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July 31, 2003

8EHQ-80-373

TELECOPY AND FEDERAL EXPRESS

Richard H. Hefter, Chief
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U.S. Environmental Protection Agency
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Washington, D.C. 20460-0001

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Washington, D.C. 20460-0001

Re: TSCA Section 8(e) Reporting For PFOA

Dear Mr. Hefter:

This letter serves as a supplement to our letter of July 3, 2003, in connection with the referenced matter providing additional information relating to the extent of E.I. duPont de Nemours and Company's ("DuPont's") knowledge of health effects related to exposure to ammonium perfluorooctanoate (a/k/a APFO/PFOA/FC-143/C-8) (hereinafter "C-8") at the time that DuPont obtained the pregnancy outcome and drinking water contamination information referenced in our July 3, 2003 letter. Because of the potential likelihood of substantial harm to our Class members or the public interest from a lack of complete information on this topic, we submit the following additional supplemental information obtained from DuPont for consideration in connection with your Agency's evaluations of the statements made by DuPont's counsel on this matter in its June 20, 2003, letter responding to your May 22, 2003, letter on this topic:

1. November 9, 1961 - DuPont's Toxicology Section Chief, Dorothy B. Hood, upon review of available information relating to toxicity of Teflon® dispersing agents, concluded that C-8 has "the ability to increase the size of the liver of rats at low doses," and "recommended that . . . these materials . . . be handled with extreme care. Contact with the skin should be strictly avoided." (Exhibit A (HLAB000232-233))

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2. February 14, 1962 - DuPont studies on C-8 in rats "proved lethal in high dose concentrations through injury to the stomach, intestine, brain, lung and pancreas. At lower dose concentrations the chemical induced enlargement of the liver, pancreas and kidney, the least dose which included a change in liver being 1.5 mg/kg." (Exhibit A (HLAB000240))
3. August 19, 1965 - DuPont's medical research projects on the effects of C-8 and related chemicals on the livers of rats and dogs confirmed that "the most striking abnormality in animals surviving a single sub-lethal dose was gross enlargement of the liver." (Exhibit B (HLAB000003-20))
4. August 31, 1966 - DuPont determined that "[s]ome of the solids wastes from the Fine Powder and Dispersion Area of the [DuPont Washington Works] "Teflon®" plant contain small amount of toxic perfluorocarboxylic dispersing agents" and that "[w]ithout a pretreatment, a small amount of the perfluorocarboxylic acid dispersing agent would be leached into the groundwater." (Exhibit C (EID193614-8))
5. October 28, 1966 - DuPont's Washington Works decided that wet "'Teflon®' scrap is no longer going to the city land-fill" and that "[a]ll wet 'Teflon®' containing C-8 or C-9 dispersing agents (must be kept on the plant for disposal at sea at a future date)." (Exhibit D (EID193613))
6. February 18, 1970 - DuPont's Washington Works plant sent a memo to DuPont's Experimental Station in Wilmington, Delaware stating that:

Past studies made at Haskell Laboratory have indicated that ammonium perfluorooctanoate (C-8 APFC), which is used in the preparation of Teflon®" dispersions, is highly toxic when inhaled and moderately toxic when injected. . . . We are interested in determining the systemic effect for repetitious skin contacts of short duration with C-8 APFC powder and with the aqueous dispersion of polytetrafluoroethylene containing C-8 (or chlorendic acid). We are also interested in determining the chronic effect of inhalation of minute quantities of C-8 APFC. In addition to knowing these effects, we would like guidance on

the personnel equipment necessary for adequate protection against these effects.

(Exhibit E (EID123138-43))

7. May 8, 1970 - DuPont's Bio-Sciences Group Research Manager informed DuPont's Washington Works plant that "C-8 APFC and C-9 APFC cause liver enlargement, but we don't know what is the lowest repeated oral dosage that will cause it. We have no repeated oral dosage study to indicate if C-8 APFC or C-9 APFC accumulates in the body to toxic levels. We do not know the eye or skin irritation potential for C-8 APFC or C-9 APFC and we do not know whether the liver enlargement effect occurs in rats or in other species as well." (Exhibit F (EID072196-99)) After summarizing the potential studies necessary to acquire the missing toxicology information, DuPont's Bio-Sciences Group Research Manager informed DuPont's Washington Works plant that "none of the repeated inhalation studies would be necessary" "if you can eliminate continuous exposure to C-8 APFC by inhalation." "Similarly, elimination of repeated exposure by skin absorption would eliminate the need for a repeated skin absorption toxicity study." (*Id.*)
8. 1975 - DuPont completed a Study of Myocardial Infarction at Washington Works Plant "to evaluate the incidence of cases of myocardial infarction among male wage and salary roll employees at the Washington Works Plant from 1956 to 1973 . . . because some workers had complained that the occurrence of heart attacks among employees seemed excessive." (Exhibit G (EID713127-35)) DuPont's study concluded that:

Among salaried employees, the observed incidence of myocardial infarction is significantly higher than the expected number . . . The high overall incidence is largely the result of elevated rates in recent years. In the period from 1971 to 1973, the difference between observed and predicted numbers is great: 12 observed cases versus 5.3 expected cases (P = 0.008). . . . Further investigation of occupation reveals that the high frequency of M.I. cases among salaried employees is seen largely in foreman. . . . Patrolman, a group representing three percent of the Washington Works population, also showed a somewhat elevated incidence of M.I.

(*Id.*) With respect to the increased rate of M.I. among salaried foreman, DuPont concluded that "increased incidence in this group cannot be explained by their age distribution." (*Id.*)

9. May 15, 1978 - In connection with an upcoming meeting with 3M on May 30, 1978, DuPont's Haskell Laboratory forwarded to DuPont's Medical Director, Dr. Bruce Karrh, a copy of an article published in 1976 entitled "Organic Fluoro-Compounds in Human Plasma: Prevalence and Characterization." (Exhibit H (EID107111-29)) In the 1976 study, the authors collected plasma samples from "106 individuals living in five different cities with between 0.1 and 5.6 ppm fluoride in their public water supply." (*Id.*, at EID107113) The "[h]uman plasma was obtained from blood banks in five cities." (*Id.*, at EID107116) The five cities included in the blood study were Albany, New York, Rochester, New York, Corpus Christi, Texas, Hillsboro, Texas, and Andrews, Texas. (*Id.*, at EID107121) Analysis of the blood samples revealed "chemical shifts" consistent with C-8 and shifts "consistent with the presence of amide or ester derivatives, or possibly with the presence of a sulfonic acid derivative as the functional group. One explanation for the additional peaks in the spectrum is the presence of branched isomers." (*Id.*, at EID107124) The authors of the 1976 study concluded that:

These findings suggest that there is widespread contamination of human tissues with trace amounts of organic fluorocompounds derived from commercial products. All available information on this subject is in accordance with this interpretation. A series of compounds having a structure consistent with that found here for the predominate form of organic fluorine in human plasma is widely used commercially for their potent surfactant properties. For example, they are used as water and oil repellents in the treatment of fabrics and leather. Other uses include the production of waxed paper and formulation of floor waxes. The findings presented here that the concentration of organic fluorine was not related to the concentration of inorganic fluoride either in blood or in the public water supply, and the early finding that they was little or no organic fluorine in the blood of animals other than human are all in keeping with environmental sources such as these.

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The prevalence of organic fluorine in human plasma is probably quite high since 104 of the 106 plasma samples tested here and all 35 in an earlier study had measurable quantities. The prevalence of the particular compounds isolated and characterized here, *i.e.*, perfluoro fatty acid (C-6 - C-8) derivatives, is not known since the starting material for each batch shown . . . was pooled from between 25 and 30 individuals and since only about one third of the original organic fluorine content was accounted for in the fractions containing these compounds.

(*Id.*, at 107126-7)

10. June 16, 1978 - DuPont reported that the 3M Company "has reported finding FC143 plus other unidentified fluorochemicals in the blood of potentially exposed workers." (Exhibit I (EID080229-31)) In response, DuPont's Medical Director, Dr. Bruce Karrh, recommended that DuPont "[r]eview the medical records of all . . . persons [who currently work or have worked jobs in which there is or was potential for exposure to "Telomer A and its non-polymeric derivatives"] still employed by DuPont, looking for consistent or unusual health occurrences or trends," and to begin obtaining "blood fluorochemical levels" of exposed and unexposed workers. (*Id.*)
11. June 22, 1978 - DuPont initiated a program to inform employees of its Chambers Works, New Jersey facility of 3M's finding of organic fluorine in the blood of its employees and DuPont's program to begin analyzing the blood and medical records of Chambers Works employees exposed to Telomer A sold under the "Zonyl" trademark. (Exhibit J (EID110651-3)) (*See also* Exhibit K (EID080241-46)) DuPont also informed its Chambers Works "supervision" at the time that the testing was prompted by a "1976 report [referenced in the memo as the one authored by Guy, et al.] indicating "that the blood serum of the general population in the U.S. contains trace quantities of fluorine in both organic and inorganic form" and that the "concentration of inorganic fluorine has been shown to be related to fluoride ion in water supplies (natural and added)" but that "[t]here is no ready explanation for the presence of organic fluorine." (Exhibit J, at EID 110653) In response to the anticipated question of : "Will DuPont be informing the appropriate regulatory agencies of this situation?" DuPont's prepared response was: "At this point in time we see no significant risk associated with the fluorine content in the blood. The existence of fluorine in blood has been known for 10 years and is published in open literature." (Exhibit K, at EID 080245)

12. August 3, 1978 - DuPont's Medical Director, Dr. Bruce Karrh, advised DuPont's Washington Works plant that DuPont recommended "the same medical surveillance program" for DuPont's Washington Works employees exposed to C-8 through production of Teflon and FEP dispersions that Dr. Karrh had recommended for the DuPont Chambers Works employees exposed to Telomers through Zonyl production. (Exhibit L (EID080236-40))
13. September 20, 1978 - DuPont Washington Works' Medical Director, Dr. Younger Power, prepared a memo summarizing his "review of the medical records of eleven operators and eighteen laboratorians [at the Washington Works Plant] who have had long-term exposure to C-8." (Exhibit M (EID080233-4)) Dr. Power concluded that:

[A]s you would anticipate, a great variety of illnesses and physical findings were found . . . [s]ome of the illnesses found are two heart attacks and five employees with high blood pressure. One questionable case of skin cancer was found during an employee's physical examination in 1976. No further mention of this possible tumor could be found. Minor elevations of many blood tests did occur in larger-than-anticipated numbers. . . . One of the liver function tests (SGOT) is most frequently elevated in the operator group. . . . Since it has been previously determined that C-8 is an hepatatoxin, it is possible that C-8 may be causing very minimal, and certainly not clinically apparent, toxic effects to the liver.

(*Id.*)

14. December 22, 1978 - DuPont's Medical Director, Dr. Bruce Karrh, prepared a memo summarizing DuPont's "Chambers Works Fluorosulfactant [sic] Study," stating that "there does not seem to be any adverse health effects reported in this study, with a possible exception of an effect on the liver." (Exhibit N (EID096510))
15. February 7, 1979 - 3M forwarded to DuPont copies of 3M's new 90-day subacute C-8 rat toxicity study and 3M's 90- day subacute C-8 Rhesus monkey toxicity study. (Exhibit O (EID071855))

16. March 5, 1979 - DuPont reviewed 3M's new C-8 rat and monkey studies and agreed that there are compound-related effects indicated in both studies, and that additional adverse effects apparently were revealed in the data but not reported by 3M in the text of the studies. (Exhibit P (EID123133))
17. March 15, 1979 - DuPont's Epidemiology Section Manager, Sidney Pell, prepared a memo summarizing "a tabulation of the Dispensary Visits and Disability Wage incidence in the [Telomer /Zonyl] exposed and control groups" at DuPont's Chambers Works facility. (Exhibit Q (GK000378-79)) Mr. Pell found that:

In the category, "Allergic, Endocrine, and the Metabolic" disorders, a significantly higher incidence was found in the exposed group for both Dispensary Visits and Disability Wage incidents. This was attributed in the report to a higher number of diabetics in the exposed group. The exposed group also showed significantly higher numbers for "mental and psychoneurotic" disorders and for disorders of "skin and cellular tissues." . . . Explanations for these differences cannot be found from the available data. . . . Although the number of employees with abnormal liver function tests was notably higher in the exposed group (6 compared to 1), the difference is not statistically significant ($P < 0.05$). Nevertheless, the data do suggest that the exposed group may be at an excess risk of developing liver disease, so continued surveillance would be advisable.

(*Id.*)

18. May 22, 1979 - DuPont prepared a "Status Review: Fluorochemicals in Blood" report confirming that DuPont's blood testing had detected organic fluorine in a "control group" of presumably "non-exposed" DuPont Wilmington, Delaware employees at between 0-0.38 ppm (average of 0.094 ppm), and that DuPont had detected organic fluorine in the blood of its Chambers Works, New Jersey employees at a range of 0-0.37 ppm (average of 0.15 ppm), with one individual in the "Wilmington Control Group" testing as high as 10.6 ppm for organic fluorine in blood. (Exhibit R (EID80274)) Because the levels of organic fluorine in the blood of DuPont's Chambers Works employees were not viewed as significantly

different from the "control group" of Wilmington, Delaware employees, the recommendation was made to "discontinue program to determine fluorine in blood, advise employees that blood analysis program has been discontinued due to uniformly favorable results." (*Id.*, at EID080282) (*See also* Exhibit S (EID080267-70))

19. July 20, 1979 - DuPont representatives met with 3M to discuss the status of organic fluorine blood testing and health studies. (*See* Exhibit U (EID107173)) During the meeting "3M described a gas chromatographic method to determine perfluorooctanoic acid (FC-143) in blood, urine, liver, and other biological materials. It can measure as little as 1.5ppb." (*Id.*) 3M also disclosed to DuPont during the meeting that "3M got blood samples from 8 peasants in a Chinese village 30 miles from Canton. The organic fluorine was significantly lower (0.004-0.017 ppm), than values found in developed countries (e.g., 3M found 0.002-0.13 in 106 members of the general U.S. population)." (*Id.*, at EID107174) DuPont also apparently planned to discuss with 3M the reportability of the blood data information to U.S. EPA under TSCA Section 8(e). (*See* Exhibit T (EID107194-95))
20. July 25, 1979 - DuPont prepared a memorandum summarizing the status of its work relating to organic fluorocompounds in human blood, indicating that organic fluorine levels had been detected in DuPont Washington Works employees at between 0.4 and 21.1 ppm. (Exhibit V (EID107199)) The memorandum also confirmed that DuPont "[d]ecided not to report to EPA under 8(e) of TOSCA [sic] because fluorine in blood per se was disclosed in 1976 article and because no adverse health effect is known, therefore, no substantial risk." (*Id.* *See also* Exhibit W (EID107196))
21. July 30, 1979 - DuPont prepared a memorandum summarizing information discussed with 3M on July 26, 1978, including DuPont's decision not to report the recent blood data to U.S. EPA. (Exhibit W (EID 107196)) During the conversation with 3M, DuPont:

Advised Robert Prokop of 3M of our . . . conclusions with regard to Section 8(e) and our general practice of reporting or otherwise publicizing relevant findings even if they are not required to be reported under Section 8(e). [Eugene Berman of DuPont] asked Prokop to clarify what plans 3M had with regard to publicizing this

fluorine blood level information and/or directly advising the relevant health agency of this information. Prokop indicated that he believed 3M was favorably disposed toward disclosing this information and promised a more definitive response next week after reviewing the matter with Lester Krogh (3M's Division Vice President).

(*Id.*)

21. August 28, 1979 - DuPont Epidemiologist, William E. Fayerweather sent a memo to DuPont Washington Works' Medical Director, Dr. Younger Power, stating that DuPont's Medical Director, Dr. Bruce Karrh, had asked him "to look into the liver function test results for workers with C-8 exposure, and [that Dr. Younger] Power asked me to examine myocardial infarction cases and deaths at the Plant. Mr. Fayerweather concluded that:

My preliminary results suggest that C-8 exposed workers may possibly have positive liver function tests more often than the plant population as a whole, and that the number of active wage role employees having myocardial infarctions from 1974 through 1977 was somewhat higher than was expected based on company-wide experience. As a consequence of these preliminary findings, the following steps are being taken: (1) Liver function survey ... (2) Coronary heart disease mortality [study].

(Exhibit X (EID080214-15))

22. October, 1979 - DuPont prepared tables summarizing the levels of organic fluorine detected in Washington Works employee blood. (See Exhibits Y (EID080255-60), Z (EID080732-37), and AA (EID107158-60))
23. January 17, 1980 - DuPont obtained organic fluoride levels in blood from mechanics at its Washington Works plant, indicating an average of 0.66 ppm organic fluorine in the employees' blood. (Exhibit BB (EID080193))

24. January 28, 1980 - DuPont's Assistant Medical Director, Dr. Vann Brewster, prepared a memo summarizing conclusions reached by DuPont during a meeting on January 25, 1980 to discuss an ongoing "Liver Enzyme Study of Workers Exposed to C-8 at Parkersburg." (Exhibit CC (EID099433-34)) Dr. Brewster noted that "the mean SGOT in the TFE process operator group and the mean AP in the FEP process group are elevated when compared to other plant groups" and that "we are unable to explain why only the mean SGOT would be elevated in one group and only the mean AP would be elevated in another group." (*Id.*)
25. February 25, 1980 - DuPont prepared a memorandum summarizing the results of total, inorganic, and organic fluorine in worker blood at its Spruance, Virginia plant. (Exhibit EE (EID107155-56))
26. February 28, 1980 - DuPont prepared a memorandum summarizing the levels of total and organic fluorine in worker blood in relationship to workplace C-8 air levels at DuPont's Toledo, Philadelphia, Marshall Lab, and Fairfield sites. (Exhibit DD (EID079084))
27. March 3, 1980 - DuPont prepared a memorandum summarizing the level of organic fluorine detected in the blood of its employees at its Washington Works, Wilmington, Delaware, Chambers Works, Experimental Station, and Spruance facilities, along with DuPont's "Finishes Plants." (Exhibit FF (EID079036))
28. June 9, 1980 - DuPont's Assistant Medical Director, Dr. Vann Brewster, prepared a memo expressing his concern that a draft communication to DuPont's Washington Works employees regarding the outcome of DuPont's liver study of employees "implies that the Medical Division will not continue the study of liver tests on those employees potentially exposed to C-8." (Exhibit GG (EID102477)). In response, Dr. Brewster states that:

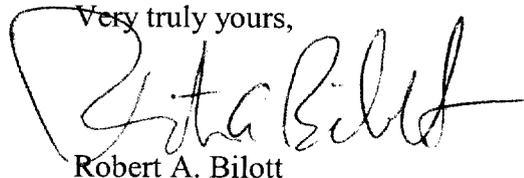
Even though we have found no "conclusive evidence of a occupationally related health problem," we still cannot explain why the mean SGOT was significantly higher among TFE process workers and that the mean AP was significantly higher among FEP process and service workers. Therefore, I recommend the following changes to the draft: At the end of the second paragraph, . . . add: "However, it was recommended that the study of liver tests continue." [and] [a]t the bottom of

page 2, add a fourth item: "Continue to evaluate the liver tests of employees with potential exposure to C-8."

(*Id.*)

29. July 31, 1980 - DuPont conducted a "C-8 communications meeting" and provided an "Outline, Talk & Charts." (Exhibit HH (EID079399-418)) In those documents, DuPont confirmed that "C-8 is toxic but can be handled safely. People working with C-8 generally accumulate organic fluorine in the blood, and levels generally correlate with job exposure potential. Although this has caused no adverse health effects, continued exposure is not tolerable." (*Id.*, at EID079401. *See also* Exhibit II (EID077237-62))
30. November, 1980 - DuPont prepared an analysis of Washington Works employee blood results, including a new analysis of the results "obtained by the C-8/GC method." (Exhibit JJ (EID080726-31) *See also* Exhibits KK (EID080717-18), LL (EID080719-24), MM (EID079382-85) and NN (EID079386))

Very truly yours,



Robert A. Bilott

RAB:mdm
Enclosures

cc: Dr. Charles M. Auer (USEPA OPPT) (w/o encls.) (letter by telecopy)
Mary Dominiak (USEPA OPPT) (for inclusion in AR-226) (w/encls.)(letter by telecopy)
Jennifer Seed (USEPA) (w/encls.) (letter by telecopy - enclosures by hard copy)
R. Edison Hill, Esq. (w/ encls.)
Larry A. Winter, Esq. (w/ encls.)
Gerald J. Rapien, Esq. (w/o encls.)

AR 226-1442

A

November 9, 1961

GERALD J. ARENSON
POLYCHEMICALS DEPARTMENT
RESEARCH & DEVELOPMENT DIVISION
EXPERIMENTAL STATION

TOXICITY OF TEFLON DISPERSING AGENTS

A brief summary of our toxicity work on Airt and other Teflon dispersing agents with emphasis on liver enlargement which seems to be the most sensitive sign of toxicity is given below. The detailed reports of work completed to date will be available within a few days.

Airt (Ammonium 3,6 dioxo 2,5 di(tert)fluoro methyl undecafluorononanoate)

The oral LD₅₀ for rats was found to be 60 mg/kg. Survivors showed definite liver enlargement in doses down to 1.5 mg/kg and with possible changes at 0.45 and 0.15 mg/kg. Single doses of 12 mg/kg produced liver enlargement which tended to increase during the two months following the dose. One one-hundredth of the lethal dose or 0.6 mg/kg given daily 5 times a week for 2 weeks produced enlargement which was significant in those rats killed on the day of final treatment and in those killed 14 days later. Histological examination of the livers indicated that the enlargement was due to increase in cell size rather than an increase in the number of cells.

The lethal dose by skin absorption in rabbits was 180 mg/kg. Although the changes in liver weight in these rabbits are more difficult to evaluate, there was a tendency toward enlargement and smaller signs of liver injury.

A 25% aqueous solution in contact with the eye caused damage which persisted through 8 days. Washing with water 20 times after immersion prevented permanent damage. Ten and twenty-five percent solutions were also irritating to guinea pig skin but did not cause skin sensitization.

Gp-ABTC (Ammonium perfluorocaprylate)

The oral LD₅₀ for rats was 670 mg/kg. Liver enlargement was definite down to a dose of 200 mg/kg with possible early signs down to 1.5 mg/kg.

BA 2'

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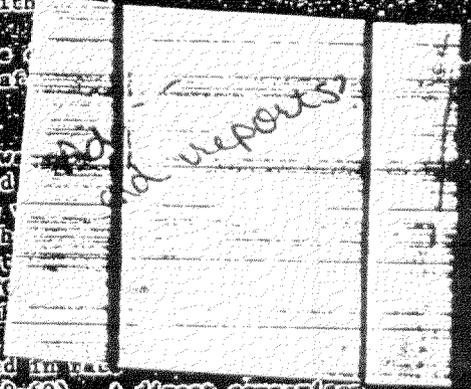
C₃-AFC - (Ammonium perhydroxy dodecafluorooctanoate)

The oral LD₅₀ was 1500 mg/kg. Survivors showed enlargement which appears evident in doses as low as 12 mg/kg.

"Teflon" Feeding Tests with "Teflon" 7, "Teflon" 6 made with C₃-AFC, "Teflon" 60 made with C₂, and "Teflon" 60 made with C₃

These compounds were fed at a level of 25% in the diet for 2, 3 and 5 weeks. Rats were sacrificed 2, 3 and 5 weeks after materials started.

Livers of rats sacrificed after two and three weeks showed slight enlargement only in the group fed "Teflon" 60 with C₃-AFC. After two-week test period the remaining rats were fed "Teflon" 60 with AFR and "Teflon" C₃ AFR. The values of these fed "Teflon" 60 with C₃-AFC are significantly different from the controls and the other groups. Although the number of rats is small and the time of feeding relatively short, this confirms the earlier liver enlargement observed in rats fed "Teflon" 60 with AFR (H. Report No. 49-60). A direct comparison among these compounds is difficult to make in these feeding tests because we do not know the concentrations of the fluoro acid dispersing agents present.



Conclusions:

AFR is a very toxic compound. Not only does it have a low lethal dose but a single dose of 1/5 the lethal dose produced liver enlargement which increased with time. And 1/100 of the lethal dose fed 10 times produced definite liver enlargement. In addition, it was easily absorbed through the skin and produced liver damage in a second species. When "Teflon" containing less than 5 ppm AFR was fed to rats, it still produced enlargement which was apparent after 2 weeks.

The C₂ and C₃ acids have much lower acute toxicity, but they too have the ability to increase the size of the liver of rats at low doses. These short experiments may indicate differences in rate of development rather than qualitative differences but completion of microscopic examination of animals in the current studies as well as dosing of greater numbers of rats at the relevant levels and holding them for longer periods would be needed to establish the lowest effective level for each compound.

It is recommended that all of these materials, especially AFR, be handled with extreme care. Contact with the skin should be strictly avoided. Tests on a third species, say dogs, should be carried out where changes in liver function could be studied over a long period of time. The results of such tests might also throw some light on any possible species differences in susceptibility.

D. B. B. H.

ROBERT H. BLOD
CHIEF, TOXICOLOGY SECTION

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USEPA 16150

HLA B000233

Toxicity Behavior of Fluorocarbon Surfactants - Carrison

Recent data obtained from Haskell Lab (via G. J. Aronson) indicate that the toxicity of AHD (the ammonium salt of PFPO dimer acid) is very low (ca. half that of sodium chloride). We also know that AHD is a poor surfactant. These data indicate a possible relationship between toxicity and surface activity. A tabulation of available data follows:

<u>Agent</u>	<u>CMC (%)</u>	<u>Surface Tension of a 0.2% Aqueous Solution</u>	<u>AR₅₀</u>
ATC ₃	0.27	23	60
AHT	0.12	31	50
C ₆ APFC	1.1	16	670
C ₆ AFD	1.5	54	1500
AHD	7	61	7500
H ₂ O	-	72	-

ATC₃ = NH₄ salt of PFPO trimer acid
 AHD values probably ± 50%

The CMC (critical micelle concentration) and surface tension data are indicative of surface activity. These data suggest that:

1. AHT (NH₄ salt of PFPO trimer acid), which is a slightly poorer surfactant than C₆APFC, should be of lower toxicity than AHD. Sewerworks trials have shown that AHT may be used as a dispersing agent.
2. The telomer acid salts higher than C₆ might possess toxicity on the order of that of AHT.
3. Fluorocarbon surfactants as a class may possess a high degree of toxicity corresponding to their surface activity.

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Toxicity Data

SOURCE: WILSON & CO.
(via E.O. FUNDATION)

<u>ANIMAL</u>	<u>MANNER OF ADMINISTRATION</u>	<u>DOSE</u>	<u>RESULTS</u>
RAT	INGESTION	15 mg/kg	LD50 3.55
RABBIT	25% SOLN ON SKIN		LD50 3.25
RAT	INGESTION	C-8	LD50 3.25
RAT	INGESTION	C-9	LD50 3.25

* LIVER ENLARGEMENT

FINE POWDER: Up to 100 ppm of AHT on resin - no effect.

DISPERSIONAL: Splashing - Be reasonably careful of the wash affected skin areas within a few days after contact. Extreme precaution not required.

FURTHER TOXICITY DATA

RABBIT	10% SOLN IN EYE	NO EFFECT
RABBIT	25% SOLN IN EYE	NO EFFECT
QUINON PIG	10% SOLN ON SKIN	NO EFFECT
QUINON PIG	15% SOLN ON SKIN	NO EFFECT
QUINON PIG	25% SOLN ON SKIN	NO EFFECT

HLABUW253

CARRIER

APPROXIMATE VOLUMES
CARRIED IN TANKS
MEASURED IN
GALLONS

CONC. AHT. SOLN. 1000

AQ. CHARGE TOWERS 1400

35% DISPERSION WATER 1100
RESID 100

12% DISPERSION WATER 2600
RESID 100

EFFLUENT FLOTATION TANK 2600

EFFLUENT DRYER 1500

BASIS GRANIS CARRIER DISC (W/10%) x 10⁶
WATER CARRIER

QUESTIONS

- (1) WHAT IS THE...
- (2) WHAT IS THE...
- (3) WHAT IS THE...
- (4) WHAT IS THE...

