

Com Chem file

Subject: MEETING MINUTES -
MEETING WITH H.C. HODGE

3M "CONFIDENTIAL"

JUNE 7, 1979

THOSE PRESENT:

M.T. CASE - 218-2
F.D. GRIFFITH - 220-2E
H.C. HODGE - U. OF CALIFORNIA
L.C. KROGH - 223-6SE
J.D. LAZERTE - 236-1
R.E. OBER - 218-2
J.A. PENDERGRASS - 220-2E
R.A. PROKOP - 236-2B
F.A. UBEL - 220-2E
R.A. Nelson - 218-3

Those present met on April 12, 1979 at the Hilton Hotel in San Francisco California 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 FC-807. FC-807 is used in combination with a hydrocarbon sizing agent to give oil and water repellency to paper and paperboard. One of its principle uses is as an indirect food additive, and a petition was granted in the late 1960's for its use as such. It is manufactured by reacting perfluorooctanesulfonyl fluoride with ethyl amine. Subsequent reaction of the sulfonamide with ethylene carbonate followed by sequential reaction with $\text{POCl}_3/\text{H}_2\text{O}$ and ammonia give FC-807. (See attached flowsheets) It is sold as a 35-40% solution in isopropyl alcohol.

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.

The serum organic fluorine level of the individual who was previously removed from fluorochemical exposure when his serum organic fluorine level rose to 70 ppm has recently been measured. The level was found to be 45 ± 5 ppm. The amount of FC-143 in his urine was found to be 220 ug for a 24 hour period.

Exhibit
1210

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

Serum organic fluorine levels have recently been measured on selected employees at Cordova, Decatur and Chemolite. In comparison with levels measured in 1976 and 1977, there has been little change.

The serum organic fluorine levels of 15 Chemolite employees were measured in 1978 prior to their being involved in the packaging of FC-143. Repeat measurements of their serum organic fluorine taken recently showed some unexpected elevations in levels. Inorganic levels were also higher than expected. Contamination with inorganic fluoride is suspected to be the cause of the high inorganic levels in serum, but the entire set of results will be reviewed to see if any errors were made to relate exposure to serum organic fluorine levels.

Eight serum samples from rural China were analyzed for organic and inorganic fluorine levels. Organic fluorine levels ranged from 0.004 ppm to 0.017 ppm and inorganic fluoride levels from 0.044 to 0.076 ppm. In the U.S. serum organic fluorine levels range from 0.002 to 0.13 ppm and inorganic levels from 0.003 to 0.17 ppm.

The epidemiology study is still in progress. The study involves tracing about 3500 people and involves about 100 deaths. So far there does not appear to be what might be considered as "unusual causes of death".

H.C. Hodge commented that data from this epidemiology study is very important and that the study should be carried out carefully. Criteria set forth by the N.C.I. should be followed. Dr. Hodge further stated that he would rather accept data from this type of study for identifying human health effects than data from animal studies, but that the National Cancer Institute would not agree.

F.A. Ubel summarized a conversation with two Mayo Clinic physicians regarding the significance of slightly elevated liver enzyme levels in some of the Chemolite employees. No definite conclusions were reached, except that the values were very slightly elevated and in some instances were felt to be compatible with their history of alcohol ingestion. They could not make any statement unless they had a chance to examine the employees personally.

Dr. Hodge was shown a summary of the abnormal findings in those 3M employees who had known fluorochemical blood levels. He was given a copy.

The results of the physical examinations done on Decatur and Cordova employees look very good. There does not appear to be evidence of a work related problem. The Chemolite employees showed more abnormalities, but the majority of these appeared to be related to a known medical problem or medication. It was the conclusion of the physicians who supervised the examinations that there did not appear to be a problem which could be identified as work related. Additional analysis of the data will be done.

J.A. Pendergrass reviewed data on workplace concentrations of various fluorochemicals in Alabama and Minnesota plants. In most cases the workplace concentrations of fluorochemicals are low-lower than some time weight averages recommended for known or suspected carcinogens. Fluorochemical salts are exceptions. Due to their dusty nature workplace concentrations are higher. Levels of one of these materials, FC-143, have been reduced to an acceptable value. Work is underway to reduce exposure to other fluorochemical salts.

