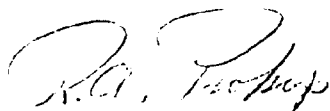
V. Analytical

1. Distribution
  - a. % binding and saturation
2. Metabolites
3. Contaminents from Manufacture
4. Route of exposure  $\longrightarrow$  disposition

During the summary Dr. Mitchell placed emphasis on epidemiology. Information on categories should be obtained immediately. This should be correlated with levels of organic fluorine in the blood. Deaths, haemopoetic effects rare tumors should be investigated.

Dr. Mitchell also commented on capabilities at the Baylor School of Medicine for analyzing for trace amounts of chemicals in serum and tissue. By combining negative ion plasma chromatography with a nuclear quadropole unit, amounts at the parts per trillion level can be detected. Besides being a more rapid method of analysis than we are now using, this technique might be used to determine fluorochemicals in tissue from fat and liver biopsies. This would allow one to determine the distribution of fluorochemicals in humans.

It was agreed that J.R. Mitchell will investigate the possibility of using the above technique to analyze trace amounts of 3M fluorochemicals. After consulting with analytical personnel at the Baylor School of Medicine, he will contact R.E. Ober as soon as possible and a decision as to how to proceed will be agreed upon.



RAP/ko  
Attachments