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Drug 3561

ACUTE ORAL TOXICITY TEST

MATERIAL: *Ammonium Perchlorate*
 MR. NO. *601* DEPT. *Pathology* BK. NO. *101*
 DEPT. SAMPLE NO. *70-101* HASK. NO. *101* DENSITY
 Solid () Solution () gms/100 ml ()
 Liquid () Paste () gms/100 gms ()
 Semi-Liquid () Powder () ml/100 ml ()
 Material given by stomach tube or by *gavage*
 Form or as a % solution of active ingredient in *water*
 suspension of *1:1* sample

Date	Animal Number	Init. Wt.	Dose (ml)	Dose (mg/kg)	% Sol	Weight Change (grams)	Results	WTS
9-28	48405	373	280	250	30	48405-9	48405-9	YES
10-3	48456	425	377	350	30	48456-10	48456-10	NO
9-28	48390	398	434	1000	30	48390-9	48390-9	YES
10-3	48453	430	388	670	10	48453-10	48453-10	NO
10-3	48438	435	448	550	10	48438-10	48438-10	YES
10-3	48416	401	415	500	10	48416-10	48416-10	YES
10-3	48450	572	734	500	10	48450-10	48450-10	YES
9-28	48345	345	734	500	30	48345-9	48345-9	YES
10-3	48495	350	350	500	10	48495-10	48495-10	YES
10-10	48425	530	734	500	10	48425-10	48425-10	YES
10-10	48486	535	400	500	10	48486-10	48486-10	YES

AEDC: 676 mg/kg

REMARKS:

Grams per 100 ml

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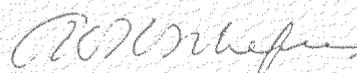
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AMMONIUM PERFLUOROCAPRYLATE
(C8AFFC)

NR-004 - H-203 - P-62-172

SUMMARY

Oral administration of C₈AFFC, in three experiments involving forty-one rats, proved lethal in high dose concentrations through injury to the stomach, intestine, brain, lung and pancreas. At lower dose concentrations the chemical induced enlargement of the liver, pancreas and kidney, the least dose which induced a change in the liver being 1.5 mg/kg.


G. W. H. Schepers, M.D.
Pathologist

GWHS/ah
2-14-62

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ML-104
C8 APPC

AMMONIUM PERSULFATE POLYMERIZATE (CPA1-C) (FC-115)

Ammonium Persulfate Polymerizate Single Oral Acute Inhalation

Male C57BL/6J Mice

NR-1 - 1-10-72 - 1-12-72

The chemical is soluble in water, acetone, and ethanol. The sample contained 25% of the active agent, which has the formula $CF_3(CF_2)_8COONH_4$. The polymer was used as a dispersing agent in PFE polymerizations.

The animals were treated as aqueous solution concentrations ranging from 1.5 to 2250. Quantities of these solutions varying from 1 to 2 ml were administered by intragastric intubation. Initially eleven dose levels were administered, ranging from 2250 mg/kg through 1500, 1000, 670, 450, 300, 200, 120, 60, 12 to 1.5 mg/kg. Subsequently two confirmatory tests were conducted. In the first, three rats received 12 mg/kg of the CPAFFC and were killed 14 days later. In the second, groups of 3 rats received 130, 60, 26, 12, 5.1, 2.3 and 1 mg/kg and were killed 14 days later. The incidence and severity of lesions found at necropsy are listed in Table 1. Organ weight data are presented in Table 2 to 6.

Four rats died within one day after administration of the 2250, 1500, 1000 and 670 mg/kg doses. These deaths were due primarily to injury to the stomach and intestine, but there were secondary effects on the lungs, brain, and pancreas. Post-mortem autolysis partially obscured the effects of the chemical in these four instances.

The principle change was in the liver which showed morphological deviations and weight changes. The 12 mg/kg dose level appears to be the transition dose for this effect.

The chemical also produced changes in the kidneys down to the 12 mg/kg level, which were accompanied by an increase in weight at 26 mg/kg and higher.

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While no morphological changes were found, the splenic weight showed significant deviations from those of the control rats.

The sporadic occurrence of changes in the thymus and spleen may be related to the moderately severe chronic pneumonitis in these rats. These changes were not clearly dose-related, but may represent indirect effects of the chemical.

Comments:

The effect of this chemical on the liver is of special interest since similar (fluorinated) aliphatics have produced persistent increases in liver weight. It is of interest to note that the liver weight was increased even at the 1.5 mg/kg level in rats which had a relatively high body weight at the start of the experiment, whereas in rats with the standard initial body weight, liver enlargement was not noted for doses below 20 mg/kg. The same observation applied for the kidney. The weight response of the pancreas was more irregular but suggests a dose relationship to a degree, especially in the second confirmatory test (Table 5). A decisive weight increase for the pancreas was demonstrated even at the low dose of 5.1 mg/kg. It would seem, therefore, that the pancreas is more responsive to this compound than is the liver.

It would be of interest to see if the change in liver weight progresses, as occurred with AHT.

Carl Johnson
Carl Johnson, D.V.M.

G. W. H. Schepers
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Pathologist
2-8-62

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LEGEND FOR TABLE 1

1. Liver - edema
 2. Liver - pale or brownish
 3. Liver - soft
 4. Liver - lobular markings prominent
 5. Kidneys - surface speckled
 6. Kidneys - pale
 7. Thymus - petechiated
 8. Lungs - edema
 9. Lungs - irregular congestion
 10. Lungs - focal atelectasia
 11. Lungs - semi-consolidation
-
- D₁. Chemical gastroenteritis with pneumonic
 - D₂. Advanced autolysis
 - D₃. Hemorrhagic gastritis
 - K. Killed
-
- a. Diffuse congestion of lung
 - b. Hyperinflation of lung
 - c. Subpleural plaques +++ (lung)
 - d. Adrenals: pale
 - e. Spleen: enlarged
 - f. Pancreas: pale
 - g. Brain: congested and edematous
-
- + = Slight reaction.
++ = Moderate reaction.
+++ = Marked reaction.

Prepared By: Cary Johnson
Cary Johnson, D.V.M.

Approved By: G. W. F. Schepers
G. W. F. Schepers, M.D.
Pathologist
2-8-52

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TABLE 1
GROSS PATHOLOGIC SUMMARY

Haskell No: 3035 Material: Amiprium Parthenocaprylate
Species: Male CRCD Rats Procedure: Gastric Incubation
SRR No: 601 Test: AID Excipient: Water
Report No: P-62-172 Experiment Period: 9-21-61 - 12-12-61 T. I. A. D. B. G. Prosecutor: G. W. Schepers

Group	Dose mg/kg	Animal No.	Survival Days	Cause of Death	Gross Pathology											Gross Pathology Possible	
					1	2	3	4	5	6	7	8	9	10	11		
	2250	48455	3/4	D1	-	-	-	-	-	-	-	-	-	-	-	-	No
	1500	48450	3/2	D2	-	-	-	-	-	-	-	-	-	-	-	-	No
	1000	48390	1	D1	-	-	-	-	-	-	-	-	-	-	-	-	No
	670	48453	2	D2	-	-	-	-	-	-	-	-	-	-	-	-	No
	450	48438	15	K	+	-	++	-	-	-	-	-	-	-	-	-	Yes
	300	48416	15	K	+	-	-	-	++	+	-	-	-	-	-	-	Yes
	200	48453	14	K	+	+	+	-	-	-	-	-	-	-	-	-	Yes
	100	48315	14	K	++	+	-	++	+	++	-	-	-	-	-	-	Yes
	45	48295	14	K	+	+	-	+	++	-	-	-	-	-	-	-	Yes
	12	48425	14	K	++	+	+	-	++	-	-	-	-	-	-	-	Yes
	1.5	48486	14	K	-	-	-	-	-	-	-	-	-	-	-	-	Yes
	12	48685	14	K	-	-	-	-	+	-	-	-	-	-	-	-	Yes
Comment:	12	48685	14	K	-	-	-	-	-	-	-	-	-	-	-	-	Yes
	12	48593	14	K	-	-	-	-	-	-	-	-	-	-	-	-	Yes

Prepared By: Carl Johnson, D.V.M.
Approved By: G. W. Schepers, M.D., Pathologist
2-8-62

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TABLE 2
ORGAN WEIGHTS

Castell No: 3035 Material: Ammonium Perfluorocaprylate
 Exp: _____
 No: 64 Species: _____ Test: _____
 Procedure: _____
 T. I. A.P. _____
 Report No: P-62-17 Experiment Period: _____
 Director: _____

Group	Animal No.	Survival Days	Body Weight		Age Days	Brain	Heart	Lungs	Liver	Pancreas	Stomach	Spleen	Kidneys	Testes	Adrenal	Thyroid	Tongue
			Init.	Final													
225	48405																
1500	48456		NO														
100	48390		ORGAN														
670	48453																
450	48438	15	435	452		1.71	1.30	1.80	28.20	0.73	1.83	0.83	2.85	3.19	.058	0.56	
300	48416	15	440	474		2.00	1.35	1.60	25.17	0.52	2.15	0.82	3.78	3.72	.056	0.75	
200	48250	14	512	542		2.10	1.52	2.00	30.61	0.82	2.07	0.85	4.73	3.09	.063	0.72	
120	48345	4	440	374		1.85	1.05	1.39	16.18	0.35	1.76	0.61	2.71	3.18	.057	0.46	
07	48295	4	515	530		2.06	1.40	1.51	24.10	0.89	1.92	0.75	4.28	3.31	.054	0.69	
21	52781	4	555	58		2.15	1.75	2.15	25.20	0.75	2.20	0.90	4.85	3.75	.063	0.65	
1.5	98787	4	535	592		2.14	1.73	2.16	24.01	0.96	2.18	0.92	4.88	3.88	.062	0.75	

Comments: _____
 Prepared by: August H. Steinfeld
 August H. Steinfeld
 Approved by: [Signature]
 G. W. H. [Signature] Pathologist
 29-8-2
 29-8-62

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TABLE 3

ORGAN WEIGHTS

Instell No: 3035 Material: Ammonium Perfluorocaprylate Excipient: _____
 R No: 604 Species: Male C57BL/6J Mice Test: Oral - 1 dose 12 mg/kg Procedure: _____
 Report No: P-62-172 Experiment Period: _____ P.I. S.G. Projectors: G. J. S. S.

Group	Animal No.	Survival Days	Body Weight Init.	Body Weight Final	Age Days	Brain	Heart	Lungs	Liver	Pancreas	Stomach	Spleen	Kidneys	Testes	Adrenals	Thyroids	Uterus
	49685	14	333	403		1.82	1.18	2.36	17.51	0.63	1.76	0.88	3.25	3.04	.053	0.57	4.21
	49686	14	300	363		1.83	1.02	1.48	15.01	1.73	1.38	0.61	3.22	3.48	.047	0.61	3.38
	49693	14	325	405		1.96	1.43	1.62	18.03	0.68	1.72	0.76	3.37	2.73	-	0.78	4.11
	Average	14	319	390		1.87	1.21	1.82	16.52	0.68	1.62	0.75	3.28	3.08	.050	0.65	4.22
	Control			390		2.02	1.25	1.55	15.51	0.83	1.76	0.76	3.03	3.48	.053	0.71	
	Deviation from normal			0		-2.5	-3.2	+17	0	-18	-8	0	+8	-11	-6	-8	

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Comments:

Prepared by: August H. Stenholm

Approved by: O. W. H. Schepers, M.D.
 Pathologist

TABLE 5

AMMONIUM PERFLUOROCAPRYLATE

MR-604 - H-2015 - 7-62-172

Group	Animal No.	Doses mg/kg	Body Wt.	Liver Wt.	R	D	Kidney		Pancreas		R	D
							Wt.	D	Wt.	D		
1	50555	130	322	21.11	-	-	3.23	-	.70	-	-	-
	50556	130	316	18.15	-	-	2.72	-	.88	-	-	-
	50557	130	329	21.23	-	-	3.00	-	.71	-	-	-
	Average		319	19.83	6.2	+35	2.98	.96	.76	.25	+22	
2	50561	60	308	22.30	-	-	3.19	-	1.01	-	-	-
	50562	60	305	20.24	-	-	3.01	-	.78	-	-	-
	50563	60	315	17.78	-	-	3.02	-	.61	-	-	-
	Average		309	21.11	6.4	+38	3.07	.93	.83	.24	+18	
3	50564	26	305	20.93	-	-	3.13	-	1.22	-	-	-
	50565	26	332	17.51	-	-	3.00	-	.51	-	-	-
	50566	26	305	15.33	-	-	2.96	-	.91	-	-	-
	Average		312	17.91	5.4	+17	3.03	.91	.81	.24	+17	
4	50567	12	319	15.20	-	-	2.62	-	.80	-	-	-
	50568	12	300	16.50	-	-	2.85	-	.76	-	-	-
	50569	12	326	15.35	-	-	2.91	-	.72	-	-	-
	Average		315	16.18	4.9	+7	2.79	.85	.76	.26	+25	

* Dose 1 on 1-18-62
 (Survival time - 14 days)
 S = Deviation X
 R = Organs weight/body weight ratio X

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 Pathologist
 2-13-62

TABLE 5 (Continued)

AMMONIUM PERBICROMATE

NR-604 - H-1055 - P-62-72

Gr. q	Animal No.	Pose# mg/kg	Body Wt. Wt.	Liver Wt. Wt.	R	D	Kidney Wt. Wt.	H	I	Pancreas Wt. Wt.	R	D
	3-575	5.1	329	13.60	-	-	2.73	-	-	.64	-	-
	5-576	5.1	321	14.83	-	-	3.20	-	-	.77	-	-
	5-577	5.1	395	11.67	-	-	2.52	-	-	.90	-	-
	Average		315	13.03	4.1	-10	2.81	.70	+4	.77	.24	+17
	1-578	1.1	402	11.65	-	-	2.77	-	-	.60	-	-
	6-579	1.1	429	15.01	-	-	2.86	-	-	.91	-	-
	1-580	1.1	305	14.8	-	-	2.52	-	-	.66	-	-
	Average		312	14.10	4.1	-8	2.71	.87	-	.77	.23	+9
1	5-581	1.1	316	15.	-	-	2.86	-	-	.85	-	-
	5-582	1.1	404	14.01	-	-	3.10	-	-	.71	-	-
	5-583	1.1	411	11.0	-	-	2.60	-	-	.62	-	-
	Average		411	13.74	1.1	-11	2.93	.88	+1	.73	.22	+5
9	Control	Control	351	15.08	-	-	2.36	-	-	.62	-	-
	Control	Control	321	11.82	-	-	2.72	-	-	.52	-	-
	Control	Control	311	14.78	-	-	3.11	-	-	.95	-	-
	Average		328	14.85	4.5	-	2.83	.87	-	.68	.21	-

Control group with 100 mg/kg body wt. of ammonium perbichromate (Supplied by Dr. J. H. Johnson, D.V.M.)

J. H. Johnson
 Dr. J. H. Johnson, D.V.M.

G. W. H. Schryvers
 G. W. H. Schryvers, M.D.
 Pathologist
 2-13-62



TITLE OF PROJ. OR STUDY _____ PROJ. OR STUDY No _____

SUBJECT H# 3035 _____ WORKS _____

COMPUTER _____ DATE _____ 19 _____

Gross pathology on rats dosed at levels of 130, 60, 26, 12, 5.1, 2.3, and 1 mg/kg of H² 35 and killed fourteen days later revealed increased pancreatic weight at doses of 5.1 mg/kg and above, and enlarged livers and kidneys in rats at doses of 26 mg/kg and above. The liver weight were increased even at the 1.5 mg/kg level in rat which had a relatively high body weight at the start of the experiment, whereas in rat with the standard initial body weight, liver or kidney enlargement was not found for doses below 26 mg/kg.

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Clinical Signs of Toxicity

Treatment Period

First Week: Five oral 6.7 mg/kg doses of H# 3035 administered over a one week period produced no clinical signs of toxicity in all the treated animals.

Second Week: Five oral 6.7 mg/kg doses of H# 3035 administered during the second week produced no clinical signs of toxicity in all the treated animals.

Observation Period

First Week: Three of the rats were sacrificed four hours after the tenth treatment. The remaining three animals exhibited no clinical signs of toxicity.

Second Week: The remaining three animals exhibited no clinical signs of toxicity during the second week of observation.

Summary and Conclusion

Clinical

H# 3035 produced no observable clinical signs of toxicity during the treatment or observation period.

Conclusion: Based upon its effect upon weight gain, Ammonium Perfluorocaprylate is not considered cumulatively toxic.

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Table of Liver Weights

Test Group

Day of 10th Treatment

Rat No.	Body Wt.	Liver Wt.	Liver Wt. / Body Wt. x 100
	gm.	gm.	
49852	312	19.91	6.38
49954	303	18.00	5.94
50011	305	18.25	5.99

14 Days After 10th Tr.

49855	364	21.60	5.93
49988	402	20.80	5.52
49987	377	18.84	4.69

Control Group

Day of 10th Treatment

50006	316	13.50	4.27
50009	305	12.20	4.00
49988	332	14.72	4.43

14 Days After 10th Tr.

49964	356	16.10	4.47
49987	354	14.95	4.04
50002	375	18.63	4.84

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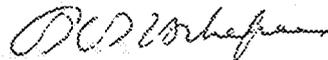
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AMMONIUM PERFLUOROCAPRYLATE (CoAPFC)

MR-604 - H-5035 - P-62-1,2

SUMMARY

Administration of ten successive doses of 6.7 mg/kg to six rats caused moderate enlargement of the liver and slight enlargement of the kidneys, adrenals and testes. Simultaneously there was slight depression of pancreatic weight and the lungs of the rats showed slightly enhanced pneumonitis.



G. W. H. Schepers, M.D.
Pathologist

GWHS/ah
2-9-62

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HLA800254

14 day study

ADVERSE TOXIC PERFLUOROCAPRYLATE (C8PFC) (T-148)

Pathologic Activity Following Repeated Oral Administration

Male OECD Rat

MR-64 - H-3135 - F-62-172

The chemical was administered by intragastric intubation as an aqueous solution. Each of 6 rats received 10 daily doses of 6.7 mg/kg over a period of 12 days. Three rats were killed 2 hours after receiving the 10th dose, and the remainder were killed 14 days later. Six un dosed rats served as controls. The incidence and severity of lesions are supplied in Table 1 and organ weights are presented in Tables 2 and 3.

As could be predicted from the experiment with single doses (Report 62-172) the most prominent effect of the chemical again was enlargement of the liver, which, at the end of the dosage regimen, was about 45% heavier than the average liver weight of the control rats. This change persisted after cessation of dosage, but the weight discrepancy was somewhat less since 14 days later the livers were only 20% heavier than those of control rats. The increase in liver size was accompanied by slight discoloration in one rat in the group killed after the 10th dose and in one rat in the group killed 14 days later.

The renal weights were 20% heavier than those of the corresponding control rats, and this increase persisted after cessation of dosage, being 22% above that of the control rats 14 days later. These weight changes were not accompanied by morphological changes.

The pancreatic weights were slightly depressed, being 8% and 12% lower than those of controls at the end of the test and recovery phases, respectively. The adrenals and testes were slightly increased

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in weight after the last dose, +14% and +11%, respectively, but returned to normality 14 days later.

Comment

It is not clear why a dose of 6.7 mg/kg was selected for this repeated dosage experiment since decisive liver injury was demonstrable for mature rats after a single dose of 1.5 mg/kg. However, the experiment served the purpose of showing that cumulative liver, kidney and pancreatic changes can be induced in young rats by relatively low doses of CBAPFC.

It may be worthwhile to extend the test to include rats killed at 30, 60, and 90 days after dosage, to determine the remote consequences of the various organ changes.

Carl Johnson

Carl Johnson, D.V.M.

G. W. H. Schepers

G. W. H. Schepers, D.D.
Pathologist

CJ:mfs
2-7-62

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TABLE 1
GROSS PATHOLOGICAL SUMMARY

Haskell No: 3035 Material: Ammonium Perfluorooctylate
 Excipient: Water
 MR No: 604 Test: Oral Repeated Dose Species: Male CHOD Rats Procedure: Gastric Intubation
 Report No: P-62-173 Experiment Period: 11-26-61 - 12-22-61 R.I. B.G. Prospector: [illegible]

Group	Dose mg/kg x 10	Animal No.	Survival Days Test after	Cause of Death	Observations					
					1	2	3	4	5	
0	1,9988	12		K	-	++	-	+++	++	Hydronephrosis, right ++
0	50006	12		K	-	+++	-	++	++	
0	50009	12		K	-	++	++	+	++	
6.7	1,9952	12		K	+	++	+	++	-	
6.7	1,9954	12		K	-	++	+	++	-	
6.7	50011	12		K	-	+	++	-	+	
0	1,9964	12	14	K	-	++	++	-	-	Hydronephrosis, bilateral, ++
0	1,9989	12	14	K	-	++	-	-	-	
0	50002	12	14	K	-	+	+	-	-	
6.7	1,9955	12	14	K	-	-	-	-	-	Hydronephrosis, right +++
6.7	1,9956	12	14	K	+	++	-	-	-	
6.7	1,9987	12	14	K	-	++	++	-	-	

- Comments:
1. Liver pale or brownish
 2. Lungs irregular congestion
 3. Lungs focal detelestasia
 4. Lungs subploural plaques
 5. Lungs mediastinal lymph nodes enlarged
- + = Slight reaction
 ++ = Moderate reaction
 +++ = Marked reaction

Prepared by: Carl Johnson
 Cary Johnson, D.V.M.
 Approved by: G. W. H. Schepets, M.D.
 Pathologist
 2-7-62

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TABLE 2

ORGAN WEIGHTS

Material: Controls for H-3035 & 3036

Excipient:

Procedure:

P.I. B.O.

Prospective:

Report No: P-62-17 Experiment Period:

No Exposure	Animal No.	Survival Days	Body Weight Init.	Body Weight Final	Age Days	Brain	Heart	Lungs	Liver	Pancreas	Stomach	Spleen	Kidneys	Testes	Adrenals	Thymus
Test	49988	12	253	332		1.91	1.18	1.55	14.72	0.61	1.70	0.65	2.60	2.75	.048	0.75
Phase	50006	12	254	316		1.90	1.00	1.72	13.50	0.38	1.35	0.58	2.72	2.90	.039	0.85
	50009	12	245	305		1.80	1.22	1.38	12.20	0.50	1.58	0.70	2.48	2.80	.051	0.64
	Average	12	251	318		1.87	1.13	1.55	13.47	0.50	1.54	0.64	2.60	2.82	.046	0.75
Recovery Phase	49964	26	249	370		1.91	1.35	1.50	16.10	0.82	1.80	0.54	2.85	2.88	.054	0.19
	49989	26	256	360		1.99	1.30	1.83	14.95	0.79	1.65	0.75	2.81	3.30	.052	0.70
	50002	26	250	385		2.09	1.14	1.75	18.63	0.79	1.65	0.63	3.29	3.13	.052	0.60
	Average	26	252	372		2.00	1.26	1.69	17.56	0.80	1.70	0.64	2.98	3.10	.053	0.60

Comments:

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Prepared by: August H. Stenholm

Approved by:

Deborah Schepers
D. W. Schepers
Head of Division
1971-1972

Animal No: 3035
 Species: Male PCDU Rats
 Report No: P-62-173 Experiment Period:

Dose Group 6.7 mg/kg	Animal No.	Survival Days	Body Weight		Age Days	Brain	Heart	Lungs	Liver	Pancreas	Spleen	Thymus	Adipose	Kidney	Testis	Ovary	Uterus	Bladder	Stomach	Intestine	Spleen	Liver	
			Initial	Final																			
Test Phase	19952	12	255	312		1.80	0.98	1.72	19.91	0.42	1.54	0.50	0.85	3.02	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60
	19951	12	250	303		1.85	1.02	1.51	18.00	0.45	1.51	0.50	0.70	3.15	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	
	50011	12	248	305		1.89	1.08	1.42	18.25	0.42	1.51	0.72	3.51	2.91	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60
	Average	12	251	307		1.85	1.03	1.55	18.72	0.44	1.53	0.57	3.02	3.02	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60
Recovery Phase	19955	26	255	361		1.89	1.15	1.58	21.60	0.73	1.67	0.72	3.60	2.28	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60
	19968	26	252	402		2.03	1.51	1.80	20.80	0.81	1.91	0.68	3.91	3.23	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60
	19987	26	245	377		1.91	1.34	2.11	18.81	0.63	1.79	0.53	3.61	3.49	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60
	Average	26	251	381		1.94	1.33	1.83	20.11	0.72	1.79	0.64	3.72	3.00	0.02	0.61	0.50	0.60	0.60	0.60	0.60	0.60	0.60

Comments:

Prepared by:

August H. Seemolm

Approved by:

[Signature]
 W. H. Schaeffer

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ACUTE ORAL TOXICITY TEST

DATE January 7, 1962

MATERIAL Commercial Polymer

MR- 601 DEPT. Chemistry BK. NO. 5 P. 72 TECH. H. J. ...

DEPT. SAMPLE NO. _____ HASK. NO. 3025 DENSITY _____

Solid (x) Solution () gms/100 ml ()
 Liquid () % Paste () gms/100 gms () in water
 Semi-Liquid () Powder () ml/100 ml ()

Material given by stomach tube or by _____ to act in original
 form or as a 1% solution of active ingredients in water
 suspension original sample

Date	Animal Number	Init Wt.	Dose (ml)	Dose (mg/kg)	% Sol	Weight Change (grams)	Results	TS
11-28	49685	333	4.0	12	0.1	333/343/344/355/366/44	Survived 12-12-61	
11-28	49686	308	3.6	12	0.1	308/317/318/330/339/46	Survived 12-12-61	
11-28	49693	335	3.9	12	0.1	335/345/346/358/370/46	Survived 12-12-61	

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ALD: 270 mg/kg

REMARKS: Three (3) rats received a single oral dose to enable investigation to compare its acute toxicity with that of polymerized in Teflon polymerization.

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*Grams per 100 ml

Sherman

TOXICITY STUDIES ON FLUOROCARBON DISPERSING AGENTS

Medical Research Project Nos. MR-689 and 10-D-1

BIOCHEMISTRY

Ammonium perfluorocaprylate (C₈FDA), ammonium 11-hydroheradecafluoro-nonanoate (C₉FDA) and ammonium-3,6-dioxo-2,5-(trifluoromethyl)-undecafluoro-nonanoate (AHT) are dispersing agents used in the polymerization of tetrafluoroethylene. In acute toxicity studies with these compounds, the most striking abnormality in animals surviving a single sublethal dose was gross enlargement of the liver. A similar but less marked effect was observed in rabbits that had absorbed AHT through the skin.

The preliminary experiments reported here were designed to measure some of the biochemical changes that accompany the accelerated growth of rat liver; to determine whether functional impairment of the liver occurs as well; and whether there is a species difference in receptibility. The liver function studies were undertaken to find some clinical laboratory procedure that might be useful to medical supervision in detecting fluorocarbon liver injury. The latter phase of the work was supported by the Plastics Department under Medical Research Project No. MR-639.

1. DOGS

Procedure: Three male beagles from the stock colony were given a single oral dose of AHT, equivalent to 4, 6, or 9 mg/kg. Samples of blood were taken at frequent intervals for three weeks and then weekly thereafter until the animals were sacrificed or given an additional dose of the compound. Four other male beagles were given a single oral dose of either C₈FDA or C₉FDA, or C₉FDA, equivalent to 450 mg/kg and a similar series of measurements made. Since both dogs receiving the C₈FDA died within 48 hours, the experiment was repeated later with a lower dose (200 mg/kg) of this dispersing agent. The two dogs that survived the exposure to the C₉FDA were given an additional oral dose, equivalent to 670 mg/kg.

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at this time. Blood sugar and amylase activity were measured on these dogs in an effort to detect an effect on the pancreas.

The following biochemical measurements were made routinely on the blood: sugar, urea nitrogen, total cholesterol, and alkaline phosphatase (APase). When high doses of the dispersing agents were administered, the level of activity of lactic dehydrogenase (LDH), isocitric dehydrogenase (ICDH), aldolase, glutamic oxaloacetic (GOT) and glutamic pyruvic (GPT) transaminases were also measured. The free and esterified cholesterol, phospholipids, dehydrocholesterol (24-dehydrocholesterol), thymol turbidity, albumin and globulin were also determined on one or more samples of blood from the dogs given low doses of AHT. In addition a routine hematological examination and analysis of a 24-hour urine specimen was made at intervals on these animals.