R.A. Nelson reviewed results of 90 day subacute toxicity studies using FC-95, FC-143 and FM-3422. (Slides attached) Of these compounds FC-95 was the most toxic. It produced deaths in the monkey at 4.5 mg/Kg and in the rat at ~10 mg/Kg. Target organs in the rat were liver hematopoietic tissue, stomach and small intestine. In monkeys, the apparent target organ was the upper G.I. tract.

The liver and possibly the kidney and G.I. tract were target organs in the rats fed FM-3422. In the case of monkeys there was clinical evidence of G.I. toxicity.

FC-143 produced liver changes in rats at the highest dose. In monkeys hematopoietic tissue was affected at lethal doses and there was evidence of gastrointestinal toxicity. H.C. Hodge also presented his summary of results of the 90 day studies on FC-143, FM-3422 and FC-95 (attached). His projected no-effect levels were 1.5 mg/Kg for FC-143 and FM-3422 in the rat, and 3 mg/Kg in the monkey. For FC-95 there was no no-effect level in the rat and no data for estimating a no-effect level in the monkey. There appears to be an indication of liver effects from FC-95, FM-3422 and FC-143 at all dose levels in the rat studies.

H.C. Hodge questioned whether some of the toxic effects observed in the animal studies might be due to low surface tension. Surface active agents are known to be capable of causing a problem in the gut. It was pointed out that some fluorochemicals are the most potent surfactants known.

F.A. Griffith pointed out that toxic effect such as those observed with FC-95, FM-3422 and FC-143 are common with surfactants.

R.A. Nelson pointed out that the liver effects are probably reversible, but this would require further study to prove.

H.C. Hodge pointed out that a buildup of fluoride ion can be detected most rapidly in the bone. Thus evidence of breakdown of fluorochemicals to fluoride ion could be detected in the bone. Bone should be collected at the end of a chronic study and analyzed for fluoride.

H.C. Hodge was then asked for his recommendations on future work. After a brief review of customer exposure to 3M fluorochemicals Dr. Hodge recommended the following:

1. It does not appear that there is a toxicity problem outside 3M. However we do not know if there are toxicity problems due to employee exposure. Reduction in exposure should have top priority.
2. Metabolic instead of chronic studies should be done next. Sequestering kinetics and metabolites should be looked at.
3. Reproduction studies, including teratology, should be given high priority. Two generations should be used. Such studies should take less than one year.
4. Carcinogenicity of fluorochemicals should be looked at. Start with Ames testing and continue to more sophisticated mutagenicity tests. If any of these turn out positive it will be necessary to go on to a chronic study.

R.A. Nelson questioned the reliability of tests other than the Ames. The transformation test may be on the way out. Different regulatory agencies are not getting results which agree.

M.T. Case outlined proposed studies on FC-807 and studies being considered for FC-95 and FC-143. (Slides attached) A question was raised on the FC-807 study as to whether the F.D.A. should be asked about the protocol. It was suggested that we should proceed without consulting the F.D.A. since the study is scientifically valid.

R.E. Ober outlined planned work in the metabolic area. (Slides attached) This proposed work involved metabolism of FC-807, persistence of FC-95 and FC-143, and skin absorption studies.

It was suggested that H.C. Hodge be given more time to consider the proposed slides on FC-807, FC-95, FC-143 and the metabolism work before being asked for an opinion.

ADDENDUM

I called Dr. Hodge on April 20, 1979 to give him the acute oral toxicity data on FC-95, FC-143 and FM-3422 which was generated at IRDC prior to the 90 day studies. He asked that the following be added to the meeting minutes:

The study of levels of FC-807 or its metabolites is of utmost importance in determining possible future problems. It should be determined if FC-807 or its metabolites are present in man, what level they are present, and the degree of persistence (half-life) of these materials.



RAP/ko
Attachments