The level of the various components of the blood following the dose of fluorocarbon dispersing agents was compared with an average value observed prior to the exposure and with a similar measurement made at the same time on specimens from stock colony dogs.

For the enzyme activities, a normal range was established from measurements made on a number of stock dogs. The activity was also measured at least once, prior to treatment, on the dogs dosed with the dispersing agents.

Results: The significant biochemical and clinical findings are summarized briefly in Table 1.

The principal finding indicative of some injury or dysfunction in the dogs that received AHT was a decrease in the plasma cholesterol and an increase in bromsulfalein retention (BSP) and APase activity. These

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changes began to occur within one week after the dose was administered. The changes in cholesterol and APase became "abnormal", i.e. exceeded an arbitrary limit of two standard deviations from the pre-exposure mean, one or two weeks later. The increase in dye retention occurred during the first week or ten days and then began to return to normal. The depression of plasma cholesterol in all three dogs occurred earlier and began to return to normal sooner than the rise in plasma APase activity. The dog that received the highest dose of AHT showed the greatest change from the pre-exposure mean. For doses of AHT up to 26 mg/kg, however, the actual values observed for all three dogs did not differ greatly. (See figures 1 and 2.)

Some qualitative and quantitative changes in the serum proteins of one of the three dogs were noted. All three showed decreases in the plasma phospholipids. There were also some changes in red cell morphology and a decrease in the number of red blood cells of the dogs receiving low doses of AHT. All other measurements made on the blood or urine showed no significant deviation from the normal.

When high doses of AHT, CgFDA or CgFDA were administered the activity of a number of enzymes, reported to be sensitive indicators of liver injury, were measured in the plasma. The results of the biochemical measurements are presented in Table 2.

When a high dose (60 mg/kg, equivalent to the rat lethal dose) of AHT was administered to the one dog that had previously received 16 and 26 mg/kg, all the plasma enzymes measured were elevated within the first three days after the dose was given. The greatest changes were in the GPT (25X) and APase (10X). Within one week all but these were within the

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normal range. The depression of the plasma cholesterol occurred more slowly, but there was no evidence of a return to normal after three weeks. Bilirubinuria was also observed.

With the lower dose of the CoFDA (30% of rat lethal dose) the transaminases were elevated in both dogs within 48 hours and continued to rise during the first week after the exposure. Thereafter there was a return to normal. The dog that appeared to have retained the largest portion of the dose showed the greatest effect. The APase was also elevated in this dog and paralleled the GPT. The cholesterol was normal or only slightly elevated within one week after the treatment. There was no effect on the blood sugar and a decrease in amylase activity. When a higher dose of this compound was administered (2/3 of the rat lethal dose) all of the enzymes measured were markedly elevated within 24 to 48 hours. The greatest changes occurred in the GPT and TUDH. There was no change in the plasma cholesterol. Both animals expired within 48 hours after dosing.

With a dose of the CoFDA equivalent to 30% of the rat lethal dose, elevated values of all enzymes measured occurred within 48 hours in one of the two dogs exposed. These returned to the normal range within seven to ten days. The plasma cholesterol was normal or only slightly elevated after one week. The other dog showed no effect from the treatment. At the higher dose (45% of the rat lethal dose) of this compound, the more susceptible dog again showed a rise in GOT and GPT during the first 48 hours and a return to normal within two weeks. There was a slight rise in APase and in the plasma cholesterol. Similar, but less marked changes occurred in the other dog. The amylase activity was lower than normal during the first 48 hours, but a rise did occur during the week following the exposure. There was a rise in the blood sugar at this time. Within three weeks after the exposure all measurements were normal.

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The biochemical data have shown that the three fluorocarbon dispersing agents affect the liver. Very high doses of AHT or the C₈FDA that are lethal or near lethal for dogs, produce elevated plasma levels of enzyme activity indicative of cellular destruction. The depression of cholesterol seems to be peculiar to AHT. The C₉ dispersing agent may also affect the pancreas but this follows the liver injury. Low doses of the C₈ compound do not show this effect. Of all the measurements made the APase and GPT seem to be the most sensitive in detecting an effect from all three dispersing agents. Of these, the latter may be more useful in that there is a narrower range of normal values. Depressed cholesterol levels may be useful in detecting an exposure to AHT.

2. RATS

The experiments with rats were conducted with only one of the three fluorocarbon dispersing agents, AHT, and were divided into two parts. The first part was a study of the biochemical changes in liver tissue which might reflect functional impairment; the second dealt with the effects of AHT on degenerating or regenerating liver tissue.

1. Biochemical Changes

Procedure: Thirty young albino rats (Chr-CD) were given a single oral dose, equivalent to 12 mg/kg of body weight, of AHT by stomach tube. Fifteen to twenty-three days later eight of these were sacrificed and their livers examined for biochemical evidence of abnormality. A similar number of untreated control animals were examined to establish a normal range of values for the various biochemical measurements in rats of this age and strain.

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Sixty to sixty-eight days after the single dose, a second group of eight AHT-treated rats and eight controls were sacrificed and the same measurements made. At this time, samples of blood were also taken for measurement of the plasma alkaline phosphatase activity (APase) and cholesterol concentration. Approximately 5 1/2 months after the AHT treatment the remaining animals were sacrificed.

Results: The results of the biochemical examination of the livers are summarized in Table 3. In the group of rats sacrificed fifteen to twenty-three days after a single oral dose of AHT, the principal changes in the liver, in addition to the relative and absolute increase in liver size, were an increase in alkaline phosphatase activity, phospholipids and a decrease in glycogen, non-protein nitrogen (NPN), and deoxyribonucleic acid (DNA). Small but significant increase in oxygen consumption, water and protein occurred and a slight but significant decrease in respiratory quotient (RQ), choline oxidase and ribonucleic acid (RNA). All other measurements were in the range of normal.

Sixty days after the single dose, the livers of the AHT-treated rats were still quite large, although they were apparently no longer growing at the accelerated rate. The growth depression as measured by live body weight however, was greater than observed previously.

The increase in phospholipid and decrease in glycogen were still the most outstanding change. Small but significant decreases in RQ, RNA and DNA again occurred. The alkaline phosphatase was no longer significantly different from the controls, while the choline oxidase had actually increased. Unlike the dogs these rats showed no increase in plasma alkaline phosphatase, and a rise rather than a fall in plasma cholesterol.

Approximately five and one-half months after the exposure to AHT, the livers were still slightly larger than in untreated rats, but absolute

size of the liver had decreased appreciably. Although small differences were still observed between the control and treated animals, all of these were within the range of normal for rats of this age, sex and strain, as established by the untreated controls.

The results indicate that the enlarged livers resulting from a single dose of AHT are biochemically as well as anatomically abnormal. The rise in O_2 consumption or decrease in CO_2 production and RQ reflect some change in the metabolic behavior of the liver, ~~for these are a measure of the integrated reactions that go on in living tissue.~~ The difference in respiratory quotient was small and after two months greater variation was seen in the AHT-treated group as more of the animals approached the normal range.

Some individual enzymes were affected to a greater degree than the RQ between 15 and 23 days. After two months, however, two of the enzyme activities were in the normal range, and the third was actually more active than the controls. These changes, together with the respiratory changes in the tissue, suggest that some modification in the effect of AHT had occurred.

The liver was depleted of glycogen at both two weeks and two months. The depletion became less marked, however, with time. ~~The glycogen was replaced by water and protein in the early stages of its liver enlargement, but later by protein and fat.~~

The decrease in DNA and RNA probably resulted from a decrease in cell density as the number of cells in a given amount of tissue decreased. This would agree with the observation that the early enlargement is due principally to cellular hypertrophy rather than proliferation. After two

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months there was less difference between control and AHT-treated rats, suggesting either a decrease in the size of the cells or an increase in mitosis.

The results reported seem to indicate that the livers of rats stimulated by a single oral dose of AHT undergo alteration in their biochemical behavior and metabolism during the period of rapid growth. Later, when the accelerated growth has slowed down or ceased, the biochemical aberrations also tend to disappear. The greatest changes occur during the first few weeks or month after the exposure. By the end of two months some evidence of a reversal of these effects is already apparent; between five and six months recovery of the organ is virtually complete.

2. Regenerating and Degenerating Liver

Procedure: Regenerating liver tissue was induced by partial hepatectomy (60-70%) in six male rats from the stock colony. Forty-eight hours after the operation a single oral dose of AHT, equivalent to 12 mg/kg body weight was administered by intubation. Fourteen days later the animals were sacrificed, the livers removed, weighed and analyzed. The experiment was repeated a second time, reversing the procedure by performing the partial hepatectomy forty-eight hours after the dose of AHT had been administered.

Degenerating liver tissue was induced chemically by administering, intraperitoneally, 0.1 ml of carbon tetrachloride per 100 gm of body weight to rats 48 hours after intubating them with 12 mg/kg of AHT. Animals which received only carbon tetrachloride served as controls.

Results: The results are summarized in Table 4. Hepatectomy alone produced an accelerated growth of the liver tissue for within two weeks all or nearly all of the tissue was restored. The DNA, RNA and protein were higher than in normal tissue.

AHT caused an accelerated growth of the liver so that it was more than twice normal size two weeks after the exposure. It also caused a decrease

in DNA and glycogen as well as an increase in APase and phospholipid. These changes occurred regardless of whether two-thirds of the liver was removed before or after the dose of AHT, although there was somewhat less of an effect on the nucleic acids, phospholipids and APase when hepatectomy followed treatment with AHT.

This remarkable growth of the liver even after two-thirds of it has been surgically removed, is quite interesting. Apparently removal of much of the affected tissue does not appreciably alter the unusual growth rate of that remaining. From another point of view, AHT would appear to have an even greater stimulus on regenerating tissue. If one assumes that the amount of liver remaining after partial hepatectomy was between 4 and 5 grams, it increased 2 to 3 fold within two weeks after hepatectomy; about the same accelerated growth that occurred in normal tissue after treatment with AHT. The 4 or 5 grams of tissue remaining after partial hepatectomy, however, had increased 5 or 6 fold when treated with AHT.

One of the six rats dosed with carbon tetrachloride died eight days later, but all six rats dosed with AHT prior to the carbon tetrachloride died within 48 hours. No analysis of the liver was possible for all of the animals were found dead and post-mortem changes had begun. When examined grossly, however, the livers were massive in size (i.e. 30 to 40 grams) and yellow in color, probably from acute fatty infiltration.

Biochemical measurements on the surviving carbon tetrachloride rats showed no appreciable differences from controls aside from small changes in the nucleic acids.

The biochemical data suggest that there are probably qualitative differences in the effect of AHT fluorocarbon dispersing agent on rats and

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dogs. Liver enlargement occurs in rats but in dogs, hypocholesterolemia is the most unusual finding. It would be useful to investigate these in several other species -- mice, guinea pigs, rabbits. The combined effect of carbon tetrachloride and AHT may be of practical significance since such multiple exposures could conceivably be experienced by personnel handling AHT. Further study of this problem is recommended.

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TABLE 1.

Compound	No. Dogs	Dose		Clinical	Mortality	Biochemical
		mg/kg	Est ASD			
AHT	1	6	10	None	0	Hypocholesterolemia, elevated APase
	1	9	15	None	0	Hypocholesterolemia, elevated APase, BSP
	1	4	7	None	0	Hypocholesterolemia, elevated APase, BSP
	1	26	43	None	0	Hypocholesterolemia, elevated APase, OPT BSP retention
	1	60	100	Vomiting; anorexia, polydipsia, weakness, weight loss, black tarry feces for 4 days	0	Hypocholesterolemia, elevated APase, OPT LDH, ICDA, aldolase, jaundice, bilirubinuria
89	2	200	30	Vomiting, polydipsia	0	Elevated APase (1/2), OPT, OPT (2/2) lowered amylase
	2	150	67	Vomiting, polydipsia, blood feces and vomitus, tremors, convulsions, anorexia, death, 1-3 days	2	Elevated APase, OPT, ICDA, LDH, aldolase, jaundice
99	2	150	30	Vomiting, 2-4 hours	0	Normal or slightly elevated cholesterol APase, OPT, ICDA, LDH, (1/2)
	2	670	45	Vomiting	0	Normal or slightly elevated cholesterol elevated OPT, OPT (2/2); slightly elevated APase (1/2); amylase and sugar (2/2) elevated after 1 week

TABLE 2

PLASMA LEVELS OF BLOOD CONSTITUENTS AFTER
EXPOSURE TO FLUOROCARBON DISBURSING AGENTS

1. AHT

Dose	Days After Dose	Cholesterol mg %	APase Bod. Units	GPT Units	LDH Units	LDH Units	Aldolase Units
	0*	133	2.3	3.5	230	150	<20
26 mg kg	8	66	5.5				
	15	49	5.5				
	22	47	7.3				
	37	86	7.2				
60 mg kg	3	74	21.7	850	3900	360	47
	7	78	15.7	270	145	60	11
	10	64	13.4	135	-	40	10
	14	50	13.1	91	290	100	13
	21	48	11.4	77	145	-	-

* Average pre-exposure

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There are also recovery records

Table 2 (Continued)

2. C₈ FDA

Dose mg/kg	Days after Dose	Cholesterol mg%		A Base Bod. Units		GPT Units		GOT Units		ICDR Units		LDH Units		Sugar mg%		Amylase Units	
		1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
200	0*	101	112	2.8	1.7	42	36	23	21					80	95	997	676
	1	102	93	2.6	2.1	38	50	20	36					89	69	530	240
	2	109	111	2.6	6.9	56	845	38	880					85	85	670	350
	5	126	126	2.5	10.1	108	425	34	52					94	94	760	610
	7	106	112	1.8	8.0	56	166	18	12					92	92	780	560
	12	100	127	1.4	5.4	40	70	12	14					90	90	860	580
	21	92	109	1.8	3.7	36	44	16	30					96	96	890	410
27	89	106	2.4	3.3	42	40	16	16					83	83	850	440	
50	0*	114	148	1.2	2.1	19	22			117	138	70	60				
	1	136	164	7.3	20.5	280	8500			2100	114000	300	302				
	2	-	145	-	38.7	-	8500			-	3860	-	1320				

* average pre-exposure

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Summary and Conclusion

Procedure:

Single oral 12 mg/kg doses of H# 3035 were given to three(3) rats, which observed for 14 days and sacrificed. This procedure was employed so as to enable investigators to compare results with other dispersing agents administered in a similar manner.

Clinical

H# 3035 given in single oral 12 mg/kg doses produced no clinical signs of toxicity.

Conclusion

H# 3035 may be considered relatively harmless when administered to rats in single oral doses of 12 mg/kg, having produced no clinical signs of toxicity.

Table of Liver Weights

<u>Rat No.</u>	<u>Body Wt.</u> <u>gm.</u>	<u>Liver Wt.</u> <u>gm.</u>	<u>Liver Wt.</u> <u>Body Wt.</u> x 100
49685	403	17.51	4.34
49686	363	14.03	3.86
49693	405	18.03	4.45

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B

Distribution List

EFFECT OF FLUOROCARBON DISPERSING AGENTS
ON THE LIVERS OF RATS AND DOGS

Medical Research Project Nos. MR-639, 10-B, 10-C and 10-D

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EFFECT OF FLUOROCARBON DISPERSING AGENTS
ON THE LIVERS OF RATS AND DOGS

Medical Research Project Nos. MR-639, 10-B, 10-C and 10-D

Report No. 123-65

Ammonium perfluorocaprylate (C₈APFC), ω-hydrohexadecafluorononanoate (C₉APC) and ammonium 3,6-dioxo-2,5-di(trifluoromethyl)undecafluorononanoate (AHT) are powerful surfactants. In acute oral toxicity studies with these compounds, the most striking abnormality in animals surviving a single sublethal dose was gross enlargement of the liver (Haskell Laboratory Report Nos. 54-61, 55-61 and 70-61). A similar but less marked effect was observed in rabbits that had absorbed AHT through the skin. Although liver enlargement is not an uncommon finding in chemical intoxications, the effect of AHT was remarkable in that 56 days after a single dose of 12 mg/kg the liver was approximately three times larger than normal.

The experiments reported here were preliminary studies designed to determine more details concerning:

- (1) the histological changes, that occur with increasing periods of time, in the livers of rats after a single oral dose of AHT;
- (2) the biochemical changes during the period of rapid growth and recovery in the livers of rats treated with AHT;
- (3) the combined effects of oral administration of ethanol and AHT in the rat;
- (4) the effect of AHT upon the pentobarbital sleeping time in the rat; and
- (5) the effect on liver function in dogs treated with AHT, C₈APFC and C₉APC in order to find some clinical laboratory procedure that might be useful in detecting liver injury in personnel exposed to fluorocarbon dispersing agents.

I. HISTOLOGICAL CHANGES DURING THE TIME OF RAPID GROWTH

A. Procedure: In order to study the changes in size and structure of the liver following a single oral dose of AHT, 14 male rats were each given a dose of 12 mg/kg. A second group of animals of the same age and weight served as controls. One test and one control animal were killed at intervals over a period of 56 days and two test and two control animals at 75 and 128 days. The livers were removed, weighed and a section taken for microscopic examination.

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B. Results: The rapid growth of the liver, in terms of both weight and per cent of whole body mass, is shown in Figure 1. The increase in size was most marked during the first ten days, reached a maximum between 40 and 60 days, and then began to decrease in size, although some enlargement was still evident after 126 days.

Morphological changes in the liver were evident 24 hours after the single dose. The initial change was characterized by markedly enhanced mitosis of the hepatocytes. This was less evident by the second day; by the ninth day, the mitotic activity had decreased. After the 36th day, most of the features which characterized the response were less intense.

The structural changes in the cells were quite evident upon microscopic examination and appeared to result principally from an enlargement of the individual cells.

II. BIOCHEMICAL AND METABOLIC CHANGES IN RAT LIVER

1. Changes in the Liver of Intact Animals

A. Procedure: Thirty male Chr-CD rats were given 12 mg/kg of AHT as a single oral dose. Two to three weeks later, eight of the rats were sacrificed by decapitation, the livers removed, weighed, and analyzed. An equal number of untreated controls were examined to establish the normal range of values that might be expected in rats of this age and strain. Two AHT-treated rats and two controls were also sacrificed for microscopic examination of the tissue. Eight to ten weeks after the single oral dose of AHT, a second group of ten rats was sacrificed and the remaining ten rats three months later. Tissue slices were prepared from a portion of the median lobe for respiration and choline oxidase measurements in a Warburg respirometer. One portion of the left lateral lobe was homogenized for measurement of alkaline phosphatase activity (APase), esterase activity, and the nucleic acids. Another portion was used for glycogen determination. The remaining tissue was used to measure water, protein, fat, ash, cholesterol, phospholipids, and potassium. An average value was calculated for each group of animals and compared with the controls. Differences between groups were tested for significance with the "t" test.

B. Results: The results of the biochemical measurements are given in Table 1. Two weeks after the single dose of AHT, the livers of the treated rats were quite large in size, more than twice that of the controls, and comprised approximately 9% of the body weight. An increase in the alkaline phosphatase activity and phospholipids and a decrease in glycogen were the most important changes. Small but statistically significant ($p < 0.05$) increases in oxygen consumption, non-protein nitrogen, water and protein and decreases in the respiratory quotient, choline oxidase, RNA and DNA occurred.

Two months after the single oral dose of AHT, the livers were no longer growing at an accelerated rate, for there was no further increase in the absolute size of the liver and its portion relative

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to the whole body had decreased. The increase in phospholipids, protein and non-protein nitrogen, and decrease in glycogen respiratory quotient, RNA and DNA again was observed.

Five and one-half months after the dose of AHT, the livers of the treated rats were still slightly larger than normal, but the small differences in the biochemical measurements were no longer significant.

These results indicate that AHT produces significant biochemical as well as morphological changes in the liver of rats. A number of these changes point to disturbances in the normal metabolic and synthetic functions of the liver. The lowered concentration of nucleic acids is consistent with the observed arrested mitotic activity. These effects are most evident when the liver is rapidly increasing in size. Later, when the accelerated growth has slowed down or ceased, a reversal of biochemical changes is apparent. Five or six months after the dose of AHT, when the liver is nearly normal in size, the recovery of the organ is virtually complete.

2. Biochemical Changes and Liver Enlargement in Hepatectomized Rats

A. Procedure: To study the effect of AHT on liver tissue already in a state of rapid growth or regeneration, six male Chr-CD rats were subjected to partial hepatectomy by removing 60 to 70% of the organ. Forty-eight hours after the operation, the rats were given a single oral dose of AHT of 12 mg/kg. The experiment was also conducted reversing the order of treatment by removing 60 to 70% of the liver of rats which had been treated with AHT 48 hours previously. Sham-operated animals dosed with AHT and hepatectomized animals served as controls. Fourteen days after the single oral dose of AHT, the livers of the rats were removed, weighed and analyzed for glycogen, phospholipids, DNA, RNA and alkaline phosphatase activity.

B. Results: The results of these experiments are shown in Table 2. Two weeks after the operation, the livers of the partially hepatectomized control animals were normal in size for rats of this age, sex, and strain, but the alkaline phosphatase activity and DNA were higher than in normal livers. When partially hepatectomized rats were treated with AHT, the livers grew very rapidly; two weeks after treatment with the trimer, the livers were more than twice those of the hepatectomized controls. The phospholipid content and alkaline phosphatase activity were increased while the glycogen content decreased. The DNA was again decreased as in the livers of intact AHT-treated rats, but the RNA had increased. Except for this increase in RNA, the results were in agreement with the previous measurements on livers from AHT-treated rats shown in Table 1. The biochemical changes in the liver occurred whether partial hepatectomy preceded or followed treatment with AHT, although the effects were somewhat less when hepatectomy followed the treatment with AHT.

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3. Effect of Chemical Injury on AHT-treated Rat Livers

A. Procedure: Six male Chr-CD rats were given a single oral dose of 12 mg/kg of AHT and then, 48 hours later, a single sub-lethal dose of carbon tetrachloride, equivalent to 0.1 ml per 100 gm of body weight, intraperitoneally. Animals which received only carbon tetrachloride served as controls.

B. Results: The results of this experiment are also shown in Table 2. One of the six rats dosed with carbon tetrachloride died eight days later, but all six rats treated with AHT prior to the carbon tetrachloride died within 48 hours. No analysis of the liver was possible, for all of the animals were found dead and post-mortem changes had begun. When examined grossly, however, the livers were massive in size, approximately 30 to 40 gm, and yellow in color, probably from acute fatty infiltration. The rapidly enlarging liver, with a greater than normal lipid:glycogen ratio, is more susceptible to the toxic effect of CCl₄ than normal liver.

Biochemical measurements on the surviving carbon tetrachloride rats showed no appreciable differences from controls two weeks after the treatment.

III. COMBINED EFFECTS OF ORAL ADMINISTRATION OF ETHYL ALCOHOL AND AHT IN THE RAT

A. Procedure: The study was designed as an additional evaluation of the effects of combining hepatotoxic agents. The objective was to determine, by oral administration to rats, whether repeated sublethal doses of ethyl alcohol would enhance the effect of a single hepatotoxic dose of AHT. The outline of the study, in tabular form, is presented in Table 3.

Male Chr-CD rats, weighing between 300-400 gm, were used in the study. They were offered water and Purina Laboratory Chow on an ad libitum basis and were weighed daily.

At the time of the prescribed sacrifices, the animals were subjected to gross pathological evaluation. The liver was removed, weighed, and preserved in appropriate fixatives.

B. Results: A summary of the liver weights obtained at the various scheduled autopsies is given in Table 4. The preliminary results of this study, wherein AHT was administered to rats in a single dose of 12 mg/kg, simultaneously with, or after, their exposure to ethyl alcohol, indicate that the increase in liver weights observed in this experiment was not any greater than that produced by AHT alone at a dose of 12 mg/kg.

IV. THE EFFECT OF AHT UPON PENTOBARBITAL SLEEPING TIME IN THE RAT

A. Procedure: Changes in liver function or liver morphology have served as traditional indicators of hepatotoxicity. More recently, a quick and simple pharmacologic test has been developed

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which has been used to determine liver damage - Pentobarbital Sleeping Time (PST).

Pentobarbital is metabolized in the liver; a change in particular liver enzymes is reflected by a prolongation, or shortening, of the sleeping time induced in animals by this compound's normal anesthetic action. Therefore, alteration in the PST has been correlated with changes in liver function and liver morphology. When young adult male ChR-CD rats are given 30 mg/kg Na pentobarbital in an aqueous solution intraperitoneally, their average sleeping time was found to be 58 ± 19 minutes (for 110 rats).

In studying the effect of AHT administration upon PST, groups of ten rats were employed. A control value for PST was obtained for each group of ten rats, usually 24 hours before the test began. Twenty-four hours later, the rats were given a single oral dose of AHT at the rate of 12 mg/kg. PST was determined on each group of rats four hours, 24 hours, 48 hours, and at other time intervals after the oral administration of the AHT. Control groups were similarly examined for PST at the same time intervals. The results of two of these tests are summarized in Table 5.

B. Results: The PST of rats that received AHT was first prolonged; it then became shorter and shorter until, at approximately six days after dosing, none of the rats could be anesthetized by a dose of Na pentobarbital that still affected untreated rats. Approximately seven weeks later, the PST of AHT-treated rats could again be determined, but it was still much shorter than that observed in control animals. The same observations were made for the next two weeks, at the end of which time the experiment was terminated.

V. EFFECT OF FLUOROCARBON SURFACTANTS ON LIVER FUNCTION IN DOGS

A. Procedure: Three male beagles from the stock colony were given a single oral dose of AHT, equivalent to 4, 6, or 9 mg/kg. Samples of blood were taken at frequent intervals for three weeks and then weekly thereafter. The dog that received 4 mg/kg was later given doses of 26 and 60 mg/kg. Four other male beagles were given a single oral dose of either C₈APFC or C₉AFC, equivalent to 450 mg/kg and a similar series of measurements made. Since both dogs receiving the C₈APFC died within 48 hours, the experiment was repeated with two other dogs which were given a 200 mg/kg dose of this dispersing agent. The two dogs that survived the exposure to the C₉AFC were given an additional oral dose, equivalent to 670 mg/kg, at this time.

The following biochemical measurements were made routinely on the blood: sugar, urea nitrogen, total cholesterol and alkaline phosphatase. When the 60 mg/kg dose of AHT, 470 mg/kg dose of C₈APFC or the 670 mg/kg dose of C₉AFC were administered, the level of activity of lactic dehydrogenase (LDH), isocitric dehydrogenase (ICDH), aldolase, glutamic oxalacetic (GOT) and glutamic pyruvic (GPT) transaminase were also measured. A routine hematological

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examination and an analysis of a 24-hour urine specimen were made at intervals on these animals.

The level of the various components of the blood following the dose of fluorocarbon dispersing agents was compared with an average value observed prior to the exposure and with a similar measurement made at the same time on specimens from stock colony dogs.

For the enzyme activities, a normal range was established from measurements made on a number of stock dogs. The activity was also measured at least once, prior to treatment, on the dogs dosed with the dispersing agents.

B. Results: The significant biochemical and clinical findings are summarized briefly in Table 6.

The principal finding indicative of some injury or dysfunction in the dogs that received AHT was a decrease in the plasma cholesterol and an increase in bromsulfalein retention (BSP) and APase activity. The effects on cholesterol and APase are shown in Figures 2 and 3. These began to change within one week and became "abnormal", i.e., exceeded an arbitrary limit of two standard deviations from the pre-exposure mean within three weeks after the dose was administered. The increase in BSP retention occurred during the first ten days and then began to return to normal. The depression of plasma cholesterol in all three dogs occurred earlier and began to return to normal sooner than the rise in plasma APase activity. The dog that received the highest dose of AHT showed the greatest change in plasma APase from the pre-exposure mean. The activity of a number of enzymes considered to be sensitive indicators of liver injury was measured in the plasma when a 60 mg/kg dose of AHT was administered. The results of these biochemical measurements are presented in Table 7. All the plasma enzymes measured were elevated within the first three days after the dose of 60 mg/kg of AHT was administered. The greatest increases were in the GPT and APase. Within one week, all but these were within the normal range. The depression of the plasma cholesterol occurred more slowly, but there was no evidence of a return to normal after three weeks as occurred in the dogs receiving 6 or 9 mg/kg.

With the 200 mg/kg dose of C₈APFC, the GPT and GOT were elevated in both dogs within 48 hours. One week later, they were in the normal range. When 450 mg/kg of this compound was administered, all of the enzymes measured were markedly elevated 24 to 48 hours later. The greatest change occurred in the GPT and ICDH. Both animals expired within 48 hours after dosing.

The 450 mg/kg dose of C₆APC caused elevated levels of all the enzymes measured within 48 hours in one (No. 2) of the two dogs exposed. On the tenth day after the dose was administered these were within the normal range. The other dog showed no effect from the treatment. At the 670 mg/kg dose of this compound,

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Dog No. 2 showed a rise in GOT, GPT, and APase during the first 48 hours, and a return to normal within two weeks. There was a slight rise in the APase, GPT and GOT in Dog No. 1.

SUMMARY

Single oral doses of 12 mg/kg of AHT, administered to rats, cause a rapid growth of the liver that continues for as long as two months after the treatment. Morphologically, the change is characterized by an enlargement of the hepatocyte. Changes in the biochemical composition, enzyme activity and respiration, accompany this enlargement and indicate a disturbance in the normal metabolic functions of the organ. The changes in nucleic acid content and morphology of the cell suggest an interference in mitotic activity. Reversal of these changes begins in two months and is nearly complete in five to six months.

Rats that have been subjected to excision of 60 to 70% of the liver 48 hours before or after a single oral dose of 12 mg/kg of AHT regenerate larger than normal livers.

Carbon tetrachloride is more toxic for rats that have been given a single oral dose of 12 mg/kg of AHT. This may result from the accumulation and retention of the CCl_4 in the enlarging liver which has more fat and less glycogen than normal liver.

When AHT is administered to rats in a single dose of 12 mg/kg simultaneously with or after their exposure to repeated sublethal oral doses of ethyl alcohol, the increase in liver weight observed is not any greater than that produced by AHT alone at the same dose.

Following an initial depressant effect by AHT on enzymes that metabolize sodium pentobarbital, there is apparently an increase in the rate of metabolism of sodium pentobarbital so that it cannot exert its anesthetic action at usually anesthetic dose levels.

Liver function studies in dogs have shown that AHT, C_8 APFC and C_9 AFC dispersing agents affect the liver. On the basis of mg/kg dose, AHT is most, and C_9 AFC least, toxic to the liver. Doses of 26 mg/kg of AHT or 200 mg/kg of C_8 APFC produce elevated plasma levels of enzyme activity indicative of cellular damage. Only AHT lowers the cholesterol level in dogs given 4 mg or more per kg of body weight in a single oral dose. Of all the measurements made, alkaline phosphatase and GPT are the most sensitive in detecting an effect on the liver in dogs from all three dispersing agents.

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EFFECT OF FLUOROCARBON DISPERSING AGENTS
ON THE LIVERS OF RATS AND DOGS

Medical Research Project Nos. MR-639, 10-B, 10-C and 10-D

Report No. 123-65

HASKELL LABORATORY FOR TOXICOLOGY
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TABLE 1

BIOCHEMICAL CHANGES IN RAT LIVER

	2-3 Weeks		2 Months		5 1/2 Months	
	Control	AHT	Control	AHT	Control	AHT
Body Weight gm	345	324	546	476	640	602
Liver Weight gm	13.5	28.5	18.0	27.9	18.8	21.4
Liver % Body	3.94	8.80	3.30	5.86	2.93	3.52
O ₂ ml/hr.	7.23	7.97	7.00	6.99	6.10	5.93
CO ₂ ml/hr.	5.84	5.73	5.67	5.08	4.68	4.50
RQ	0.81	0.72	0.81	0.72	0.77	0.76
APase BU/gm	2.45	3.60	2.66	2.86	3.41	3.04
Esterase U/gm	245	180	210	245		
Choline Oxidase	69	61	65	78	74	78
Water %	68.8	69.8	68.0	68.2	68.3	68.3
Protein %	18.1	19.6	17.2	18.3	16.7	16.9
Fat %	4.14	4.18	5.03	5.31	4.87	4.81
Glycogen %	4.54	2.60	3.86	2.93	4.44	4.05
Ash %	1.38	1.36	1.36	1.32	1.36	1.37
Cholesterol %	0.43	0.40	0.44	0.40		
NPN %	0.23	0.26	0.21	0.23	0.29	0.30
Phospholipide %	3.15	3.96	3.29	4.17	3.08	3.20
Potassium %	0.34	0.33	0.42	0.40	0.42	0.42
RNA %	0.907	0.872	0.834	0.786	0.824	0.815
DNA %	0.160	0.124	0.176	0.158	0.185	0.176
Plasma APase BU			51	51		
Plasma Cholesterol mg%			93	144		

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TABLE 2

BIOCHEMICAL CHANGES IN RAT LIVER TISSUE 2 WEEKS AFTER HEPATECTOMY AND/OR TREATMENT WITH AHT AND AFTER TREATMENT WITH AHT AND/OR CCL₄

Treatment 1	Treatment 2	No. of Rats	Mortality	Liver Weight	Liver % Body	Oly-cogen	APace	Phospho-lipids	RNA	DNA		
0	Hepatectomy	4	0	12.6	3.15	4.60	3.80	3.3	0.95	0.20		
AHT ^a	Sham Operated	6	0	30.5	8.24	2.47	3.94	3.8	1.15	0.12		
Hepatectomy	AHT ^a	6	0	29.2	7.29	2.07	4.55	4.3	1.04	0.12		
AHT ^a	Hepatectomy	6	0	24.6	7.18	1.74	3.82	4.0	0.93	0.15		
CCL ₄ ^b	0	6	1/6	13.6	3.71	4.16	2.69	3.0	0.96	0.19		
AHT ^a	CCL ₄ ^b	6	6/6	All animals died within 48 hours after receiving AHT								

a) 12 mg AHT/kg body weight

b) 0.1 ml CCL₄/100 gm body weight

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TABLE 2

DOSING AND SACRIFICE SCHEDULE OF ANIMALS GIVEN ETHYL ALCOHOL AND AHT

Group	Total No of Animals	Number of Animals Sacrificed			
		4 Hrs After 10th Dose	14 Days After 10th Dose	28 Days After 10th Dose	2 Months After 10th Dose
Control (no dosing)	8	2	2	2	2
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks)	8	2	2	2	2
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks) + AHT (12 mg/kg on day of first alcohol dose)	6	2	2	2	2
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks) + AHT (12 mg/kg on day of 10th alcohol dose)	6	2	2	2	2
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks) + AHT (12 mg/kg on 14th day after 10th alcohol dose)	4			2	2

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TABLE 4

LIVER WEIGHTS OF ANIMALS RECEIVING REPEATED DOSES OF ETHYL ALCOHOL AND A SINGLE DOSE OF AHT

Group	Liver Weights (gm) of Animals Sacrificed		
	4 Hrs. After 10th Dose	14 Days After 10th Dose	28 Days After 10th Dose
Control (no dosing)	16; 15	16; 20	19; 23
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks)	13; -*	24; 19	25; 21
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks) + AHT (12 mg/kg on day of first alcohol dose)	23; 30	42; 32	40; 30
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks) + AHT (12 mg/kg on day of 10th alcohol dose)		39; 44	36; 33
C ₂ H ₅ OH (2250 mg/kg/day, 5 x week for 2 weeks) + AHT (12 mg/kg on 14th day after 10th alcohol dose)			30; 41
			36; 36
			37; 36

* 1 animal died after the fourth dose

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TABLE 5

AVERAGE SLEEPING TIMES OF RATS GIVEN Na PENTOBARBITAL INTRAPERITONEALLY AT A DOSE LEVEL OF 30 mg/kg

Treatment	Pre-Exposure		4 Hours		24 Hours		48 Hours		6 Days		7 Days	
	PST ± SD	R	PST ± SD	R	PST ± SD	R	PST ± SD	R	PST ± SD	R	PST ± SD	R
Control	49 ± 14	10/10	52 ± 8	10/10	56 ± 11	10/10	40 ± 9	9/10	41 ± 12	8/10		
AHT (12 mg/kg)	47 ± 6	10/10	121 ± 14	10/10	36 ± 8	7/10	25 ± 6	8/10				
Control	50 ± 12	10/10	47 ± 8	10/10	47 ± 6	10/10	46 ± 11	8/10	56 ± 12	10/10		
AHT (12 mg/kg)	56 ± 15	10/10	143 ± 18	10/10	33 ± 12	7/10	22 ± 6	7/10				

PST ± SD = Average Pentobarbital Sleeping Time ± Standard Deviation (minutes)

R = $\frac{\text{Number of rats which went to sleep}}{\text{Total number of rats dosed}}$

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TABLE 5 (Cont'd)

AVERAGE SLEEPING TIMES OF RATS GIVEN Na PENTOBARBITAL
INTRAPERITONEALLY AT A DOSE LEVEL OF 30 mg/kg

Treatment	Post-Exposure											
	9 Days		16 Days		27 Days		49 Days		56 Days		64 Days	
	PST ± SD	R	PST ± SD	R	PST ± SD	R	PST ± SD	R	PST ± SD	R	PST ± SD	R
Control } AHT (12 mg/kg)	72 ± 10	9/10	65 ± 18	8/10	80 ± 25	9/10	81 ± 20	10/10	76 ± 16	10/10	82 ± 17	10/10
AHT (12 mg/kg)	-	0/10	-	0/10	-	0/10	18 ± 4	7/10	22 ± 6	6/10	18 ± 2	7/10

-----Discontinued after seven days-----

PST ± SD = Average Pentobarbital Sleeping Time ± Standard Deviation (minutes)

R = $\frac{\text{Number of rats which went to sleep}}{\text{Total number of rats dosed}}$

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TABLE 6

CLINICAL AND BIOCHEMICAL OBSERVATIONS IN DOGS ADMINISTERED FLUOROCARBON DISPERSING AGENTS

Compound	No. Dogs	Dose		Clinical	Mortality	Biochemical
		mg/kg	% Rat ALD			
AFT	1	6	10	None	0	Hypocholesterolemia, elevated APase
	1	9	15	None	0	Hypocholesterolemia, elevated APase, BSP retention
	1	4	7	None	0	Hypocholesterolemia, elevated APase, BSP retention
	26	43	None	0	Hypocholesterolemia, elevated APase, GPT, BSP retention	
C8FDA	2	200	30	Vomiting, polydipsia	0	Elevated APase (1/2), GGT, GPT (2/2), lowered amylase
	2	450	67	Vomiting, polydipsia, blood, feces and vomitus, tremors, convulsions, anorexia, death 1-3 days	2	Elevated APase, GPT, ICDH, LDH, aldolase, jaundice
C9FDA	2	450	30	Vomiting, 2-4 hours	0	Normal or slightly elevated cholesterol, APase, GPT, ICDH, LDH (1/2)
	2	670	45	Vomiting	0	Normal or sl. elevated cholesterol, elevated GGT, GPT (2/2), sl. elevated APase (1/2), amylase and sugar (2/2), elevated after 1 week

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TABLE 7

LIVER FUNCTION TESTS IN DOGS - AHT

Dose (mg/kg)	Days After Dose	Cholesterol mg %	APase Bod. Units	GPT Units	ICDH Units	LDH Units	Aldolase Units
0*	0	133	2.3	35	230	150	<20
26**	8	66	5.5				
	15	49	5.5				
	22	47	7.3				
	37	86	7.2				
60	3	74	21.7	850	3900	360	47
	7	78	15.7	270	145	60	11
	10	64	13.4	135		40	10
	14	50	13.1	91	290	100	13
	21	48	11.4	77	145		

* Average pre-exposure

** Previously received 4 mg/kg 61 days before a dose of 26 mg/kg

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TABLE 7 (Cont'd)

Dose (mg/kg)	Days After Dose	Cholesterol mg %		APase Bod. Units		OPT Ur. lts		GOT Units		ICDH Units		LDH Units	
		1	2	1	2	1	2	1	2	1	2	1	2
C ₆ APFC 200	0*	101	112	2.8	1.7	42	36	23	21				
	1	102	93	2.6	2.1	38	50	20	36				
	2	109	111	2.6	6.9	56	845	38	880				
	5	126	126	2.5	10.1	108	425	34	52				
	7	106	112	1.8	8.0	56	166	18	22				
	12	100	127	1.4	5.4	40	70	12	14				
	21	92	109	1.8	3.7	36	44	16	30				
	27	89	106	2.4	3.3	42	40	16	16				
C ₆ APFC 450	1	118	164	7.3	20.5	280	8500			2100	114,000	300	302
	2		145		38.7		8600				3660		1320
C ₆ APFC 450	0*	112	112	1.2	2.4	25	33	14	16	153	150	72	43
	2	126	126	1.6	3.8	30	116			116	595	74	200
	4	102	124	2.0	4.4	33	84						
	7	128	152	1.7	3.8								
	10	100	123	1.3	2.3	27	43			145	189	68	48
	14	121	135	1.7	2.1		40						
C ₆ APFC 670	22	142	156	1.1	1.4		25						
	2	142	124	1.9	2.4	66	52	38	22				
	4	159	149	1.9	2.8	70	170	44	172				
	5	144	134	1.7	3.6	58	190	18	54				
	7	124	133	1.4	3.5	42	100	14	22				
	12	102	135	1.2	2.4	34	48	16	16				
	21	127	133	1.0	2.0	36	50	18	24				
27	140	136	1.2	2.1	36	46	14	16					

* Average pre-exposure

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AR226-1444

C

CC: A. C. Huiston
S. A. Sauvage
T. N. Shipley
R. N. Taylor
File: 81-9

August 31, 1966

TO: R. F. ANDERSON

FROM: R. G. ALSUP R. D. A.

DISPOSAL OF SOLID "TEFLON" WASTES CONTAINING C-8 APFC

Introduction

Some of the solids wastes from the Fine Powder and Dispersion Area of the "Teflon" plant contain small amounts of toxic perfluorocarboxylic dispersing agents. A cheap and acceptable method of disposing of these solids is in a land fill, provided that the toxic agents are reduced to an acceptable level. Since the dispersing agents are volatile at moderate temperatures, we set out to determine the conditions necessary to bake the resins to a non-toxic state.

Summary and Conclusions:

1. The dispersing agent level of the solids waste stream is reduced to a quite acceptable level (below 2 ppm) by baking at 175°C for 5 hours.
2. Without a pretreatment, a small amount of the perfluorocarboxylic acid dispersing agent would be leached into the ground water.

Discussion:

A system for collecting the solid wastes from the Dispersion and Fine Powder Area was proposed by Anderson and Chren. This involved the use of sumps and settling basins to concentrate the solids. Solids in the form of coagulum from wax filters and wax separator settlings were also to be collected in this system. A flow sheet of the proposed system is attached. The total amount of solids is estimated at ca. 768 pounds per day at current operating conditions.

Samples of solid wastes were obtained from the collection points in the proposed system. These samples were representative of material to be obtained from the fine powder sump, the wax trap, the bottom of the wax separator and the sump from the Dispersion Area. The make-up of these samples was as follows:

August 31, 1966

- Fine Powder Sump - This material looks like contaminated, wet, fine powder. The material contained 36.2% water and 130 ppm perfluoro-carbon dispersing agent calculated as C-8 APFC.
- Wax Trap - appears like wax. Lost 8% by weight on heating to 175°C. Contains ca. 30 ppm C-8.
- Bottom of Wax Separator - appears like wet fine powder and contains about 65% water and 240 ppm C-8.
- Dispersion Area Sump - This sample was actually obtained from the bottom of the stabilization tanks and was a mixture of a 60% dispersion liquid and a solid containing about 30% water. The material contained ca. 300 ppm water. In most of the work done with this mixture, both the liquid and solid phase were analysed.

1. Leaching

As a first step, it was determined that the dispersing agent could be leached from these solids. This was done by adding 100 grams of the sample from the different sources to 100 ml of water in a Waring Blendor. After blending for 5 minutes, the water was filtered and analysed for dispersing agent by the titration method (see below). The data shown in Table I show that the C-8 dispersing agent could indeed be extracted by water. This is the conclusion reached by Crandell in 1964 (see attachment).

Table I

The Extraction of C-8 Dispersing Agent
from "Teflon" Samples in Water

<u>Sample Source</u>	<u>PPM C-8 Extracted</u>	
	<u>1st Extraction</u>	<u>2nd Extraction</u>
Fine Powder Sump	30	19
Wax Separator	103	15
Wax Trap	39	17

2. Baking

The samples were baked at 175°C for 3, 5 and 20 hours. Analysis of these samples showed almost complete removal of the dispersing agent at 5 or 20 hours; after 3 hours treatment only the sample from the fine powder sump contained any residual C-8.

TABLE II

ANALYSIS OF PERFLUOROCARBON DISPERSING AGENT
IN "TEFLON" SOLIDS WASTE

<u>Sample Source</u>	<u>Hours Heated @ 175°C</u>			
	<u>0</u>	<u>3</u>	<u>5</u>	<u>20</u>
Fine Powder Sump	130	100	2.7	0.24
Bottom of Wax Trap	240	<10	2.4	----
Wax Trap #8	(30)	0	0.73	----
Stabilization Tank				
Liquid	460	0	1.1	0.20
Solid	130	<40	0.77	0.41

APFC. The temperature of 175°C was chosen as one easily reached by most ovens and because it is below the flash point of the wax used (205°C).

3. Analysis

Two methods of analysis were used for the determination of perfluorocarbon dispersing agents in the waste streams. The procedures are included here for completeness. One made use of the property that perfluorocarbon dispersing agents can be distilled with water from a strongly acidified slurry. This distillate can then be titrated to determine the amount of acid (as perfluorooctanoic acid ($C_7F_{15}CO_2H$ — MW 431). In these studies the following procedure was followed:

1. A 100 gram sample (+200 ml of distilled water) was cut in a Waring Blendor. The slurry was added to a 500-ml flask and 25 ml of concentrated phosphoric acid added.
2. The flask was fitted with a distilling head and condenser. The slurry was heated to boiling and the condensate collected in an Erlenmeyer flask containing 50-ml of distilled water that had been carefully neutralized to a pink end-point with phenolphthalein indicator. Distillate samples were collected each 5 minutes and titrated with 1/100 N sodium hydroxide.
3. When the titrations indicated that no additional acid was being distilled (ca. 3 titrations or 15 minutes) the titre was added and the amount of dispersing agent calculated according to the following.

$$\text{ppm C-8} = \text{ml} \times 43.1$$

This method checked very well with known spiked amounts of C-8 in the slurry.

The other method is based on the formation of a complex between methylene blue and the dispersing agent. While methylene blue is not extracted from acid solution into chloroform, the complex is partitioned into the chloroform layer. The intensity of the coloration in the chloroform layer is related to the concentration of dispersing agent in the aqueous phase. Nonionic dispersing agents, such as "Triton" X-100, do not interfere. The method is sensitive to 0.05 ppm dispersing agent in the aqueous phase.

In this method, the following procedure was used:

1. The sample was prepared (as in the method above) by cutting a 100 gram sample in a Waring Blendor,

August 31, 1966

with water, acidifying with H_3PO_4 and distilling..
For this test, 500-ml of distillate was collected..

2. A measured portion of the distillate was added to a 100 ml volumetric flask and diluted with water.. The measured amount depended on the amount of C-83 in the distillate. For instance, in the baked samples, a 25 ml portion, diluted to 100 ml, was used; for the as-received sample from the stabilization tank, a 0.2 ml sample, diluted to 100-ml was used.
3. The 100-ml from the dilution of step 2 was added to a 250-ml separating funnel and 1.0 ml of 1-9 HCl solution, 1.0 ml of methylene blue solution (0.500 gms/liter), and 10.0 ml of chloroform were added. The mixture was shaken vigorously for 2 minutes, allowed to settle and the chloroform layer withdrawn.
4. The chloroform layer was analysed in a spectrophotometer in a 11-cm glass cell by scanning from 700 $m\mu$ to 600 $m\mu$ using chloroform in the reference cell. The peak absorbance for the sample at 650 $m\mu$ was measured.
5. For these studies, it had been shown that 0.0057 units on the spectrophotometer = 1×10^{-6} grams of C-8. From the amount of absorbance and the factor from step 2, the amount of C-8 in the sample was calculated.

The two methods checked within 10% for the wax separator sample.

RGA:sc
Attachment

AR226-1445

D

CC: W. L. Smith
R. N. Taylor
G. L. Dean
R. F. Anderson
A. L. Douglas

6.18.0

October 28, 1966

TO: B. A. HERBERT
J. L. OSMOND
R. J. PACOFKY
A. L. WHITE
F. MANZO

FROM: J. E. HIGGINBOTHAM

"TEFLON"® SCRAP

"Teflon" scrap is no longer going to the city land-fill. Scrap accumulated on the plant must immediately be separated (physically) into 2 categories. Each category must be identified.

CATEGORIES

- A. All wet "Teflon" containing C-8 or C-9 dispersing agents (must be kept on the plant for disposal at sea at a future date).
- B. All dry "Teflon", regardless of type, all wet granular "Teflon" except 6091, all wet FEP scrap except "Teflon" 110 (can be moved to the plant land-fill by plant transportation).
- C. Scrap accumulated at Building 22 is to be placed in categories using A & B guidelines above.

PROCESS SCRAP AS FOLLOWS

- 1. All wet scrap (other than dispersion) must be placed inside 2 "Leverpak" liners and a lid and lock-ring must be in place.
- 2. All dispersion scrap is to be handled in steel drums.

Identify category "A" above

"SEA DISPOSAL"

Identify category "B" above

"Land-Fill"

*LABELS ON ORDER
DUE WK. OF 11-7-66*

INFO - Steel drums are on order to replace "Leverpaks" for handling category "A" scrap.

JEH/jwd

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EID193613

CF020524

AR 226-1446

E

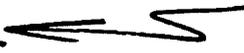
E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
P. O. Box 1217
PARKERSBURG, W. VA. 26101

CC: J. W. Amacher
T. L. Miller
File: 11-0-4

PLASTICS DEPARTMENT

February 18, 1970

COMPANY CONFIDENTIAL

TO: J. MITCHELL, JR. 
PLASTICS DEPARTMENT
EXPERIMENTAL STATION

FROM: W. E. HILTON
FLUOROCARBONS DIVISION
WASHINGTON WORKS

(8-181-7239)

REQUEST FOR TOXICOLOGICAL INFORMATION
"TEFLON"® DIVISION CHEMICALS

Past studies made at Haskell Laboratory have indicated that ammonium perfluorooctonate (C-8 APFC), which is used in the preparation of "Teflon"® dispersions, is highly toxic when inhaled and moderately toxic when injected. However, data are not available on the chronic local or chronic systemic effect of the compound in the solid state or dissolved in "Teflon" dispersions.

A review of the medical history of employees in the dispersion's area revealed that with the exception of two cases of dermatitis, which were probably due more to temperature and moisture than specific chemicals, there have not been any indications of toxicological effects of chemicals. The plant Medical group is aware of the potential effects of the area chemicals and monitor area employees, both individually and statistically.

We are interested in determining the systemic effect for repetitious skin contacts of short duration with C-8 APFC powder and with the aqueous dispersion of polytetrafluoroethylene containing C-8 (or chlorendic acid). We are also interested in determining the chronic effect of inhalation of minute quantities of C-8 APFC. In addition to knowing these effects, we would like guidance on the personnel equipment necessary for adequate protection against these effects. Would you determine the cost of each separate study, the potential for beneficial data

3/3/70 RSW handling cost estimates & proposals

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*W. E. Hilton
2/19/70*

DUP001005

J. MITCHELL, JR.

- 2 -

February 18, 1970

beyond our ability to extrapolate existing qualitative data, and if the following data is sufficient for Haskell Lab's purposes.

C-8 APFC Charging

REDACTED

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J. MITCHELL, JR.

- 3 -

February 18, 1970

REDACTED

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HASKELL LABORATORY FOR TOXICOLOGY AND INDUSTRIAL MEDICINE

SAMPLE SUBMITTED FOR TOXICITY EVALUATIONDepartment Plastics Division Fluorocarbons Location Washington Works

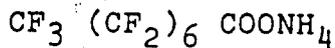
Systematic Name of Chemical:

Ammonium Perfluorooctanoate

Synonym, Product Name and/or Designations:

3M's Wetting Agent FC-143, C-8 APFC

Formula:



Sample: Code No. _____ Lot No. _____ Amount _____

Grade _____ Color White Form _____ Mol. Wt. _____

Special Handling Requirements _____

Is it explosive in air? No in oxygen? ? if so, at what concentrations? _____Active Ingredient C-8 APFC 95 %

Composition, if a mixture (are percentages by weight or volume?)

C-8 95% Minimum

C-6 5% Maximum

Impurities (Identity and amounts; are percentages by weight or volume?)

C-6 5% Maximum

Properties: Decomposes 150°C @ 25°C Negligible (Attach MP curve if available)
MP _____ BP _____ VP _____ @ Max. Process Temp. 100°C
2% Aqueous SolutionSp.Gr. _____ pH 4 Min Vapor Density (air = 1) _____

Flash Point (Open cup) _____ (Closed cup) _____

Solubility (Quantitative, if possible) in water Yes Acetone _____

Ethanol _____ Vegetable oil _____ Other Solvents _____

Proposed Use:

Ingredient in Polymerization Recipe _____

Present Stage of Development: Research _____ Sales _____ Mfg. _____ Sales _____

(OVER)

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EID123141

Employee Exposure

1. Concentration of material in process 1200 PPM
2. Solvent and other chemicals present Water, Disuccinic Acid Peroxide
3. Is exposure by inhalation X skin absorption X other _____
4. Maximum temperature of material in process 100°C
5. Is the compound present in the atmosphere in the form of vapor No
mist No dust Slight
6. Maximum concentration likely to be present in atmosphere Unknown
7. What type of ventilation is in use? High Volume
8. What type of protective clothing is worn? Gloves, Goggles, Dust Mask
9. Exposure is for _____ hours _____ minutes per day See Attached Letter

Consumer Exposure

By Employee

What is possibility of:

- | | | |
|-----------------|----------------|--|
| 1. Ingestion | Very Slight | NOTE: See Attached Letter for Write-Up |
| 2. Inhalation | Minor Quantity | |
| 3. Skin contact | Fair | |
| 4. Eye contact | Slight | |

Experience to Date

Have any clinical signs of toxicity such as headaches, difficulty in breathing, dizziness, nausea, skin or eye irritation, etc., been reported by persons who have been in contact with the chemical? If so, please list them and describe circumstances under which they occurred.

No

NOTE: Haskell Laboratory will retain the unused portion of stable, nonflammable, nonvolatile, low toxicity samples for 5 years unless requested to return to sender immediately after testing. After 5 years, the samples will be discarded or returned to the appropriate department. It is suggested that the sender also retain a suitably identified portion of the sample sent for toxicity evaluation for his own future reference.

Signature W. E. Hilton Date 2/13/70

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EID123142

DUP001009

TABLE I

Ammonium Perfluorooctanoate (C-8 APPC)

Formula: $\text{CF}_3 (\text{CF}_2)_6 \text{COONH}_4$

Manufacturer: 3M (FC-143)

Previous Tests:

Inhalation, MR No. 1198, Haskell Laboratory Report
No. 160-69

Oral, MR No. 604, Haskell Laboratory Report No. 55-61.

Chlorendic Acid

Formula: $\text{C}_9\text{H}_4\text{O}_4\text{Cl}_6$

Manufacturer: Hooker Electrochemical Company

Previous Tests:

Oral, MR No. 604, Haskell Laboratory Report No. 1-63.

EID123143

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DUP001010

AR 226 - 1447

F

cc: J. Mitchell, Jr., Plastics
J. A. Zapp/G. J. Stopps, Haskell Lab.
J. F. Morgan, Haskell Lab.
C. F. Reinhardt, Haskell Lab.
H. Sherman, Haskell Lab.
F. D. Griffith) In turn, Haskell Lab.
C. S. Hornberger)

May 8, 1970

W. E. HILTON
FLUOROCARBONS DIVISION
WASHINGTON WORKS
PARKERSEURG, W. VA.

TOXICOLOGICAL INFORMATION ON C₈ APFC

I'm sorry for the delay in replying to your recent request for an evaluation of employee hazard from C₈APFC in your polymerization operations. I hope this letter will sufficiently amplify my telephone comments of April 16.

As I understand it, you currently are using C₉APFC, but are phasing it out and will be using C₈APFC for ca. 80 per cent of the Teflon® polymerizing and chlorendic acid for the other 20 per cent. AHT is not used.

I have summarized the available toxicity information on C₈APFC and chlorendic acid in the attached table. We have even less information on C₉APFC and some of it is internally conflicting. The information is inadequate for a complete evaluation of the toxicity of these materials. Your principal exposure is by skin absorption. We have no skin absorption toxicity information on any of the three. C₈APFC and C₉APFC cause liver enlargement, but we don't know what is the lowest repeated oral dosage that will cause it. We have no repeated oral dosage study to indicate if C₈APFC or C₉APFC accumulates in the body to toxic levels. We do not know the eye or skin irritation potential for C₈APFC or C₉APFC and we do not know whether the liver enlargement effect occurs only in rats or in other species as well. Except for the knowledge that chlorendic acid does not cause liver enlargement, our data for this material are similarly sketchy. We have no information on the toxicity of disuccinic acid peroxide.

To answer the initial toxicity questions on C₈APFC, I suggest the following tests:

- I. Determination of lethal concentration by single oral doses and determination of lowest oral dosage causing liver enlargement in rats (histopathology of liver only).

\$600

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DUP01001

May 8, 1970

II. Accumulation in the rat to cause liver enlargement (two-week subacute, oral dosing).	\$ 750
III. Accumulation in the rat to lethal levels (with histopathologic examination of tissues, oral dosing).	\$1400
IV. Recovery study for regression of liver enlargement in the rat after oral dosing.	\$1000
V. Single administration skin absorption toxicity (this is done in the rabbit and can be done with enough rabbits to measure liver enlargement).	\$ 800
VI. Repeated application skin absorption study without histopathology but with examination of livers.	\$1500
VII. Primary skin irritation and sensitization (this is done in the guinea pig and can be done with enough guinea pigs to determine if there is significant liver enlargement).	\$1200
VIII. Eye irritation.	300
IX. Repeated (two-week) inhalation administration with histopathology.	\$2000
X. Coordination of the above program, interim reports and final evaluation.	+15%

The liver enlargement evaluation in the above studies has not added materially to the cost. In addition, we recommend a 90-day feeding study in rats and dogs including a one-generation reproduction-teratogen study in rats. This would cost ca. \$30,000. This study is recommended because we have no chronic studies on any of these surfactants and no adequate studies in non-rodent species. Depending on the results of this 90-day study, a protracted study in dogs or dogs and rats, might be indicated.

None of the above studies would allow us to set an atmospheric level of CRAPFC that would be hygienically acceptable on a chronic basis. This would require a chronic inhalation study. The exact cost would depend on final test design, but it would be in excess of \$100,000.

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DWS 1036534

DUP001002

May 8, 1970

If you can eliminate continuous exposure to CgAPFC by inhalation, none of the repeated inhalation studies would be necessary. Similarly, elimination of repeated exposure by skin absorption would eliminate the need for a repeated skin absorption toxicity study. I suggest a visit by our industrial hygienist, Mr. Morgan, as the most beneficial next step to determine the extent of the toxicity testing program. This would also give us better insight into developing the necessary toxicity testing program for chlorendic acid.

RSW

RICHARD S. WARITZ
RESEARCH MANAGER, BIO-SCIENCES GROUP

RSW:ljm
Attachment

C. J. J.

EID072198

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DWS1036535

DUP001005

SUMMARY OF TOXICITY DATA ON C₈APFC AND CHLORENDIC ACID

<u>Test</u>	<u>C₈APFC</u>	<u>Chlorendic* Acid</u>	<u>Chlorendic* Anhydride</u>
Oral Approximate Lethal Dose	670 mg/kg	5000 mg/kg**	1000 mg/kg not lethal
Oral liver enlargement	60-90 mg/kg	No	No
Oral Subacute	ND	8 x 1000 mg/kg caused seven deaths (10 rats used)	8 x 1000 mg/kg caused six deaths (10 rats used).
Approximate Lethal Dose	0.8 mg/L (caused liver enlargement)	ND	ND (Respiratory irritant in rats).

ND - Not determined

* - Data from Hooker Chemical

** - Haskell Laboratory found 2250 mg/kg

‡ - On rats only

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DW\$ 1036536 ★

AR 226-1448

G

STUDY OF MYOCARDIAL INFARCTION

AT WASHINGTON WORKS PLANT

This study was conducted to evaluate the incidence of cases of myocardial infarction among male wage and salary roll employees at the Washington Works Plant from 1956 to 1973. Dr. Y. I. Power, Plant Physician, requested the investigation because some workers had complained that the occurrence of heart attacks among employees seemed excessive.

DESIGN AND METHODS

A computer search of the morbidity files in Wilmington produced a list of cases for this retrospective study. A case is defined as any male employee who suffered a first myocardial infarction (M.I.) between January 1, 1956, and December 31, 1973. This definition includes persons who recovered from an acute M.I. and those who died suddenly from coronary heart disease. Persons who had left work for any reason were considered potential propositions during only those years in the study period when they were active employees. Females were excluded from the study, as they represent a group too small in size for statistical analysis.

Additional data concerning plant population statistics and occupational profiles for each case were obtained from records at Washington Works.

Sixty-one cases of M.I. were observed during the eighteen-year period. A breakdown by age categorization within three-year periods for salary roll and for wage roll men is presented in Table I.

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Age-specific Du Pont Company rates for male wage roll and salaried personnel were used to compute the expected number of M.I.'s at Washington Works. Again, three-year time periods were selected for this determination. It would not have been sufficient to have referred to the 1973 figures, nor to have averaged or otherwise aggregated the rates over the eighteen years, because a trend toward lower incidence in the Du Pont Company has occurred in recent years. The Company rates are shown in Table II. The observed number of myocardial infarctions at Washington Works and the number of cases predicted according to Company statistics are presented in Table III for wage roll and for salary roll employees.

ANALYSIS

No excess incidence of M.I. is evident among the male wage roll employees. The expected number of M.I.'s is 34.0; 32 were observed. One notices that the number of cases has been increasing over the years at Washington Works. One suggested explanation is that with an increasing percentage of employees over the age of fifty, both at Washington Works Plant and in the Company (Table IV), more M.I.'s are to be expected.

Among salaried employees, the observed incidence of myocardial infarction is significantly higher than the expected number, under the assumption that cases follow a Poisson distribution: 29 M.I.'s were observed; 21.5 is the expected number ($P \approx .06$). The high overall incidence is largely the result of elevated rates in recent years. In the period from 1971 to 1973, the difference between observed and predicted numbers is great:

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12 observed cases versus 5.3 expected cases ($P = 0.008$) whereas in the preceding years no differences between observed and expected numbers were significant. ($P > .10$ for all comparisons).

Further investigation of occupation reveals that the high frequency of M.I. cases among salaried employees is seen largely in foremen. Twenty of the twenty-nine cases occurred among the population of foremen at Washington Works: 8 were mechanical foremen, 9 were production foremen, 2 were laboratory foremen, and 1 was a yard and transportation foreman. Approximately thirty-five percent of the salaried men at the plant are foremen. Since the age distribution of foremen is comparable to that of all salaried employees at Washington Works, one would expect that only 10 of the observed M.I.'s would present in this occupational class (35% of 29), compared to the 20 which occurred among foremen.

The foremen studied range in age at onset of the attack from 35 to 65 years. Both the mean and the median number of years of experience as foremen prior to M.I. is 9.0. The range is 1 week to 25 years.

Patrolmen, a group representing three percent of the Washington Works population, also showed a somewhat elevated incidence of M.I. Four cases were observed among patrolmen, whereas the expected number is 1.4 (3% of 29). The age at onset for these patrolmen, however, ranges from 55-59 years; this is older than the median age at onset for the entire group, which is about 50 years. This consideration explains the increased incidence among patrolmen. Distribution of M.I. cases among employee work classifications is presented in Table V.

: SUMMARY

This study examines incidence of myocardial infarction among male employees at Washington Works over an eighteen-year period. Using Du Pont Company rates as the referrent, it was found that no excess of M.I. cases occurred among wage roll persons, whereas among salaried men, elevated morbidity rates obtain. The target group among salaried employees is foremen. Increased incidence in this group cannot be explained by their age distribution. One asks, then, if some aspect of the work routine is a causal link in the development of coronary heart disease, or if some personal characteristic which predisposes one to become a foreman is a risk indicator for M.I. As a result of the findings of this study, the Biostatistics Group in Wilmington will explore the possibility of a Company-wide investigation of morbidity among foremen.

Maureen T. O'berg
MAUREEN T. O'BERG
Biostatistician

TABLE I
AGE DISTRIBUTION OF M.I. CASES BY THREE-YEAR
PERIODS AT WASHINGTON WORKS, 1956-1973

Age	Male Wage (Number of Employees)						Total
	<u>1956-58</u>	<u>1959-61</u>	<u>1962-64</u>	<u>1965-67</u>	<u>1968-70</u>	<u>1971-73</u>	
20							0
20-24					1		1
25-29							0
30-34			2				2
35-39		2			3	1	6
40-44		2	1				3
45-49		1	1	2	3	1	8
50-54	1	1		3	1		6
55-59				1		3	4
60-64						2	2
Total	1	6	4	6	8	7	32

Age	Male Salary (Number of Employees)						Total
	<u>1956-58</u>	<u>1959-61</u>	<u>1962-64</u>	<u>1965-67</u>	<u>1968-70</u>	<u>1971-73</u>	
20							0
20-24							0
25-29							0
30-34			1				1
35-39			1				1
40-44							0
45-49		3			1	2	6
50-54		1	1	2	1	1	7
55-59		1		1	1	7	10
60-64				1			1
Total	0	5	3	4	5	12	29

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EID713131

TABLE II

Age-Specific Du Pont Company Rates,
Per 100,000, of MI Cases

WAGE - MEN

Age	1956-58	1959-61	1962-64	1965-67	1968-70	1971-73
20	0.0	0.0	0.0	0.0	0.0	0.0
20-24	0.0	0.0	0.0	5.1	12.4	0.0
25-29	4.0	0.0	6.0	4.2	11.7	4.5
30-34	18.6	21.3	34.4	10.6	15.8	0.0
35-39	88.7	117.7	114.6	55.8	111.8	86.2
40-44	178.2	282.7	254.9	191.2	242.0	183.6
45-49	484.7	384.0	358.4	385.4	372.9	422.5
50-54	707.9	812.1	630.7	674.4	565.3	648.2
55-59	883.3	962.5	713.8	895.9	919.6	804.4
60-64	940.8	910.3	857.4	989.7	1,064.9	1,169.8
*TOTAL	280	357	259	267	275	271

222
401
673

SALARY - MEN

Age	1956-58	1959-61	1962-64	1965-67	1968-70	1971-73
20	0.0	0.0	0.0	0.0	0.0	0.0
20-24	0.0	0.0	0.0	0.0	0.0	0.0
25-29	0.0	0.0	0.0	0.0	7.0	0.0
30-34	6.2	13.8	56.4	8.3	7.6	0.0
35-39	57.9	84.0	68.8	119.9	43.5	20.5
40-44	247.2	184.4	237.7	175.2	206.4	64.9
45-49	458.7	451.7	450.7	342.7	312.4	180.0
50-54	703.9	683.1	552.3	645.5	459.9	343.4
55-59	1,001.0	1,007.1	936.7	849.8	776.5	476.2
60-64	1,327.9	903.3	1,165.6	1,024.2	1,141.0	707.0
*TOTAL	354	330	331	303	271	215

*Age-adjusted rate

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EID713132

TABLE III

OBSERVED NUMBER OF M.I. CASES AT WASHINGTON
WORKS AND EXPECTED NUMBER OF M.I. CASES,
BASED ON DU PONT COMPANY MORBIDITY

		Male Wage						
		<u>1956-58</u>	<u>1959-61</u>	<u>1962-64</u>	<u>1965-67</u>	<u>1968-70</u>	<u>1971-73</u>	<u>Total</u>
Observed		1	6	4	6	8	7	32
Expected		2.2	3.8	4.9	6.0	8.2	8.9	34.
		Male Salary						
		<u>1956-58</u>	<u>1959-61</u>	<u>1962-64</u>	<u>1965-67</u>	<u>1968-70</u>	<u>1971-73</u>	<u>Total</u>
Observed		0	5	3	4	5	12	29
Expected		1.5	2.5	3.5	3.9	4.8	5.3	21.5

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EID713133

TABLE IV

Age Categorization of Male Employees at
Du Pont Company and Washington Works, 1956-1973

DU PONT COMPANY
WAGE AND SALARY COMBINED*

Age	1956-58	1959-61	1962-64	1965-67	1968-70	1971-73
< 50	203,712	181,142	186,413	205,110	197,957	183,441
≥ 50	44,287	49,733	58,954	67,960	72,259	74,020
% ≥ 50	18%	22%	24%	25%	27%	29%

WASHINGTON WORKS
WAGE AND SALARY COMBINED*

Age	1956-58	1959-61	1962-64	1965-67	1968-70	1971-73
< 50	3,136	4,421	4,712	5,528	6,370	6,031
≥ 50	151	322	526	744	1,000	1,225
% ≥ 50	4%	7%	10%	12%	14%	17%

*Each number represents the cumulative mid-year population for the three-year period.

TABLE V

OBSERVED NUMBER OF M.I. CASES BY OCCUPATION
AND EXPECTED NUMBER OF M.I. CASES, BASED ON
OCCUPATIONAL DISTRIBUTION AT WASHINGTON
WORKS, MALE SALARIED EMPLOYEES

<u>OCCUPATION</u>	<u>% OF SALARIED EMPLOYEES AT WASHINGTON WORKS</u>	<u>OBSERVED NUMBER OF M.I.'S</u>	<u>EXPECTED NUMBER OF M.I.'S*</u>
Foremen	35%	20	10.2
Supervision through Management	23%	3	6.7
Specialists	2%	1	1.4
Analysts, Accountants	3%	0	.9
Engineers	22%	0	6.4
Clerical	10%	0	2.9
Patrolmen	3%	4	.9
Draftsmen	2%	1	1.4
TOTAL		<u>29</u>	

*expected number = % x 29

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EID713135

AR 226 - 1449

H

DON'T SAY IT-WRITE IT

To FRANK A. BOWER Location PETCHEM-FREON PRDTS LAB-CHESTNUT RUN
From RAY MORROW *Rwm* Location HASKELL LAB Phone No. 366-4356
Subject MEETING WITH 3M MAY 30 Date 5/15/78

cc: [REDACTED]
T. L. Cairns, CR&D-Wilm.
CFR/BCM
J. R. Gibson

Attached is a copy of a paper by Guy and Taves concerning organic fluorocompounds in human plasma. The discussion section deals specifically with possible environmental sources of perfluorinated fatty acids. The paper was presented at a symposium sponsored by Divisions of Fluorine and Biological Chemistry at the 170th Meeting of the American Chemical Society, Chicago, Illinois, August 26, 1975 and published in the ACS Symposium Series 28, by the American Chemical Society, 1976.

RWM/taa
Attachements

G-88 REV. 10-62

SECURITY IS AN INDIVIDUAL RESPONSIBILITY

RECEIVED
MAY 16 1978
BRUCE W. KARRH, M.D.

EID107111

RL001539

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Presented at a symposium sponsored by the Divisions of Fluorine and Biological Chemistry at the 170th Meeting of the American Chemical Society, Chicago, Ill., Aug. 26, 1975.

Published by the American Chemical Society, 1976. 7

Organic Fluorocompounds in Human Plasma: Prevalence and Characterization

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Taves discovered that samples of his own blood serum contained two distinct forms of fluoride (1-4). Only one of these was exchangeable with radioactive fluoride. The other, non-exchangeable form was detectable as fluoride only when sample preparation included ashing. This paper is concerned with three aspects of this newly discovered, non-exchangeable form: 1) its prevalence in human plasma, 2) how its presence in human plasma affects the validity of certain earlier conclusions about the metabolic handling of the exchangeable form of fluoride, and 3) its chemical nature.

Preliminary work in this laboratory suggested that the non-exchangeable form was widespread in human plasma but did not exist in the plasma of other animals. Ashing increased the amount of fluoride an average of 1.6 ± 0.25 SD μM (range 0.4-3.0) in samples of plasma from 35 blood donors in Rochester, N.Y. (5). No such fluoride was detectable (above 0.3 μM) in blood serum from eleven different species of animal including horse, cow, guinea pig, chicken, rabbit, sheep, pig, turkey, mule and two types of monkey (6).

Standard methods for analysis of exchangeable fluoride in serum have in the past included ashing as a step in sample preparation (7). Taves showed that the amount of fluoride in serum that would mix with radioactive fluoride was only about one-tenth the amount generally thought to be present based on analyses using these older methods (4). When plasma samples from individuals living in cities having between 0.15 and 2.5 ppm fluoride in their water supply were analysed by these older methods, no differences were found between the averages for the different cities. This led to the conclusion that "homeostasis of body fluid fluoride content results with intake of fluoride up to and including that obtained through the use of water with a fluoride content of 2.5 ppm" (8). If the non-exchangeable form of fluoride predominated in these samples, differences in the exchangeable fluoride concentration would probably not have been apparent, and it would be unnecessary to postulate such rigorous

homeostatic control mechanisms for fluoride.

In this study plasma samples were collected from a total of 106 individuals living in five different cities with between 0.1 and 5.6 ppm fluoride in their public water supply. These were analyzed for both forms of fluoride. In this way the relationship between exchangeable fluoride concentration in the plasma and the consumption of fluoride through drinking water was re-evaluated, and the prevalence of the non-exchangeable form was further studied.

With respect to the chemical nature of the non-exchangeable form of fluoride several lines of evidence suggested that it was some sort of organic fluorocompound of intermediate polarity, tightly bound to plasma albumin in the blood. It migrated with albumin during electrophoresis of serum at pH nine (3) and was not ultrafilterable from serum (2). Attempts at direct extraction from plasma with solvents of low polarity like heptane, petroleum ether and ethyl ether were generally unsuccessful. Treatment of albumin solution (prepared by electrophoresis of plasma) with charcoal at pH three did remove the bound fluoride fraction. And finally, when plasma proteins were precipitated with methanol at low pH the fluoride fraction originally bound to albumin appeared in the methanol-water supernatant in a form which still required ashing to release fluoride as inorganic fluoride (5). Based on these considerations the non-exchangeable form of fluoride in human plasma is referred to as "organic fluoride" throughout the rest of this paper.

In order to further characterize the organic fluoride fraction, it was purified from 20 liters of pooled human plasma and characterized by fluoride nmr.

Materials and Methods

Analytical Methods. Values for organic fluoride were calculated by taking the difference between the amount of inorganic fluoride in ashed and unashed portions of the same material.

The following procedure was used to prepare ashed samples: 1) samples (sample size for plasma was 3 ml) were placed in platinum crucibles and mixed with 0.6 mmoles of low fluoride $MgCl_2$ and 0.1 mmoles of NaOH, 2) these were dried on a hotplate and then ashed (platinum lids in place) for 2-4 hr at 600° C in a muffle furnace which had been modified so that the chamber received a flow of air from outside the building (room air increased the blank and made it more variable), and 3) ashed samples were dissolved in 2 ml of 2.5 N H_2SO_4 and transferred to polystyrene diffusion dishes using 2 rinses with 1.5 ml of water.

The following procedure was used for separation of fluoride from both ashed and unashed samples: 1) samples (sample size for unashed plasma was 2 ml) were placed in diffusion dishes (Organ Culture Dishes, Falcon Plastics, Oxnard, Calif., absorbent

removed, rinsed with water and agitated with a gentle stream for 30 min to remove CO_2 ; 2) solution (0.5 ml, 0.01 N NaOH) was placed in a small polystyrene diffusion dish, 1 drop of sample to decrease surface tension, more uniform between sample and lid with a small hole was placed into place with petroleum ether (Dow Corning, Fluid 1) was injected through the hole was sealed immediately with paraffin film; and 3) sealed for at least 6 hr, diffusion and trapping solutions were checked at this point to ensure and dried in a vacuum oven in the presence of a NaOH desiccant.

Fluoride was determined with a fluoride electrode. The system was oriented in an inverted position (Cambridge, Mass.), a calcium plastic vapor shield was used, electrodes forming an electrode, saturated tissue paper was used for evaporation of the sample (model 401, Orion).

Samples were prepared in a 1 M HAc was drawn into a Micro Sampling Kit, Spiro (San Jose, Calif.) and deposited into the trapping solution a micropipette was used to transfer solution was then transferred to the electrode and the reference electrode. Surfaces of the two electrodes were cleaned.

Samples were read with a fluoride ion selective electrode and sets of sample standards. These standards were used during a run. First, the electrode surfaces to equilibrate with the samples and to make the measurement. The analyst to take readings every one minute. Secondly, the electrode readings used in preparation of the standards.

Values for individual samples were averaged and the average value was then divided by the sample size.

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removed, rinsed with water), acidified with 2 ml of 2.5 N H_2SO_4 , and agitated with a gentle swirling action on a laboratory shaker for 30 min to remove CO_2 ; 2) for each sample the trapping solution (0.5 ml, 0.01 N NaOH + phenolphthalein-p-nitrophenol indicator) was placed in a small polystyrene cup in the center-well of the diffusion dish, 1 drop of 10% Triton-X 100 was added to the sample to decrease surface tension and make the diffusion rate more uniform between samples containing plasma and those not, the lid with a small hole made near its lateral margin was sealed into place with petroleum jelly, 0.02 ml of 4% hexamethyldisiloxane (Dow Corning, Fluid 200, 0.65 cs, Midland, Mich.) in ethanol was injected through the hole in the lid into the sample, and the hole was sealed immediately with petroleum jelly and a strip of paraffin film; and 3) samples were diffused with gentle swirling for at least 6 hr, diffusion was terminated by breaking the seal, and trapping solutions were removed (the indicator color was checked at this point to insure that they were still alkaline) and dried in a vacuum oven (60° C, 26 in-Hg vacuum, in the presence of a NaOH desiccant).

Fluoride was determined by potentiometry with the fluoride electrode. The system used consisted of a fluoride electrode oriented in an inverted position (model 9409A, Orion Research Inc. Cambridge, Mass.), a calomel reference electrode (fiber type), a plastic vapor shield which just fitted over the bodies of both electrodes forming an enclosed sample chamber in which water-saturated tissue paper was placed above the sample to prevent evaporation of the sample, and a high impedance voltmeter (model 401, Orion).

Samples were prepared and read in the following way: 10 μ l of 1 M HAc was drawn into a polyethylene micropipette (Beckman Micro Sampling Kit, Spinco Div., Beckman Inst. Co., Palo Alto, Calif.) and deposited into the cup containing the residue from the trapping solution after drying; the flexible tip of the micropipette was used to wash down the walls of the cup; and the solution was then transferred to the surface of the fluoride electrode and the reference electrode brought into position. Surfaces of the two electrodes were blotted dry between samples.

Samples were read in order of increasing expected concentration and sets of samples were read between bracketing calibration standards. These standards were used in two different ways during a run. First, they were flooded onto the electrode surfaces to equilibrate them to concentrations expected for samples and to make them uniform. This procedure permitted the analyst to take reasonably stable readings for samples within one minute. Secondly, they were used in 10 μ l volumes for readings used in preparing the standard curve.

Values for identical samples (usually triplicates) were averaged and the average blank was subtracted from sample means. These were then divided by the average fractional recovery of

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fluoride (usually 90 to 95%) in standards treated the same way as the sample set.

Plasticware (Falcon Plastics) was used for all analytical procedures to avoid contamination by fluoride from glass. Liquid volume measurements were made with 1, 5 and 10 ml polystyrene pipettes and a polycarbonate volumetric flask (100 ml).

Reagents were purified to insure uniformly low blanks. Water was redistilled and deionized. Acetic acid and ammonia were redistilled. Fluoride contamination in $MgCl_2$ (analytical grade) was reduced by preparing a 1 M solution containing HCl to pH 1 and scrubbing with hexamethyldisiloxane vapor in a column through which the solution was continuously recycled. Following scrubbing the solution was boiled to one third volume to remove any residual volatile silicones and then made just basic with NH_4OH . Fluoride contamination in H_2SO_4 was reduced by repeated extractions of a 6.7 N solution with hexamethyldisiloxane and then boiling to one third volume to remove the residual silicone.

Buffered calibration standards were made from the same NaOH and HAc stock solutions as for samples.

The blanks for ashed samples ranged between 0.2 and 1.5 nmoles fluoride and were typically about 0.5 nmoles. The blanks were smaller for unashed samples; these ranged between 0.05 and 0.2 nmoles fluoride and were typically about 0.1 nmoles.

Factors affecting recovery of fluoride during diffusion were investigated with F^- tracer. Recovery during diffusion was 97% after 80 min from 5 ml containing 2 ml of plasma. Increasing the acidity of the sample up to 5 N, the volume of the sample up to 7.5 ml, the amount of cold F^- up to 1 μ mole, the amount of fluoride complexors up to 1 μ mole of $Th(NO_3)_4$ had no material effect on the rate of fluoride diffusion. The absence of both plasma and detergent in the sample compartment markedly slowed the rate of diffusion. Not shaking the sample also slowed the rate of diffusion. Increasing the alkalinity of the trapping solution to 0.1 N increased the rate of diffusion but the lower concentration, 0.01 N, was required here to permit a lower ionic strength in the sample reading solution.

Overall recovery of added cold fluoride was measured. In samples containing neither plasma nor detergent the recovery after 6 hr diffusion averaged 93% and 95% for ashed and unashed samples, respectively. In samples containing plasma the recovery was 95% after 3 hr diffusion.

The degree to which fluorine from organic fluorocompounds could be fixed as inorganic fluoride by ashing varied from less than 1% for volatile compounds like p-aminobenzotrifluoride, m-hydroxybenzotrifluoride, benzyl fluoride and benzotrifluoride to over 80% for less volatile compounds like 5-fluorouracil, fluoroacetate and p-fluorophenylalanine.

Methods used here for separation of fluoride (diffusion at room temp.) (9) and its quantitation (fluoride electrode) (10) are considered to be quite specific for fluoride. One potentially

important interference which might partially lower the pH of the buffer found that samples containing acetic acid (e.g., from purification system) over a few hours. The significant fluoride in blood plasma of four samples of human blood over weeks, and no change in the amount of fluoride in the trapping solution containing the same plasma up to 158 hr and the results were observed between time.

The sensitivity of the blank rather than the sample was measured. Reproducibility varied between 10% and 20%. The coefficient of variation range (samples containing the high range (10-12

Blood Plasma. Blood plasma was collected in five cities. Accuracy was not changed the fluoride supply for at least a month. Samples were received as part of the Fenwall A collection using this method containing 67.5 ml of solution. When the fluoride in the plasma. Because of a factor of 1.3 was appropriate concentration of fluoride was ± 0.1 because of hematocrit and minimum blood was obtained at a concentration of 1 liter per

Electrophoresis. A separator (model FF-1) was employed. Sample flow was 72 ml/hr, voltage was 1000 V, run time took 19 hr. Fluorescence was between 2 and 3. The pH was made by bubbling CO_2 and the pH reached 9.0.

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important interference, however, was codiffusible organic acids which might partially neutralize the trapping solution and thus lower the pH of the buffered reading solution. Indeed, it was found that samples containing relatively large concentrations of acetic acid (e.g., fractions 2, 3 and 4 from step 4 in the purification system) completely neutralized the trap within a few hours. The significance of this problem in the analysis of fluoride in blood plasma was investigated in two ways. First, four samples of human plasma were allowed to diffuse for three weeks, and no change in the color of the phenolphthalein indicator in the trapping solution was observed. Secondly, samples containing the same plasma were diffused for different periods up to 158 hr and the apparent fluoride was determined. No changes were observed between samples which correlated with diffusion time.

The sensitivity of the analytical method was limited by the blank rather than the sensitivity of the instruments used. Reproducibility varied with the amount of fluoride being measured. The coefficient of variation averaged 55% in the low range (samples containing 0.25 to 0.75 nmoles F^-) and 6.6% in the high range (10-12 nmoles F^-).

Blood Plasma. Human plasma was obtained from blood banks in five cities. According to public records these cities had not changed the fluoride concentration of their public water supply for at least six years prior to obtaining the samples. Samples were received in individual polyethylene bags which were part of the Fenwall ACD blood collection system. In blood collection using this system 450 ml of blood is drawn into a bag containing 67.5 ml of anticoagulant acid citrate dextrose (ACD) solution. When the cells are removed the ACD solution remains in the plasma. Because of this dilution of plasma a correction factor of 1.3 was applied to values obtained here for the concentration of fluoride. The potential error in this factor was ± 0.1 because of variation between standard limits for hematocrit and minimum volume of the blood donation. Bovine blood was obtained at slaughter and mixed immediately with ACD solution in 1 liter polyethylene bottles.

Electrophoresis. A continuous flow electrophoretic separator (model FF-3, Brinkman Inst., Inc., Westbury, N.Y.) was employed. Sample flow rate was 2.3 ml/hr, buffer flow rate was 72 ml/hr, voltage was 0.67 kv, and current was 140 mamp. Separation took 19 hr. Plate separation was 1 mm and operating temperature was between 2 and 4° C. The buffer was 0.12% $(NH_4)_2CO_3$, made by bubbling CO_2 from dry ice into redistilled NH_4OH until the pH reached 9.0.

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Purification System. Steps in the purification system are summarized in table I. In the first step one liter of plasma (pooled from 5-6 individuals) was dialysed in seamless cellulose tubing (1 in. diameter) against 20 liters of water at 4° C. The dialysate was changed twice at 24 hr intervals. In the second step dialysed plasma was freeze dried.

In the third step the dried powder from electrophoresis was extracted with methanol in a soxhlet extraction apparatus (model 6810 G, Ace Glass, Inc., Vineland, N.J.). Cellulose extraction thimbles (model 6812 G, Ace Glass) were soaked overnight in methanol. Operating conditions were 25° to 30° C under a vacuum of 24 in-Hg. Coolant for the condenser was 80% ethanol; inlet temperature was -10° to -20° C and outlet temperature was -10° to 0°. Two liters of methanol were refluxed through the apparatus for a period of 4 hr and approximately 400 ml were lost to evaporation during that period. Glass beads were placed in the flask to prevent bumping.

In the fourth step the residue from the methanol extract was fractionated according to the method described by Siakotos and Rouser (11) for separating lipid and non-lipid components. The method is based on liquid-liquid partition in a column containing a dextran gel (Sephadex G-25, coarse, beaded, Pharmacia Fine Chemicals, Inc., N.Y.). Four eluents are used: 1) 500 ml chloroform/methanol, 19/1, saturated with water, 2) 1000 ml of a mixture of 5 parts of chloroform/methanol, 19/1, and 1 part of glacial acetic acid, saturated with water, 3) 500 ml of a mixture of 5 parts chloroform/methanol, 19/1, and 1 part glacial acetic acid, saturated with water, and 4) 1000 ml of methanol/water, 1/1. Their method was modified for use here by increasing the column length to that attained by using a full 100 grams of dextran beads. Sample size corresponded to that from 2.5 liters of the original plasma.

In the fifth step the residues from eluents 2 and 3 from two runs of step four were combined, applied to a silicic acid column, and eluted by reverse flow with an exponential gradient of increasing amounts of methanol in chloroform. The column (model SR 25/45, 2.5 cm i.d. x 45 cm, Pharmacia) was filled to a height of 30 cm with silicic acid (Unisil, 100-200 mesh, Clarkson Chem. Co., Inc., Williamsport, Pa., heat activated at 110° C for 2 days) and was washed with a complete set of elution solvents before use. The gradient maker (model 5858, set 4, Ace Glass Co.) was filled with 1 liter of methanol in the upper chamber and 2 liters of chloroform in the lower. The flow rate was adjusted by the height of the solvent reservoirs to an average of 3 ml/min for the first liter of eluent. The sample had to be transferred to the column by repeated washings with chloroform because of its low solubility in this solvent. This usually required about 30 ml of chloroform total. Dead volume for the system as 90 ml. Fractions of 15 ml volume were collected in carefully cleaned glass tubes.

PROCE
OF FLUOROC

Fraction
Treated

blood plasma

plasma proteins &
protein-bound
substances in
water solution

plasma proteins &
protein-bound
substances

plasma lipids

polar lipids

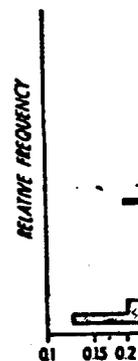


Figure 1. Fluorides in human plasma

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Table I
 PROCEDURE FOR PURIFICATION
 OF FLUOROCOMPOUNDS FROM BLOOD PLASMA

Fraction Treated	Treatment	Fraction Removed
blood plasma	step 1: exhaustive dialysis against distilled water	smaller, water-soluble components
plasma proteins & protein-bound substances in water solution	step 2: lyophilization	water
plasma proteins & protein-bound substances	step 3: methanol extraction—soxhlet, 25°C, 24 in-Hg vacuum	plasma proteins
plasma lipids	step 4: column chromatography—liquid-liquid partition on Sephadex	lipids of low polarity and residual polar contaminants
polar lipids	step 5: column chromatography—adsorption on silicic acid	unknown: several yellow fractions

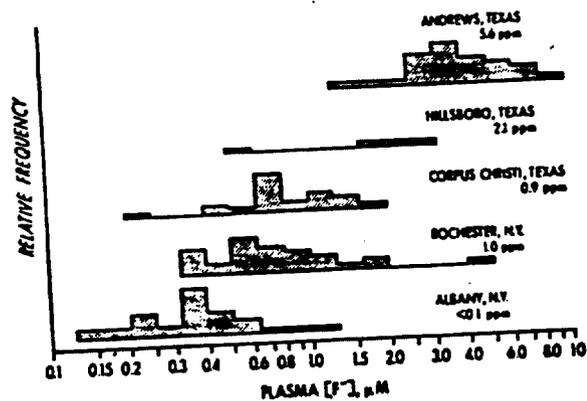


Figure 1. Relationship between the concentration of fluoride in human plasma and the concentration of fluoride in the drinking water

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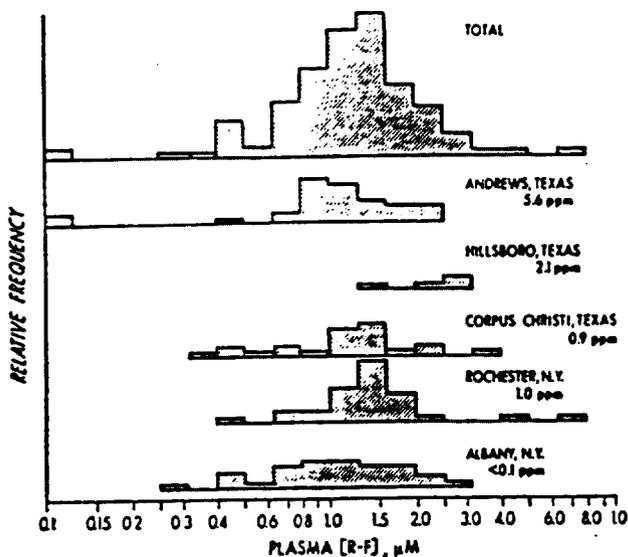


Figure 2. Relationship between the concentration of organic fluoride in human plasma and the concentration of fluoride in the drinking water

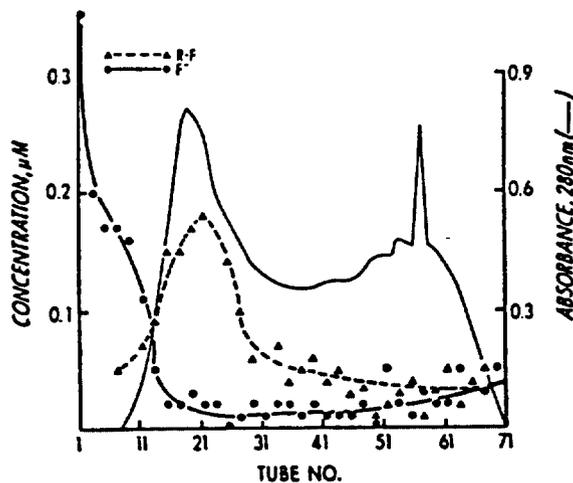


Figure 3. Separation of fluoride and organic fluoride in human plasma by electrophoresis. A sample (about 45 ml) of human plasma was electrophoresed in pH 9 buffer and fractions between the sampling port (near tube 72) and the positive pole (near tube 1) were analyzed for the fluoride content of both ashed and unashed aliquots. Relative concentrations of proteins were estimated by absorbance at 280 nm.

Tubing and fittings were supplied largely by...
All solvents were ACS certified (Fisher Scientific, St. Louis). Solvents were evaporated.

NMR. The nmr spectrum was obtained with a Nicolet spectrometer with Nicolet... The sample was dissolved in CH_3OH and CDCl_3 and spectra were referenced to CFCl_3 was... are expressed with positive frequency). External lock pulse length of 15 microcycles of 2.5 sec, and a processing.

Results

Values for inorganic fluoride (R-F) in 106 plasma samples are shown in table II. The concentration in plasma and the concentration in the water and the fluoride concentration in the fluoride in plasma and... by inspection of values of the values within cities both cases the distribution with only 3 or 4 individuals of the two individuals were (figure 2, Andrews group) levels were both in excess for organic fluoride. The organic fluoride was 1.0.

Plasma was electrophoresed. Findings of Taves (3) were shown in figure 2. Results shown in figure 2 that a predominant form with albumin at pH 9, and were clearly separated.

The recovery, mass balance in the purification system is shown in table III. These data show that the amount of organic fluoride peak from silicic acid was for in other fractions presumably because of a...

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Tubing and fittings to the columns were polytetrafluoroethylene (supplied largely by Chromatronix, Inc., Berkeley, Calif.).

All solvents were redistilled. Methanol and chloroform were ACS certified (Fisher Scientific Co.) and acetic acid was analytical reagent grade, U.S.P. (Mallinckrodt Chemical Works, St. Louis). Solvents were removed from samples in a flash evaporator.

NMR. The nmr spectrum was obtained on a Varian XL-100 spectrometer with Nicolet Technology Fourier Transform accessory. The sample was dissolved in an approximately 1/1 mixture of CH_3OH and CDCl_3 and spectra were run in a 5 mm tube. External referencing to CFCl_3 was used for the chemical shifts, and these are expressed with positive numbers to lower field (i.e., higher frequency). External lock was used. Typical conditions were a pulse length of 15 microseconds, a delay time between pulse cycles of 2.5 sec, and a time constant of -1 sec for exponential processing.

Results

Values for inorganic fluoride (F^-) and organic fluorine (R-F) in 106 plasma samples from humans living in five cities are shown in table II. These data show that the average fluoride concentration in plasma is directly related to the fluoride concentration in the water supply, and that the average organic fluorine concentration in plasma is not. No relationship between fluoride in plasma and organic fluorine in plasma was apparent by inspection of values for individual samples. The distributions of the values within cities are shown in figures 1 and 2. In both cases the distributions appear to be log normally distributed with only 3 or 4 individuals surprisingly deviant. In the cases of the two individuals with little or no apparent organic fluorine (figure 2, Andrews group, left margin), the inorganic fluoride levels were both in excess of 7 μM , making the difference measurement for organic fluorine difficult. The overall mean value for organic fluorine was 1.35 ± 0.85 SD μM .

Plasma was electrophoresed in an attempt to reproduce the findings of Taves (3) using plasma from another individual. Results shown in figure 3 closely match those found earlier in that a predominant form of organic fluorine appeared to migrate with albumin at pH 9, and in that organic and inorganic forms were clearly separated.

The recovery, mass balance and purification factors for steps in the purification system listed in table I are recorded in table III. These data show that about one-third of the original amount of organic fluorine in plasma is recovered in the major peak from silicic acid chromatography. Another third is accounted for in other fractions and the rest is not accounted for, presumably because of adsorption to surfaces of containers in

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Table II

CONCENTRATION OF FLUORIDE (F^-) AND ORGANIC FLUORINE (R-F) IN BLOOD PLASMA SAMPLES FROM FIVE CITIES HAVING DIFFERENT FLUORIDE CONCENTRATIONS IN THEIR WATER SUPPLY

City ($[F^-]$ in Water, ppm)	$[F^-]$ in Plasma ^a , μM			$[R-F]$ in Plasma ^{a,b} , μM		
	Mean \pm SD(n)	Range	Diff. ^c P<.05	Mean \pm SD(n)	Range	Diff. ^{c,d} P<.05
Albany, N.Y. (<.1)	0.38 \pm 0.21 (30)	0.14-1.1	sig.	1.2 \pm 0.6 (30)	0.3-2.6	n.s.
Rochester, N.Y. (1.0)	0.89 \pm 0.75 (30)	0.35-4.2		1.6 \pm 1.2 (30)	0.5-6.8	
Corpus Christi, Tex. (0.9)	1.0 \pm 0.35 (12)	0.60-1.7	n.s.	1.3 \pm 0.9 (12)	0.4-3.9	n.s.
Hillsboro, Tex. (2.1)	1.9 \pm 0.9 (4)	0.60-2.6	sig.	2.3 \pm 0.6 (4)	1.5-2.8	n.s.
Andrews, Tex. (5.6)	4.3 \pm 1.8 (30)	1.4-8.7		1.1 \pm 0.5 (30)	0.1-2.3	

^a Each value used in the computation was the average of at least three replicate analyses and was corrected for dilution by ACD solution by multiplying it by 1.3.

^b taken to be the difference between the amount of inorganic fluoride measured in ashed and unashed aliquots of the same sample

^c by t-test assuming equal variance in each group

^d The difference between Rochester and Andrews is statistically significant.

MASS BAL
FACTOR FOR

Fraction
human plasma
(ACD, 2.5 liter
batch)

Methanol Extractio

extract

residue

Sephadex Column

Fraction I

Fractions II + I

Fraction IV

Silicic Acid Colum

major peak

other peaks
combined

^a mean \pm SD(n)

^b percent of the
mean \pm SD

^c estimate based o
of the major

^d estimate based o

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Table III

MASS BALANCE, RECOVERY AND PURIFICATION
FACTOR FOR STEPS IN THE PURIFICATION SYSTEM

<u>Fraction</u>	<u>Dry Wt.</u> <u>grams</u>	<u>Amt. R-F^a</u> <u>nmoles</u>	<u>Recovery^b</u> <u>%</u>	<u>Purifi-</u> <u>cation</u>
human plasma (ACD, 2.5 liter batch)	200	1725 ±273(6)		
<u>Methanol Extraction</u>				
extract	10.1	1476 ±60(6)	85.6 ±14.0	17 X
residue	--	105 ±37(4)	6.1 ±1.0	--
<u>Sephadex Column</u>				
Fraction I	--	125 ±18(4)	7.3 ±1.6	--
Fractions II + III	1.29	1195 ±129(6)	69.3 ±13.3	108 X
Fraction IV	--	118 ±29(4)	6.8 ±1.2	--
<u>Silicic Acid Column</u>				
major peak	.03 ^c	630 ^d	36.5	2,440 X
other peaks combined	--	240 ^d	13.9	--

^a mean ± SD(n)^b percent of the amount of R-F in the original plasma sample,
mean ± SD^c estimate based on weighing the contents of two tubes in the center
of the major peak^d estimate based on area under peaks from graph

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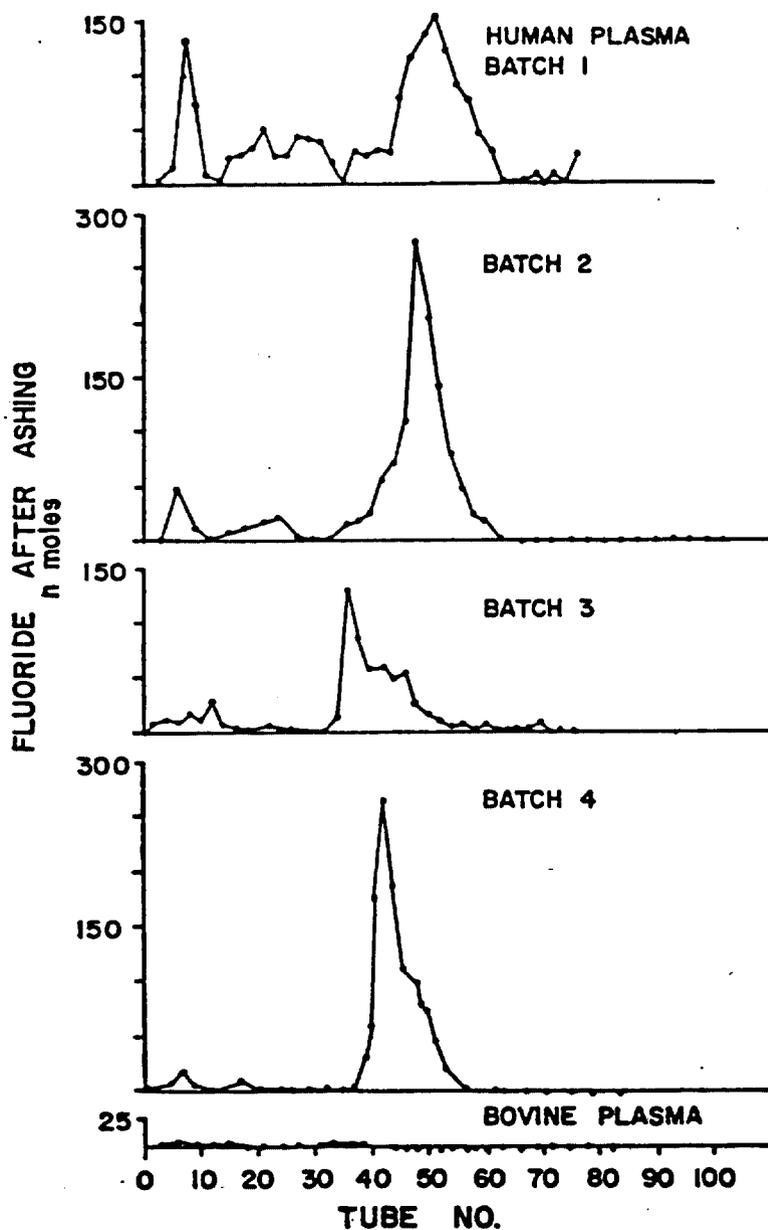


Figure 4. Distribution of organic fluorine from human and bovine plasma in fractions from silicic acid chromatography

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which samples were pla
The blank for the
using bovine rather th
detectable in the orig
the sample was dialyse
tate making the measur
Some organic fluorine
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small difference. Thi
was not found in the
from human plasma as

Human plasma had
solution. Analysis of
analysis of blood plas
showed that not more
plasma could have com

The distribution
silicic acid chromatop
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they varied in size an

The sample used
combining the fractio
the four batches. Mus
had been used for oth
combined sample was r
single sharp peak obt
central portion of the
fluorine.

Four sample runs
15,000 to 17,000 scan
in all but one run, w
were consistent with
chemical shifts shown
mixture showed no ins
contributed to the sp
perfluoro-octanoic ac
son of the shifts in
acid show that there
2 ppm except for the
E) where the shift is
be considered a signi
was used for each. 1
consistent with the p
possibly with the pre
functional group. On
the spectrum is the p

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which samples were placed.

The blank for the purification process was obtained by using bovine rather than human plasma. No organic fluorine was detectable in the original bovine sample but as a further check the sample was dialysed to remove inorganic fluoride to facilitate making the measurement for organic fluorine by difference. Some organic fluorine was apparent in dialysed bovine plasma: 0.13 ± 0.11 SD μM ($n=6$), a statistically significant though small difference. This trace amount of organic fluorine clearly was not found in the same silicic fractions as the dominant peak from human plasma as shown in figure 4.

Human plasma had been stored in polyethylene bags with ACD solution. Analysis of ACD solution from unused blood bags and analysis of blood plasma before and after placing it in the bags showed that not more than 5% of the organic fluorine in human plasma could have come from this source.

The distribution of organic fluorine in fractions from silicic acid chromatography are shown in figure 4 for four batches corresponding to 5 liters of the original plasma each. There is clearly one dominant peak lying in approximately the same elution position for each batch (the exact position varied with column use and the degree of hydration of the silicic acid adsorbant). There were always some smaller secondary peaks, but they varied in size and position relative to the major peak.

The sample used for characterization by nmr was obtained by combining the fractions containing the major peaks in each of the four batches. Much of the material from batches one and two had been used for other purposes prior to this combination. The combined sample was rechromatographed on silicic acid and a single sharp peak obtained. The final sample was taken from the central portion of that peak and contained 3.3 μmoles of organic fluorine.

Four sample runs were made on the nmr spectrometer with 15,000 to 17,000 scans each and with a sweep width of 15,151 Hz in all but one run, where it was 7,576. The results of all runs were consistent with the spectrum shown in figure 5 and the chemical shifts shown in table IV. A blank run on the solvent mixture showed no instrumental artifacts which might have contributed to the spectrum. Chemical shifts determined for perfluoro-octanoic acid are also included in table IV. Comparison of the shifts in the unknown with that of perfluoro-octanoic acid show that there is a constant difference in shifts of about 2 ppm except for the $-\text{CF}_2-$ peak next to the functional group (peak E) where the shift is about 6 ppm. Only the latter is enough to be considered a significant deviation since external referencing was used for each. The difference in shift for peak E is consistent with the presence of amide or ester derivatives, or possibly with the presence of a sulfonic acid derivative as the functional group. One explanation for the additional peaks in the spectrum is the presence of branched isomers, peaks A and B

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Table IV

RESULTS OF NMR SPECTROSCOPIC ANALYSIS

Peak Designation	Chemical Shift ^a , ppm		Suggested Assignments
	Sample	Perfluoro-octanoic Acid	
A	-70.7		-CF ₃ groups at branch points
B	-71.9		terminal -CF ₃ in branched isomers
C	-80.0		terminal -CF ₃ in straight chain
D	-81.0	-82.6	
E	-114.3	-120.2	-CF ₂ - next to X ^b
F	-120.3	-123.1	
G	-121.5	-124.2	-CF ₂ - in -CF ₂ -CF ₂ -CF ₂ -
H	-122.3		-CF ₂ - next to branch points
I	-126.0	-127.6	-CF ₂ - next to terminal -CF ₃

^aExternal referencing to CFC1₃ was used for the chemical shifts, and these are expressed with positive numbers to lower field (i.e., higher frequency).

^bwhere X is likely to be -CO-Y

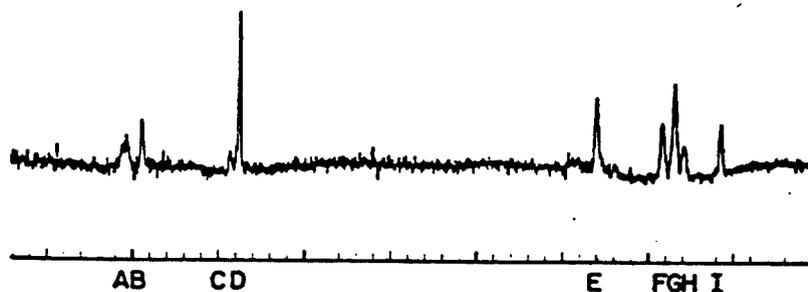


Figure 5. NMR spectrum of organic fluorocompound(s) isolated from human plasma

representing -CF₃ groups two carbons removed representing -CF₂- next to

The sample was recharacterized by nm fluorine was apparent. perfluoro-octanoic acid washing was found to be

Discussion

These findings suggest of human tissues with derived from commercial this subject is in a series of compounds here for the predominant is widely used commercially. For example, the treatment of fabric production of waxed paper (12). The findings of organic fluorine was not ic fluoride either in the earlier finding in the blood of animals with environmental sources.

The prevalence of probably quite high here and all 35 in an The prevalence of the terized here, i.e., percentage not known since the spectrum figure 4 was pooled from since only about one percent content was accounted for compounds (see table I).

Peaks other than those chromatograms shown in contains other forms of probably not volatile that these would be detected this study. They correspond since they appear in the purification step. According that step the first eluted third eluents contain certain bile acids in leucine and tyrosine. non-lipid compounds (13)

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representing $-CF_3$ groups at branch points, peak C the $-CF_3$ groups two carbons removed from the branch points, and peak H representing $-CF_2-$ next to the branch points.

The sample was reanalyzed for organic fluorine following characterization by nmr to check for contamination; no additional fluorine was apparent. The degree to which fluorine from perfluoro-octanoic acid is fixed as inorganic fluoride during ashing was found to be 21 ± 3 SD % ($n=3$).

Discussion

These findings suggest that there is widespread contamination of human tissues with trace amounts of organic fluorocompounds derived from commercial products. All available information on this subject is in accordance with this interpretation. A series of compounds having a structure consistent with that found here for the predominant form of organic fluorine in human plasma is widely used commercially for their potent surfactant properties. For example, they are used as water and oil repellents in the treatment of fabrics and leather. Other uses include the production of waxed paper and the formulation of floor waxes (12). The findings presented here that the concentration of organic fluorine was not related to the concentration of inorganic fluoride either in blood or in the public water supply, and the earlier finding that there was little or no organic fluorine in the blood of animals other than human (6) are all in keeping with environmental sources such as these.

The prevalence of organic fluorine in human plasma is probably quite high since 104 of the 106 plasma samples tested here and all 35 in an earlier study (5) had measurable quantities. The prevalence of the particular compounds isolated and characterized here, i.e., perfluoro fatty acid (C_6-C_8) derivatives, is not known since the starting material for each batch shown in figure 4 was pooled from between 25 and 30 individuals and since only about one third of the original organic fluorine content was accounted for in the fractions containing these compounds (see table III).

Peaks other than the one characterized by nmr appear in the chromatograms shown in figure 4 suggesting that human plasma contains other forms of organic fluorocompounds. They are probably not volatile compounds like freons since it is doubtful that these would be detected by the analytical methods used in this study. They correspond in solubility to very polar lipids since they appear in fractions two and three in the fourth purification step. According to the authors of the method used in that step the first eluent contains most fats, the second and third eluents contain very polar fats like gangliosides and certain bile acids in addition to compounds like urea, phenylalanine and tyrosine. The last fraction contains water soluble non-lipid compounds (11). Components of these other peaks are

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less polar than the compounds in the predominant peaks in accordance with the methanol-in-chloroform gradient used to elute them in the fifth purification step. Other forms not seen in silicic acid fractions may also exist since only about half the original organic fluorine was recovered in these fractions.

The actual amounts of the perfluorinated fatty acid derivatives in human plasma is not known both because individual plasma samples were not assayed for these particular compounds and because the degree to which organic fluorine from these compounds is converted to inorganic fluoride during ashing is not known. Metal salts of perfluorinated fatty acids have been reported to decompose at 175 to 250° C forming CO₂, volatile perfluorinated olefins one carbon shorter, and one atom of fluoride per molecule (13). About 3 fluorine atoms per molecule of perfluoro-octanoic acid were fixed as inorganic fluoride by ashing methods used here. Thus, values reported here for fluoride after ashing fractions from the major peaks in figure 4 probably represent somewhere between one-third and one times the molar amount.

Little has been published about the metabolic handling and toxicology of perfluorinated fatty acid derivatives. Computer assisted literature searches using Medline, Toxline and Chemcon developed no information on these subjects. This was surprising with respect to the widespread commercial use of such compounds. It would appear from information presented here that rapid excretion of such compounds into urine is unlikely since they are bound to albumin in the blood. On this topic it can also be stated that other chemicals are usually not toxic in blood concentrations similar to those found here for organic fluorine.

The concentration of organic fluorine in human plasma may be changing with time. In 1960 Singer and Armstrong reported that the plasma of 70 individuals residing in communities with 1 ppm or less fluoride in their public water supply had an average concentration of fluoride of 8.8 μM (8). They prepared their samples by ashing them and then distilling fluoride from the ash acidified with perchloric acid (7). Thus, it seems likely that their values for "fluoride" would have included organic fluorine had it been present. Assuming that inorganic fluoride concentrations at that time were similar to those found in this study (see table II), the organic fluorine component would exceed 7 μM. In 1969 the same investigators using the same method reported an average fluoride concentration of 4.5 μM for 6 plasma samples each pooled from at least 3 individuals supposedly living in fluoridated communities (14). This corresponds to an organic fluorine component of only about 4 μM. Organic fluorine concentration presented here averages only 1.35 μM. Therefore, there may have been a decrease in the concentration of organic fluorine in human plasma since the late 1950's. An alternate explanation might be that differences in

the analytical methods caused these values to

Organic fluorine in human blood except when drinking water is high (table II). This together with there is no apparent relationship between organic fluorine and inorganic fluoride in plasma fluoride determined from the content of the public water supply that when methods specified a clear relationship between the public water supply fluoride demonstrated. Thus, the concentrations of such rigorous homeostatic fluoride as suggested by the concentrations for individuals here reflect the balance and that in bone mineral content do not contradict a possible relationship which bone mineral density is over relatively shorter

The values presented here for the concentration of plasma fluoride having about 1 ppm fluoride in water with recent findings of

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15. Singer, L. and Armstrong

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the analytical methods or differences in the sample populations caused these values to vary.

Organic fluorine is the predominant form of fluorine in human blood except where the concentration of fluoride in drinking water is high (in which case fluoride predominates, see table II). This together with the finding reported here that there is no apparent relationship between the concentrations of organic fluorine and inorganic fluoride in plasma helps explain why in earlier studies (8) no relationship was found between plasma fluoride determined in ashed samples and the fluoride content of the public water supply. The data in table II show that when methods specific for inorganic fluoride are applied, a clear relationship between fluoride in plasma and fluoride in the public water supply (between 0.1 and 5.6 ppm) can be demonstrated. Thus, there is no need to postulate the existence of such rigorous homeostatic control mechanisms for plasma fluoride as suggested earlier (8). Average plasma fluoride concentrations for individuals living in the same city as reported here reflect the balance established between fluoride in blood and that in bone mineral over periods of years. These findings do not contradict a passive homeostatic control mechanism in which bone mineral damps swings in blood fluoride concentration over relatively shorter periods of time.

The values presented here for the average inorganic fluoride concentration of plasma from individuals living in a community having about 1 ppm fluoride in the water supply are consistent with recent findings of others using similar methods (14, 15).

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Q. I wonder if you tried to correlate within individuals the level of organic fluorine with age.

A. It would certainly be interesting to have this information but unfortunately we cannot supply it at this time. An expeditious approach might be to analyze cord blood from infants of mothers who had not received fluorine-containing anesthetics at childbirth. It would also be of interest to know whether individuals living in isolated regions have organic fluorine in their blood plasma.

Q. Did you say the sample analyzed by nmr contained methyl alcohol?

A. Yes, I did.

Q. Methyl alcohol will react very rapidly with fluorinated acids. The nmr spectrum may, therefore, represent that of methyl ester derivatives.

A. Methanol was also used in the last three steps of the purification system. The nmr spectrum is consistent with the presence of methyl ester derivatives of perfluorinated fatty acids (C₆-C₈) and their branched isomers.

Intravenous Infusion Emulsions in the Rhesus

LELAND C. CLARK, JR., EUGENE
and CAROLYN EMORY
Children's Hospital Research Foundation
Cincinnati, Ohio 45229

ROBERT MOORE
Sun Ventures, Inc., Marcus Hook, Delaware

DONALD DENSON
Stanford Research Institute, Menlo Park, California

Introduction

Interest in the possibility of using artificial blood began for animals survived the breathing apparatus (2) (pany). Since that time of FASEB Symposium (2) and several papers on the subject. Reviews have been published. A large number of emulsions were screened for this purpose and found to be in significant quantities. This is because, after performing tests in the main in the body, largely by the mononuclear phagocytes, that only those containing iodine and bromine in their structure were not completed our testing of new ones in the future, none of the perfluorodecalin (PFD) emulsions were found to be in the liver in a reasonable time with intravenous use. As the toxicity in the mouse is very low, these quantities and can be part of these, and other reasons, the artificial blood in a non-human primate was first reported (5) on the awake rhesus monkey. This was followed by further tests in 19 monkeys of a protocol for its possible use in man. Of the 19 monkeys, 11 were given PFD emulsions, and 4 with other emulsions.

The data included here have been selected to illustrate the results and is to be interpreted in terms of its contribution to this subject.

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AR 226 - 1450



E. I. DU PONT DE NEMOURS & COMPANY
WILMINGTON, DELAWARE 19898

CHEMICALS, DYES AND PIGMENTS DEPARTMENT

check 3/11/78 7746360

- cc: J. W. Nicholas
- H. E. Hiestand
- R. A. Darby
- J. C. Breckenridge
- J. B. Coleman
- G. H. Patterson - Jackson Lab
- R. E. Read - Jackson Lab
- B. C. McKusick - CR&D
- T. W. Hanavan - Legal
- H. J. Moncure - PP&R
- R. M. Shepherd - PP&R

For 4/22

Wilmington, Delaware
June 19, 1978

*Copy for: BAB-JRM
JWR*

*JC Leitinger - Parkers
for info - not an action
item*

PERSONAL & CONFIDENTIAL

P. M. HUMANICK - CH. WKS.

FLUOROCARBONS IN BLOOD

The attached memorandum describes a medical program recommended by Dr. B. W. Karrh to ensure a sound step-wise approach to determine if an occupational hazard exists to Du Pont workers exposed to certain fluorochemicals. After discussion with Wilmington Management, it has been decided to follow that program, with the following exceptions:

- Step 2 will be restricted to include only those who have handled the Telomer A-derived fluorochemicals line, and only currently (since 1/1/78).
- The program will be interrupted for Management review of the findings after the medical review in Step 6. This will occur after any findings in the study become statistically significant or after completion of the series of blood tests, whichever comes sooner.
- At that time, consideration will be given to accelerating the program, adding earlier workers, and adding workers involved with production of other fluorochemicals.

Will you please initiate this program as soon as practical. Dr. Karrh will supply additional details of physical examination procedures and G. H. Patterson's Division will carry out the blood analyses. John Coleman will coordinate the program and should be given copies of all memoranda and results.

In addition to the foregoing, the Product Center will initiate additional toxicity tests on representative fluorosurfactants in their line as well as on Telomer A, Telomer B alcohol, and on the fluoro-alkyl methacrylate.

F. E. French

F. E. FRENCH

FEF:lrg
Attachment

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ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE

J. B. Coleman, CD&P
T. W. Hanavan, Legal
H. Moncure, PP&R
S. Pell, ERD
J. Foderaro, M.D.
B. C. McKusick, CR&D

EMPLOYEE RELATIONS DEPARTMENT

June 16, 1978

F. E. FRENCH
CD&P
B 17264

FLUROCHEMICALS IN BLOOD

3M has reported finding FC143, plus other unidentified fluorochemicals in the blood of potentially exposed workers. As yet, no adverse health effect has been detected in these workers and the significance of these findings is unknown. These chemicals have also been detected by tests on the workers' urine, with good correlation with the blood test results but in very small quantities. Similar tests have not been done on the general population, although a few tests have been done on plant office workers.

The Medical Division recommends the following course of action for Du Pont employees whose jobs have potential for exposure to Telomer A and its non-polymeric derivatives.

1. Review all current operations and industrial hygiene controls to insure that the potentials for exposures are properly controlled.
2. Identify all employees who currently work or have worked jobs in which there is or was potential for exposure to fluorochemicals.
3. Review the medical records of all such persons still employed by Du Pont, looking for consistent or unusual health occurrences or trends.
4. Obtain blood fluorochemical levels on persons who have never had potential for occupational exposure to fluorochemicals to establish background levels for a baseline. These tests can be obtained on Wilmington office employees as a part of the periodic physical examinations given in the Nemours Medical facility.
5. Obtain blood fluorochemical levels on representative employees with various potentials for exposures to various fluorochemicals. If this is done at the same

*only Telomer A and
since 11/1/78*

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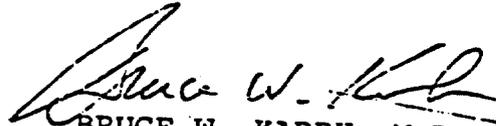
time as the employee's periodic physical examination, a comprehensive examination should be done with careful documentation of the results. A urine specimen should be obtained for later analysis for fluorochemical levels in the event the blood level is markedly elevated.

Must decision to proceed with #7

6. Review the physical findings of the workers examined for consistent or unusual health occurrences or trends. When such occurrences or trends are found and appear to be significant, consideration should be given to conducting similar physical and blood examinations on non-exposed controls for comparison.
7. If the period of potential exposure has been of sufficient duration and there is a sufficient number of employees, an epidemiologic study of the mortality of the cohort identified may be considered. A determination can be made of the likelihood of having a meaningful study after the number of previously exposed employees is determined.

The Medical Division recommends proceeding with this study in order as presented. However, we will need at least two days to obtain proper supplies and inform our technicians of the study and how to discuss the study with the employees.

BWK/ag


BRUCE W. KARRH, M.D.
MEDICAL DIRECTOR

AP001416

AR226-1451

J

DU PONT CONFIDENTIAL
SPECIAL CONTROL

H. E. Hiestand
R. L. Wright

E. O. Langer
J. T. Chesser
B. F. Galloway
R. E. Read
J. A. Thoroug

P. M. Humanick/
R. A. Shinn
E. T. Fogg
J. F. Scott
F. J. Meadow
S. L. Schenk

22 June 1978

To: T. C. Kuchler, Administration Building

From: R. D. Richardson, 1094 Building

FLUROSURFACTANTS COMMUNICATION WITH CHAMBERS WORKS EMPLOYEES

The following schedule has been developed for the communication on the presence of organic fluorine substances in human blood plasma (copy attached) to Chambers Works personnel who handle fluorosurfactants and their intermediates:

Day/Date	Time	Action	Responsible
Friday 6/23/78	Before 4 p.m.	Inform Chambers Works Executive Staff that announcement to employees will be made at 10 a.m., 6/27/78.	R. D. Richardson
	Before 4 p.m.	Supervision will be provided with a communication message.	R. D. Richardson
Tuesday 6/27/78	After 8 a.m.	Supervision will inform Union Leaders and local Union Representatives	R. J. Lyng
		Chemicals Area	R. J. Lyng
		Development Manufacturing Area	L. J. Marcot
		Jackson & Technical Laboratories	E. O. Langer
		(Engineering Department)*	F. J. Meadow
		(Environmental & Service Department)*	E. T. Fogg
		(General Analytical Laboratory)*	R. F. Stalze
	10 a.m.	Supervision will inform all personnel who handle or may contact fluorosurfactants and their intermediates in their assigned work.	
		Chemicals Area	R. J. Lyng
		Development Manufacturing Area	L. J. Marcot
		Jackson & Technical Laboratories	E. O. Langer
		(Engineering Department)*	F. J. Meadow
		(Environmental & Service Department)*	E. T. Fogg
		(General Analytical Laboratory)*	R. F. Stalze

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MEDICAL DIVISION

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Employees who are not present at 10 a.m. 6/27/78 will be informed when they next report to work.

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19 *For information only. Employees in this group will not participate in the initial medical program. They should be advised of the program, however.

VERBAL COMMUNICATION TO CHAMBERS WORKS EMPLOYEES
WHO HANDLE FLUROSURFACTANTS AND THEIR INTERMEDIATES

Through information supplied by the 3M Company, Du Pont has become aware that elevated organic fluorine levels have been detected in the blood of 3M workers exposed to certain organic fluorinated surfactants and the intermediates associated with their manufacture.

These specific fluorochemicals are not used on the Chambers Works, but we do manufacture a line of fluorosurfactants. The Chambers Works fluorosurfactants are manufactured by different technology and have not been implicated. As a precautionary measure, however, we are reviewing handling procedures, medical records and toxicological information related to our fluorosurfactants.

As a part of this program the organic fluorine level in the blood of Chambers Works employees who are working with these fluorosurfactants will be determined for comparison with the general population. This check will be made at the time of the employee's next regular plant physical examination.

A preliminary report from the 3M Company indicated that they are not aware of any adverse health effects among affected employees. 3M has manufactured fluorinated surfactants for over 20 years.

Your supervision will see that any questions you may have are answered.

RDR
6/22/78

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ADDITIONAL INFORMATION FOR SUPERVISION

A 1976 report⁽¹⁾ indicates that the blood serum of the general population in the U.S. contains trace quantities of fluorine in both organic and inorganic form. The concentration of inorganic fluorine has been shown to be related to fluoride ion in water supplies (natural and added). There is no ready explanation for the presence of organic fluorine.

A recent study by the 3M Company of their workers who manufacture and handle fluorosurfactants and their intermediates has revealed organic fluorine levels in their blood plasma in excess of those not engaged in these operations. 3M reported that a preliminary review of the medical histories and current health status of affected employees has not revealed any unusual health conditions. A more detailed epidemiological study of 3M workers has been initiated.

3M has identified two probable key sources of employee exposure in their operations. These are associated with (1) electrolytic cells in which key intermediates are manufactured, and (2) packaging operations involving powdered products.

The specific products implicated in the 3M study are not manufactured nor used on the Chambers Works. Different fluorosurfactants manufactured on Chambers Works in the Chemicals and Development Manufacturing areas and are sold under the "Zonyl" trademark. The Chambers Work processes do not involve electrolytic fluorination and the products are handled throughout in liquid forms and are also sold in liquid forms. Despite the dissimilarity between the Du Pont and 3M technology, all handling procedures for fluorosurfactants and intermediates should be reviewed for adequacy. Assistance may be obtained from R. J. Hubiak (X3415).

A special medical program will be initiated for all employees currently engaged in fluorosurfactants operations. This program will not be extended to personnel who have previously worked with fluorosurfactants, but who are no longer involved, unless the results of the initial program indicate that necessary. Similarly, Engineering Department, Environmental & Service Department and General Analytical Laboratory employees will not be included in the initial program though they should be advised of the program.

The initial special medical program will include (1) a review of the medical records of the employee, and (2) special blood analyses at the time of the employee's regular physical examination.

This program is concerned only with fluorosurfactants and their intermediates. Other fluorinated substances such as "Freon" fluorocarbons and fluoropolymers (e.g., "Teflon", "Viton", etc.) are not implicated.

(1) W. S. Guy, et.al.; Proceedings Amer. Chem. Soc., Fluorine and Biological Chemistry Symposium, Chicago, 26 August 1975, Paper 7, page 117.

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WAB

CC: R. E. Putnam

6/27 - 9:00 Division Superintendents
11:00 Line Supv'n.-TEFLON®
2:00 Affected Wage Roll

June 27, 1978

TO: ALL DIVISION SUPERINTENDENTS
CHIEF CHEMIST

FROM: C. H. FOSHEE
PRODUCT SUPERINTENDENT

FLUOROSURFACTANTS ANNOUNCEMENT

Attached is a communications package pertaining to the presence of organic fluorine in the blood of 3M workers. We plan to communicate this information on Tuesday, June 27. Information in the attached letter to TEFLON® Supervision should be communicated to TEFLON®, TEFLON® Research and TEFLON® Laboratory wage roll personnel. The Questions and Answers are to be used as reference material to respond to questions. A communications package is being transmitted to unaffected divisions for information.

CHF:sc
Attachments

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June 27, 1978

TO: TEFLON® SUPERVISION

FROM: C. H. FOSHEE

FLUOROSURFACTANTS IN BLOOD

Through information provided by the 3M Company, Du Pont has become aware that elevated organic fluorine levels have been detected in the blood of 3M workers exposed to certain fluorinated surfactants.

Du Pont does not manufacture these fluorochemicals, but does purchase one of them for use in manufacturing TEFLON® and FEP dispersions in the Fluorocarbons Division. The surfactant we use is perfluoro-octanoic acid ammonium salt and is commonly known as C-8. Du Pont does manufacture different fluorinated surfactants at Deepwater, N. J. and these have not been implicated with higher blood levels.

Fluorinated surfactants are water soluble chemicals used for their marked ability to modify the wettability of materials.

Our toxicological tests indicate that Du Pont's fluorinated surfactants have a low order of toxicity. No known ill effects which could be attributed to these chemicals or C-8 have been detected among employees in more than 20 years of experience with the products.

Du Pont's handling procedures have been designed to minimize exposure of employees to these fluorinated surfactants. As a precautionary measure, however, Du Pont is reviewing its procedures, medical records, and toxicological information relating to these materials.

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QUESTIONS AND ANSWERS

1. Q. What is the effect of elevated organic fluorine levels in blood?
 - A. Although 3M has found elevated organic fluorine levels in the blood of workers exposed to certain fluorinated intermediates, they have identified no related health effects in any of these workers or in those exposed to the surfactants but are continuing a broad investigation.

2. Q. Does Du Pont have information about organic fluorine levels in the blood of its employees exposed to these materials?
 - A. Not at this time.

- 2a. Q. Why not?
 - A. We had no reason to believe any problem of this type existed and normal blood tests would not show this kind of information unless you were looking precisely for fluorine levels. While we have not specifically looked at fluorine content in the blood, we have been satisfied that no known health effects which could be attributed to these chemicals have been detected among employees.

3. Q. Will Du Pont be conducting blood tests on employees at Washington Works who may have been exposed to the fluorinated surfactant purchased from 3M?
 - A. We will check some employee blood levels to establish a background level for fluorinated compounds.

4. Q. Are employees being notified of findings reported by 3M?
 - A. Yes.

5. Q. What products are manufactured by Du Pont using the fluorinated surfactants purchased from 3M?
 - A. The material purchased from 3M is used in the polymerization process for making TEFLON® fluorocarbon dispersions. These dispersions contain only about one tenth of one percent (.001) or 1000 parts per million of fluorinated surfactant.

ALP001428

QUESTIONS AND ANSWERS

6. Q. What are uses for the dispersions?
- A. TEFLON® fluorocarbon dispersions are used to coat glass fibers and metals. In the coating operation the surfactants are destroyed by the sintering process which is used. The only application where the fluorosurfactants are not destroyed is packings and gaskets.
7. Q. Where are gaskets and packings used?
- A. We don't know all the places, however we can assume that any operations where liquids are being transported might use pump packings and gaskets.
8. Q. If packings and gaskets are used in systems to transport liquids, could they be coming into contact with liquids ingested by humans?
- A. It is possible. However, we believe most of the applications involving our dispersions in packings and gaskets are industrial operations. Du Pont does not sanction the use of unsintered TEFLON®, such as that involved in packings and gaskets, and applications where the material would come in contact with food, beverages or potable water.
9. Q. Are any consumer products made and sold by Du Pont involved?
- A. No. All materials using fluorinated surfactants which could reach the consumer or general public are processed in such a way that the surfactant is burned off before it goes to the consumer.
10. Q. Is there any problem involved with cookware which has been coated with TEFLON®?
- A. No.
11. Q. What is meant when you say that Du Pont's fluorinated surfactants have a low order of toxicity?
- A. By a "low order of toxicity" we mean that a lethal dose would be about a cupful or eight fluid ounces of this material.

AJP001429

EID080244

000127

QUESTIONS AND ANSWERS

12. Q. In 3M's findings, what were the elevated levels of organic fluorine which they found in their workers?
- A. The highest level 3M detected was 45 parts per million of this material in a person's blood. This is equal to about one-tenth of a drop of the material in the total blood content of the average human being.
13. Q. Why aren't the fluorinated surfactants manufactured by Du Pont implicated by 3M's findings?
- A. The surfactants which Du Pont manufactures are made by a completely different process and are chemically different than those made by 3M. However, because of their similar functional activity, it is possible they may behave in a similar way but at this point we have no data to confirm or deny this.
14. Q. If Du Pont's fluorinated surfactants are not implicated, why not use these materials instead of purchasing them from 3M to make TEFLON®?
- A. Chemically Du Pont's fluorinated surfactants behave differently and are not suited to the existing process for making TEFLON® fluorocarbon resins.
15. Q. Are other companies involved and have they been alerted about 3M's findings?
- A. The 3M Company has notified its customers. To the best of our knowledge these are the only companies in the United States involved. Du Pont intends to share all of the information developed on this situation with any companies in the U.S. and worldwide who might be involved.
16. Q. Will Du Pont be notifying customers of the findings reported by 3M?
- A. We will share this information on a need-to-know basis.
17. Q. Will Du Pont be informing the appropriate regulatory agencies of this situation?
- A. At this point in time we see no significant risk associated with the fluorine content in the blood. The existence of fluorine in blood has been known for 10 years and is published in open literature.

QUESTIONS AND ANSWERS

18. Q. Are these fluorinated surfactants found in the blood persistent?
- A. Published literature indicates that fluorinated compounds containing oxygen and nitrogen are persistent. However, 3M has indicated that organic fluorinated compounds are secreted by the body as a waste product. Data are conflicting about the existence of organic fluorinated compounds in animals.

6-26-78

000129

EID080246

AJP001431

AR226-1452

L



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

PLASTIC PRODUCTS AND RESINS DEPARTMENT

PERSONAL & CONFIDENTIAL

August 9, 1978

W. A. BOWER
WASHINGTON WORKS

MEDICAL SURVEILLANCE PROGRAMS

The attached letter response of August 3 from Dr. Karrh summarizes his recommendations applicable to both C-8 and Telomer-A at Washington Works. Copies of the July 24 and June 16 letters, to which he refers, are appended also. It is assumed that the plant physicians will contact Dr. Karrh directly with any questions and in connection with medical record reviews.

R. M. SHEPHERD
ENERGY & ENVIRONMENTAL AFFAIRS
MANUFACTURING DIVISION

RMS:ldb
Attachment

EID080236



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE

EMPLOYEE RELATIONS DEPARTMENT

August 3, 1978

R. M. SHEPHERD
PP&R
D-12019

C-8 EXPOSURE -- WASHINGTON WORKS
MEDICAL SURVEILLANCE PROGRAM

Reference R.M.Shepherd to B.W. Karrh, July 31, 1978

I had received a copy of your letter to H. Moncure, and Dr. Foderaro had contacted Dr. Alvarado at Washington Works. The plan they agreed to was for Dr. Alvarado to review the medical records of employees who had been identified as previously having been exposed to C-8 compounds. He would be searching for any findings that could possibly be related to occupational factors. We have not heard from Dr. Alvarado nor have we followed up.

*Dr. French
re: summary
summary*

The Medical Division recommends that employees potentially exposed to C-8 at the Washington Works have the same medical surveillance program as was outlined in my July 24 letter to F. E. French. You will note this is our regular periodic examination and should be conducted at the same frequency, consistent with the Company's periodic examination program. There are no recommendations for special testing nor for an increased frequency of examinations for employees working with C-8. The only other recommendation is for those employees identified as having had potential exposure to these compounds ~~to~~ to have the blood test for fluorochemicals. However, these tests should not be done until we have established the background level of fluorochemicals present in the blood of nonexposed persons. We will do this in the Medical Division as soon as Jackson Laboratory can take our blood specimens.

*no change
from present*

*Test still being
developed.
Karrh to
advise us*

You also inquire regarding my June 16 letter to F. E. French about the applicability and status of the recommendations for Du Pont employees whose jobs have potential for exposures to similar fluorochemicals. I recommend that Washington Works follow the same seven action points as outlined in that letter. However, you will recognize that Action Point 4 will be done by the Medical Division.

*911
Fluorochemicals
exam
of num*

Please contact me should you have additional questions or comments.

EID080237

Bruce W. Karrh
BRUCE W. KARRH, M.D.

BWK/ag



ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY

INCORPORATED

WILMINGTON, DELAWARE

EMPLOYEE RELATIONS DEPARTMENT

July 24, 1978

F. E. FRENCH
CD&P

MEDICAL EXAMINATIONS FOR FLUORO-CHEMICAL WORKERS

3M's physical examination program for workers potentially exposed to fluorochemicals was somewhat less extensive than our routine periodic examination with one exception. A few 3M employees, selected because their jobs had the greatest potential for fluorochemical exposure, received special x-rays of the pelvis to determine if there was thickening of the bones consistent with fluorosis. Incidentally, these x-rays were negative.

Our medical surveillance examinations for fluorochemical workers should be the regular Du Pont periodic physical examination consisting of

- o a health history questionnaire,
- o an examination by or under the supervision of a physician,
- o urinalysis
- o 12 blood chemistry tests (glucose, BUN, SGOT, LDH, alkaline phosphatase, bilirubin, total protein with albumin and globulin, calcium, phosphorus, creatinine, uric acid, cholesterol)
- o 7 hematology tests (white and red blood cell counts, hemoglobin, Hematocrit, and red blood cell indices,
- o vision test,
- o audiogram,
- o 14 x 17 postero-anterior chest x-ray,
- o Height, weight, blood pressure, and pulse,
- o Screening pulmonary function tests (FEV₁ and FVC)
- o Electrocardiograms at the routine intervals.

I recommend we not include special x-ray examinations.

BWK/ag


Bruce W. Karrh, M.D.

EID080238



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE

T. W. Hanavan, Legal
H. Moncure, PP&R
S. Pell, ERD
J. Foderaro, M.D.
B. C. McKusick, CR&D

EMPLOYEE RELATIONS DEPARTMENT

June 16, 1978

F. E. FRENCH
CD&P
B 17264

FLUROCHEMICALS IN BLOOD

3M has reported finding FC143, plus other unidentified fluorochemicals in the blood of potentially exposed workers. As yet, no adverse health effect has been detected in these workers and the significance of these findings is unknown. These chemicals have also been detected by tests on the workers' urine, with good correlation with the blood test results but in very small quantities. Similar tests have not been done on the general population, although a few tests have been done on plant office workers.

The Medical Division recommends the following course of action for Du Pont employees whose jobs have potential for exposure to Telomer A and its non-polymeric derivatives.

Done

*Done
Report being typed*

*Wilmington
Medical*

*As soon as
list is ready*

1. Review all current operations and industrial hygiene controls to insure that the potentials for exposures are properly controlled.
2. Identify all employees who currently work or have worked jobs in which there is or was potential for exposure to fluorochemicals.
3. Review the medical records of all such persons still employed by Du Pont, looking for consistent or unusual health occurrences or trends.
4. Obtain blood fluorochemical levels on persons who have never had potential for occupational exposure to fluorochemicals to establish background levels for a baseline. These tests can be obtained on Wilmington office employees as a part of the periodic physical examinations given in the Nemours Medical facility.
5. Obtain blood fluorochemical levels on representative employees with various potentials for exposures to various fluorochemicals. If this is done at the same

EID080239

time as the employee's periodic physical examination, a comprehensive examination should be done with careful documentation of the results. A urine specimen should be obtained for later analysis for fluorochemical level in the event the blood level is markedly elevated.

To be determined

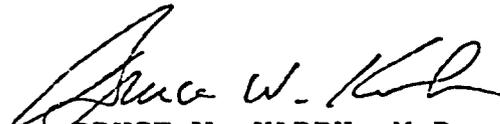
6. Review the physical findings of the workers examined for consistent or unusual health occurrences or trends. When such occurrences or trends are found and appear to be significant, consideration should be given to conducting similar physical and blood examinations on non-exposed controls for comparison.

*To be determined
would probably
be done by
Dr. Bill's Group*

7. If the period of potential exposure has been of sufficient duration and there is a sufficient number of employees, an epidemiologic study of the mortality of the cohort identified may be considered. A determination can be made of the likelihood of having a meaningful study after the number of previously exposed employees is determined.

The Medical Division recommends proceeding with this study in order as presented. However, we will need at least two days to obtain proper supplies and inform our technicians of the study and how to discuss the study with the employees.

BWK/ag


BRUCE W. KARRH, M.D.
MEDICAL DIRECTOR

AR 226 - 1453

M

September 20, 1978

PERSONAL AND CONFIDENTIAL

TO: W. A. BOWER

FROM: Y. L. POWER, M.D.

A review of the medical records of eleven operators and eighteen laboratorians who have had long-term exposure to C-8 was undertaken.

As you would anticipate, a great variety of illnesses and physical findings were found; but I do not believe any of these are caused by exposure to C-8. Some of the illnesses found are two heart attacks and five employees with high blood pressure. One questionable case of skin cancer was found during an employee's physical examination in 1976. No further mention of this possible tumor could be found.

Minor elevations of many blood tests did occur in larger-than-anticipated numbers and are listed separately. With the exception of one person, all of the elevations were borderline and not indicative of disease. One of the liver function tests (SGOT) is most frequently elevated in the operator group. However, no liver diseases were found. Many of the laboratorians also work with Perclene, which is a known hepatatoxin.

In conclusion, I could find no unusual health problems occurring in the group of people studied, with the exception of borderline elevation of liver function tests. Since it has been previously determined that C-8 is an hepatatoxin, it is possible that C-8 may be causing very minimal, and certainly not clinically apparent, toxic effects to the liver. Because the total number of records reviewed is small (31), I do not believe any findings of this study are statistically valid.

Y. L. P
YLP:vf

ALP001418

EID080233

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PERSONAL AND CONFIDENTIAL

<u>LAB TEST</u>	<u>% OPERATORS WITH ABNORMAL TESTS **</u>	<u>% LABORATORIANS WITH ABNORMAL TESTS</u>	<u>ANTICIPATED LEVEL FROM STUDY 1976 (% WITH ABNORMAL TESTS)</u>
* SGOT	60	11.2	14.21
* Alkaline Phosphatase	30	16.7	6.84
Albumin	10	16.7	1.58
Uric Acid	10	5.6	4.21
Cholesterol	30	0	1.05
BUN	30	11.2	3.68
Glucose	10	27.8	1.58
Calcium	10	0	0
Total Protein	10	0	0
* Bilirubin	0	11.2	1.05
LDH	0	11.2	1.58

* Liver function tests.

** Only 10 operators had liver function test done.

YLP:vf
9/20/78

000136

EID080234

AJP001419

AR226-1454

N



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE

EMPLOYEE RELATIONS DEPARTMENT

December 22, 1978

P. G. GILBY
CD&P
B-13265

CHAMBERS WORKS
FLUOROSULFACTANT STUDY

Dr. Pell had the study and was reviewing it. His comments are included.

SUMMARY:

There does not seem to be any adverse health effects reported in this study, with the possible exception of an effect on the liver.

DISCUSSION

The liver function tests should be tabulated to compare the number of persons, not the number of tests, in each group.

The matching variables should have included payroll class since there may be large differences between wage and salary employees in dispensary visits, absenteeisms, and the incidence of certain diseases.

Attachment I should show the number of persons for each body system. The number of visits can be inflated by one person making several visits for the same condition.

Dr. Pell would like to know how significant differences were determined.

The percentage of smokers seems high in both groups compared to about 40% in the U.S.

The table on page 3 should show the number of employees with abnormal liver function tests.

The relation to diabetes is probably not important after the initial exposure because the diagnosis was definitely made in 4 exposed employees vs. 2 definite diabetes in the control group and the diagnosis was suspected in 4 exposed employees vs. 5 in the control group.

THERE'S A WORLD OF THINGS WE ARE DOING SOMETHING ABOUT

EID096510

000137

For liver function tests, data should be tabulated to show the number of persons (not the number of tests) in each group with abnormal results. Blood sugars should be tabulated the same way, taking the diabetics into account.

To summarize, neither Dr. Pell nor I see any adverse health effects reported in this study. However, we would like to see the liver function tests tabulated to compare the number of persons in each group rather than the number of tests, as well as the other requests noted above.

I apologize for not having responded sooner.

BWK/ag



BRUCE W. KARRH, M.D.

EID096511

000138

DWAS000138/

AR 226 - 1455



GENERAL OFFICES • 3M CENTER • SAINT PAUL, MINNESOTA 55101 • TEL. (612) 733-1110

Commercial Chemicals Division

February 7, 1979

Dr. Blaine McKusic
Associate Director
Haskell Laboratory for Toxicology
and Industrial Medicine
E.I. DuFONt DENEMOURS & Co. Inc.
Wilmington, DE 19898

Dear Dr. McKusic:

At the request of Dr. L.C. Krogh, I am sending you copies of the following reports from International Research and Development Corporation:

1. One Ninety Day Subacute Rat Toxicity Study using FLUORAD[®] Fluorochemical FC-143.
2. One Ninety Day Subacute Rhesus Monkey Toxicity Study using FLUORAD[®] Fluorochemical FC-143.

If you have any questions concerning these reports please contact Dr. Frank Ubel of our Medical Department. His phone number is 612-733-5181.

Very truly yours,

R. A. Prokop
Manager, Research
Commercial Chemicals Division

*summary prepared
See Report File for
full report*

RAP/ko

Enclosures

RECEIVED

FEB 9 1979

HASKELL LAB.

EID071855

DWS 1036530

AR226 - 1456

DON'T SAY IT-WRITE IT

DATE _____

TO _____

AT _____

FROM _____

PWS, Summer 1979

Bill, (Bill Krauss)

I've reviewed the 90-day toxicity studies in the rat and agree that there are compound-related effects in the liver. In addition to the changes mentioned in RESULTS, (Histopathology) I would also mention hepatocellular necrosis and sinusoidal liver congestion. The presence of yellow-brown pigment in the epithelium of the convoluted tubules in the kidney ~~is~~ is noted in the treated but not control groups.

The ^{mean} final body wt in males of the 1,000 ppm group ~~but not~~ is only 76% of the control value, a decrease I would consider more than "slight".

I am also not clear as to the distinctions ^{among} ~~between~~ "no entry", the designation "1" (not remarkable) ^{and} "X" (condition present).

I also reviewed the monkey study and am in general agreement with their conclusions. However, there also seems to be an increased incidence of chronic interstitial nephritis in the test animals that is not mentioned. There was also slightly increased incidence of hyperkeratosis in the skin of test monkeys and a slight increase in skeletal muscle atrophy. If these are judged to be not compound-related there should be some mention of the reason why.

EID123133

Nancy
(Nancy Chirney)
PWS

ONLY TELL THOSE WHO HAVE A NEED TO KNOW

000140

AR 226 - 1457

Jan 26 99 02:02p

DuPont-Chambers Works

608-540-4654

P.2

CC: B. W. Karrh, M.D.



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE

EMPLOYEE RELATIONS DEPARTMENT

March 15, 1979

PERSONAL AND CONFIDENTIAL

P. G. GILBY
CD&P
B-13265

**CHAMBERS WORKS
FLUOROSULFACTANT STUDY**
(Ref. Letter from RDR to PGG, 1/23/79)

In response to our request to the plant for additional information to analyze the data statistically, we received a tabulation of the Dispensary Visits and Disability Wage incidents in the exposed and control groups (Attachment V). These data were broken down by body systems. We were also informed of the number of employees in each group who had abnormal liver function tests.

We performed a "chi-square" test to test the significance of differences between the exposed and control groups. The attached table shows only those differences that were found to be statistically significant.

In the category, "Allergic, Endocrine, and Metabolic" disorders, a significantly higher incidence was found in the exposed group for both Dispensary Visits and Disability Wage incidents. This was attributed in the report to a higher number of diabetics in the exposed group.

The exposed group also showed significantly higher numbers for "mental and psychoneurotic" disorders and for disorders of "skin and cellular tissues."

The control group, on the other hand, had considerably more Disability Wage incidents for circulatory diseases, 25 compared to 5. This difference is highly significant ($P < 0.001$).

Explanations for these differences cannot be found from the available data. It would be helpful to find out what specific diagnosis within these general categories accounted for the differences between the two groups.

GK000378

... THERE IS A WORLD OF THINGS WE ARE DOING SOMETHING ABOUT

GK000378

000141

Although the number of employees with abnormal liver function tests was notably higher in the exposed group (6 compared to 1), the difference is not statistically significant ($P < 0.05$). Nevertheless, the data do suggest that the exposed group may be at an excess risk of developing liver disease, so continued surveillance would be advisable.

MEDICAL DIVISION

Sidney Pell

Sidney Pell
Manager
Epidemiology Section

SP:msd
Attach.

GK000379

AR 226 - 1458

R

STATUS REVIEW
FLUOROCHEMICALS IN BLOOD
5/22/79, PGG

- On May 30, 1978, 3M informed Du Pont of findings of organic fluorocarbons in blood of employees exposed to long-chain perfluoro surface-active materials. Organic fluoride blood levels of 1 to 71 ppm were found. Higher blood levels were associated with operations where airborne mists or dusts generated were in range of 48-81 ppm. 3M reports that some trace level of organic fluorine in humans is apparently normal, i.e. less than 1 ppm.

- Du Pont Program and Status

<u>Item</u>	<u>Status</u>
● Communication	
1. Inform affected C.W. employees of 3M information.	Complete 6/27/78
● Toxicity	
1. Haskell 10-Day Subacute Feeding Tests for MPD-5004 (homolog mixture of ammonium perfluoroalkyl carboxylates); perfluoroalkyl methacrylates (ZFM, TLF-1837); "Teflon" CSF Carpet Protector (TLF-4113-D); Zonyl BA (Telomer B Alcohol, TLF-1847); Zonyl FSC (TLF-3635C); Zonyl FSN (TLF-4714C); Zonyl FSD (TLF-3176); Zonyl Tela (Telomer A, TLF 4187).	Complete
2. Analysis of rat blood	Done for rats fed Zonyl FSN and Zonyl BA.
● Medical Program	
1. Review all current operations and industrial hygiene controls to insure that the potentials for exposures are properly controlled.	Complete
2. Identify all employees who currently work or have worked jobs in which there is or was potential for exposure to fluorochemicals.	Complete
3. Review the medical records of all such persons still employed by Du Pont, looking for consistent or unusual health occurrences or trends.	Complete

EID080271

, 000143

AJP001456

Status

- | | | |
|----|---|-------------------------------------|
| 4. | Obtain blood fluorochemical levels on persons who have never had potential for occupational exposure to fluorochemicals to establish background levels for a baseline. | Complete |
| 5. | Obtain blood fluorochemical levels on representative employees with various potentials for exposures to various fluorochemicals. | Complete for 55 c
199 employees. |
| 6. | Review the physical findings of the workers examined for consistent or unusual health occurrences or trends. | Complete |
| 7. | If the period of potential exposure has been of sufficient duration and there is a sufficient number of employees, an epidemiologic study of the mortality of the cohort identified may be considered. A determination can be made of the likelihood of having a meaningful study after the number of previously exposed employees is determined. | To be decided |
-
- | | | | |
|---|---|---------|-----------|
| ● | Program Cost to Date | Total | \$149,400 |
| | 1. Toxicity Testing | MR-3089 | 17,000 |
| | | MR-3187 | 27,400 |
| | | Total | \$ 44,400 |
| | 2. Blood Analysis | | \$105,000 |
| | (Additional blood analysis,
~\$500 each) | | |

AJP001457

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CHAMBERS WORKS
FLUORO-CHEMICALS IN BLOOD STUDY

- (1) RESULTS OF STUDY - LEVELS OF FLUORINE IN THE BLOOD OF CHAMBERS WORKS EMPLOYEES, (INORGANIC AND LOW VOLATILITY ORGANIC FLUORINE)
- (2) INDUSTRIAL HYGIENE SURVEY
 - MANUFACTURE OF TELOMER B ALCOHOL
 - MANUFACTURE OF ZEPHEL® FLUOROMONOMER, ZONYL® FSN, RP, FSE, FSP, UR

R. D. RICHARDSON/AMB
18 MAY 1979

AJP001458

EID080273

000145

ORGANIC FLUORINE IN BLOOD

GROUP (SAMPLE SIZE)

PPM ORGANIC FLUORINE*

3M DATA

GENERAL POPULATION (106)	0.002 TO 0.13 [0.02]**
PLANT OFFICE WORKER	0.01 TO 0.06
PLANT WORKER - GENERAL	0.13 TO 1.18
PLANT WORKER - LONG SERVICE IN F/C AREA	
NEWER PLANT	0.9 TO 9.1
OLDER PLANT	5.9 TO 71

DU PONT DATA

WILMINGTON CONTROL GROUP (25)	(23 OF 25) 0 - 0.38 *** [0.094]
CHAMBERS WORKS GROUP (55)	(54 OF 55) 0 - 0.37 **** [0.15]

CONCLUSIONS

- CHAMBERS WORKS EMPLOYEES DO NOT HAVE ELEVATED LEVELS OF ORGANIC FLUORINE IN THEIR BLOOD AS WAS REPORTED FOR 3M WORKERS.
- THE MEAN VALUE FOR CHAMBERS WORKS EMPLOYEES WAS SLIGHTLY HIGHER THAN THE WILMINGTON CONTROL GROUP [0.15 VERSUS 0.094], BUT ALL VALUES ARE CONSIDERED TO BE "NORMAL" (<1 PPM) EXCEPT ONE VALUE IN THE WILMINGTON CONTROL GROUP (10.6 PPM).

* BY DIFFERENCE BETWEEN TOTAL AND INORGANIC FLUORINE
*** EXCEPT 2 VALUES 10.6;
0.78
** [MEDIAN VALUES] **** EXCEPT 1 VALUE 0.89 PPM

EID080274

000146

AJP001459

CHAMBERS WORKS FLUOROCEMICALS COHORT

- CHAMBERS WORKS EMPLOYEES WERE IDENTIFIED WHO
 - (1) HAVE HAD JOB ASSIGNMENTS WITH POTENTIAL FOR EXPOSURE
 - (2) ARE STILL ACTIVE OR ARE READILY AVAILABLE ON SITE
- BLOOD SAMPLES TAKEN AT REGULARLY SCHEDULED PHYSICAL EXAMINATION

<u>JOB ASSIGNMENT</u>	<u>LOCATION</u>	<u>NUMBER IDENTIFIED</u>	<u>NUMBER CHECKED TO DATE</u>	<u>(%)</u>
R & D	JACKSON LAB. TECHNICAL LAB.	50	18	(36)
DEVELOPMENT MANUFACTURING	SPEC. CHEM. WEST	36	6	(17)
MANUFACTURING	SPEC. CHEM. EAST	84	26	(31)
	OTHER	29	5	(17)
		<u>199</u>	<u>55</u>	(28)

- INFORMAL CHECK WITH SUPERVISION INDICATED THAT GROUP (55) SAMPLED WAS REPRESENTATIVE OF COHORT (199).

AJP001460

EID080275

000147

CONCLUSIONS - INDUSTRIAL HYGIENE SURVEY

A) TELOMER B ALCOHOL AND ZFM MANUFACTURE

- 1) ENVIRONMENTAL MONITORING DATA SUGGESTED CONDITIONS IN THE MANUFACTURING FACILITIES TO BE NORMALLY $<5 \text{ mg/m}^3$ TBA (8 HRS.), HOWEVER, EXCURSIONS TO RAISE THIS LEVEL TO 30 TO 40 mg/m^3 TBA (8 HRS.) HAVE BEEN OBSERVED ON MULTIPLE OCCASIONS.
- 2) ADDITIONAL ENVIRONMENTAL MONITORING REQUIRED TO IDENTIFY EXPOSURE SOURCES AND DEFINE POTENTIAL EXPOSURE LEVELS. (IN PROGRESS)
- 3) MOST PROBABLE EXPOSURE SOURCES ARE DRUMMING AND ~~DEDRUMMING~~ FACILITIES, AND TO A LESSER EXTENT SAMPLING EQUIPMENT AND PROCEDURES.
- 4) DRUMMING, ~~DEDRUMMING~~ AND SAMPLING FACILITIES ARE OF A LOW STANDARD FOR CONTAINMENT BY ENGINEERING CONTROLS, (NOT ENCLOSED, NO LOCAL VENTILATION)
- 5) A CONTRIBUTING FACTOR IS THAT THE FACILITIES ARE ENCLOSED IN A BUILDING. PROMPT ELIMINATION OF PROCESS LEAKS AND MAINTAINENCE OF VENTILATION IS ESSENTIAL.

B) TELOMER B ALCOHOL USE AREAS

LIMITED, AVAILABLE, ENVIRONMENTAL DATA SUGGEST THE POTENTIAL FOR EXPOSURE TO TBA (AND ZONYL[®] FSN) TO BE LOW.

AJP001466

000148

EID080281

RECOMMENDATIONS

- 1) DISCONTINUE PROGRAM TO DETERMINE FLUORINE IN BLOOD.
- 2) ADVISE EMPLOYEES THAT BLOOD ANALYSIS PROGRAM HAS BEEN DISCONTINUED DUE TO UNIFORMLY FAVORABLE RESULTS.
- 3) UPGRADE FACILITIES, IF REQUIRED, TO MEET HASKELL LABORATORY EXPOSURE LIMIT GUIDELINES WHEN THESE ISSUE.

18 MAY 1979

000149

EID080282

AJP001467

SUMMARY OF SUBACUTE TESTS WITH FLUOROCHEMICALS

Compound	Report #	(mg/kg/day)	Mortality	Observations at 14 Days	Observations at 28 Days	(mg/kg) ... A.D.	(mg/kg) ... Lipid
TLF-264	216-68	2250	0/5	↓ liver weight degenerative liver changes reversible histologic kidney changes mild gastroenteritis	persisted ↓ in severity ↓ in severity		
"Zonyl" KP	244-71	2250	0/6	↓ liver weight reversible histologic liver changes	returned to normal persisted	1100	
"Zonyl" KP, ammonium salt	245-71	2200	0/6	↓ liver weight reversible histologic liver changes	returned to normal persisted	2250	
"Zonyl" KP, ammonium salt of low molecular weight	246-71	2200	0/6	↓ liver weight reversible histologic liver changes	persisted with only slight recovery persisted		421
"Zonyl" KA	357-78	90 45	6/10 0/10	reversible histologic changes in: GI tract, spleen thymus, bone marrow liver, testes	returned to normal good but incomplete recovery persisted with only slight recovery		11,792
"Zonyl" SA	718-78	4470	0/10	reversible histologic spleen, bone marrow and thymus changes ↓ liver weight	returned to normal persisted	1000	
"Zonyl" SC	720-78	200	0/10	no compound-related effects	no compound-related effects		>25,000
"Zonyl" SD	721-78	1400	0/10	↓ liver weight	partial recovery		
"Zonyl" SE	744-78	5000	0/10	↓ liver weight ↓ spleen and thymus weights necrosis of hemopoietic cells in spleen, bone marrow and thymus necrosis of germ cells with ↓ sperm production	partial recovery returned to normal nearly complete recovery persisted	>25,000	
Fluoromonomer (B1)	767-78	3400	3/10	↓ liver weight ↓ erythropoietic foci in spleen	partial recovery returned to normal		
"Teflon" ASD	778-78	5000	0/10	reversible histologic liver changes	returned to normal		
Perfluoropolyether carboxylic acid, ammonium salt	44-79	300 150	9/10 3/10	↓ liver weight reversible histologic changes in: hemopoietic system, liver, kidney and G.I. tract non-reversible testicular damage	partial recovery returned to normal		
"Zonyl" BA	52-79	3400 1700 850	8/10 10/10 4/10	↓ liver weight histologic liver changes reversible histologic changes in several organs histologic testicular changes	partial recovery persisted partial recovery partial recovery returned to normal partial recovery	11,000	

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AJP001468

Ninety-Day Feeding Study with "Zonyl" KP in Rats, Report #190-65

Dietary levels: 100, 500 or 2500 ppm for 75 days adjusted to 100, 1000 and 5000 ppm for 55 days

(Observations slightly decreased probably due to ...)

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EID080283

ORGANIC FLUOROCOMPOUNDS IN BLOOD

In May, 1978, 3M informed Du Pont of findings of organic fluorocompounds in blood of employees exposed to long-chain perfluoro-surface active materials. 3M reported airborne contaminant levels up to 81 ppm in their operations and organic fluorine blood levels of 1 to 71 ppm for exposed workers. 3M reports that some level of organic fluorine in humans is normal, i.e. equal to or less than 1 ppm.

Chambers Works makes functional equivalents to the 3M fluorosurfactants and plant employees were informed of the 3M findings in June 1978. Also a program was initiated to define exposure potential in the Chambers Works fluorocompound manufacturing and use operations, review the medical records of employees assigned to these operations, determine organic fluorine levels in the blood of such employees and to gather additional toxicity information on selected plant fluorocompounds. Program results are summarized below:

- Airborne contaminant monitoring results show that the highest potential for employee fluorocompound exposure to be in the manufacturing facilities. Eight hour time weighted average measurements ranged from <0.3 ppm (5 mg/m³) to 2 ppm (40 mg/m³). The drumming, dedrumming and sampling operations are major contributors to exposures above 0.3 ppm. Engineering control programs to reduce contaminant emissions from these sources is underway.
- Blood samples were taken from a representative sample of exposed employees and analyzed for organic fluorine. The mean organic fluorine value for Chambers Works employees was slightly higher than the Wilmington control group (0.15 ppm versus 0.094 ppm) but all values for exposed employees were less than 1 ppm. This program has been discontinued.
- A review and comparison of the medical records of active fluorocompound exposed plant employees with a control group showed no adverse health effects. However, while the difference is not statistically significant, the number of employees with abnormal liver function tests was notably higher in the exposed group (6 compared to 1). Medical surveillance will be continued with study update December, 1979.

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EID080284

AIPO01469

10-day subacute feeding tests carried out by Haskell showed compound related non-reversible effects for three of the eight fluorocompounds tested. Non-reversible liver and testes effects were noted in rats fed 4,470 mg/kg/day Zonyl FSN and 850 mg/kg/day Zonyl BA. Decreased sperm production was found in rats fed 5,000 mg/kg/day Zonyl Tela. The need for further toxicity testing is being studied.

A meeting is being arranged through Haskell Laboratory to inform 3M of the results of our program.

AJP001470

EID080285

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E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

WILMINGTON, DELAWARE 19898

CHEMICALS, DYES AND PIGMENTS DEPARTMENT

- S. N. Doya
- B. C. McKusick
- B. W. Karrh, ERD
- S. Pell, ERD
- F. J. Marascia, CW
- A. Dade, F&F
- R. M. Shepherd, PP&R
- H. Serenbetz, Elas.
- W. J. Raines, PP&R

Handwritten signature and date: 6/21

PERSONAL & CONFIDENTIAL

June 20, 1979

TO: MEETING ATTENDEES

FROM: P. G. GILBY

Handwritten initials
FLUORO-CHEMICALS IN BLOOD
5/22/79 MEETING SUMMARY

This letter is to summarize discussions and decisions reached in the subject meeting. It was agreed that:

<u>Item</u>	<u>Responsible for Coordination</u>
● The Chambers Works program to determine organic fluorine blood levels will be discontinued.	--
● Chambers Works employees will be informed of the results and discontinuance of the blood analysis program.	R. Richardson
● Followup will be done in the Wilmington control group employee whose blood sample was analyzed at 10.6 ppm organic fluorine.	Dr. J. C. Bonnett (additional blood sample has now been submitted for analysis)
● Medical records review study of Chambers Works exposed and control group will be updated December 1979. Update will be limited to tabulation of abnormal liver function tests.	R. Richardson to submit updated tabulation to P. G. Gilby for transmission to Dr. S. Pell.

AJP001452

EID080267

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ItemResponsible for Coordination

- Blood analysis will be done for employees having potential for exposure to 3M's FC-143 at Washington Works. PP&R will submit samples week of 6/18/79 to G. H. Patterson, CD&P, Jackson Laboratory for analysis. R. M. Shepherd, PP&R
- Engineering control programs to reduce Telomer B Alcohol airborne contaminant levels during drumming, dedrumming and sampling will be defined and projects initiated. R. Richardson
- Acceptable airborne contaminant exposure limits recommendations will be requested for Telomer B Alcohol (Zonyl BA), Telomer A (Zonyl Tela) and ZFM. W. Darnell (Request to Haskell submitted 6/12/79)
- The need, if any, for (1) further toxicity testing of selected fluorochemicals, (2) MSDS revisions and (3) customer notifications will be determined. R. E. Read
- A meeting will be set up with 3M to review Du Pont toxicity, blood and health information. F. E. French will coordinate through B. McKusick, Haskell

Discussion Summary

- Haskell completed 10-day subacute feeding tests and issued reports for the eight fluorochemicals submitted by CD&P for testing. Of the materials tested, compound related non-reversible liver and testes effects were noted in rats fed 4,470 mg/kg/day Zonyl FSN and ~850 mg/kg/day Telomer (Zonyl) BA. Decreased sperm production was found in rats fed 5,000 mg/kg/day Zonyl Tela.
- The medical records of 221 active Chambers Works employees known to have potential for fluorochemical occupational exposure were reviewed and compared to a control group. The control group (221 employees) was randomly selected from Chambers Works employees and matched as to sex, age and A.S.D. No adverse health effects were noted. However, while the difference is not statistically significant (P < 0.05), the number of employees with abnormal liver function tests was notably higher in the exposed group (6 compared to 1). Continued surveillance is warranted.

AJP001453

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- Blood samples were taken from a representative sample (55) of the Chambers Works exposed group and analyzed for organic fluorine. Du Pont Wilmington employees (25) having no potential for fluorochemical occupational exposure were used as the control group to establish base line levels. The mean value for Chambers Works employees was slightly higher than the control group (0.15 versus 0.094 ppm organic fluorine), but all values are considered to be normal (≤ 1 ppm) except one 10.6 ppm value found in the Wilmington control group. A second blood sample from this individual will be taken and analyzed. Additional blood analysis of Chambers Works employees is not warranted in view of the low values found.
- An industrial hygiene survey of selected Chambers Works fluorochemical manufacturing and use facilities was carried out. Fluorochemical exposure potential was found to be low in the use facilities. Airborne contaminant levels in the manufacturing facilities were normally 45 mg/m^3 (0.26 ppm), 8 hr. TWA. However, levels up to 40 mg/m^3 (2.1 ppm), 8 hr. TWA were measured and additional monitoring is being done to better define exposure sources. Most probable exposure sources are drumming, dedrumming and sampling operations (facilities are not now enclosed and have no local exhaust ventilation.) Engineering control programs to reduce airborne contaminants from these operations are being developed and projects will be initiated to improve these facilities.
- 3M's FC-123 fluorosurfactant is used at Spruance (TF) and Washington Works (PP&R). PP&R will submit employee blood samples for analysis. Textile Fibers have not yet reached a decision on whether or not blood analysis is warranted for their operations.

For additional information, see attached meeting charts.

PGG/bam
Att.

AJP001454

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EID080269

Meeting Attendees:

J. C. Breckenridge
F. E. French
H. E. Hiestand
R. N. Knowles
W. H. Darnell
S. B. Cupp
L. Percival, PP&R
A. A. Wright, TF
J. C. Bonnett, ER
R. D. Richardson, CW
R. E. Read, Jackson Lab
G. H. Patterson, Jackson Lab
G. L. Thayer, Jackson Lab
H. J. Trochimowicz, Haskell
P. W. Schneider, Haskell

AJP001455

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EID080270

AR 226 - 1459



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

PLASTIC PRODUCTS AND RESINS DEPARTMENT

*File
Proceedings
in 9-20-78*

CC: R. E. JACKSON
R. M. SHEPHERD
H. V. BRADLEY
E. D. CHAMPNEY
J. C. LEITINGER/M. S. EATON - WW
W. A. BOWER/R. J. BURGER - WW
C. H. FOSHEE - WW
J. F. DOUGHTY - WW
S. N. BOYD - CD&P
B. C. MC KUSICK - CR&D, HASKELL
B. W. KARRH - ER
J. B. ARMITAGE

PERSONAL & CONFIDENTIAL

July 18, 1979

TO: J. W. RAINES
FROM: L. F. PERCIVAL *LFP*

RECEIVED
JUL 20 1979
BRUCE W. KARRH, M.D.

MINUTES
REVIEW OF PRELIMINARY DATA
ORGANIC FLUORINE LEVELS IN BLOOD - WASHINGTON WORKS

- Ref: (1) Letter J. F. Doughty to L. F. Percival,
"Data on C-8 Exposure", 7/17/79.
(2) Letter Dr. Y. L. Power, M.D. to W. A. Bower,
9/20/78.

R. E. Jackson, J. W. Raines and I met with Dr. B. W. Karrh and B. C. McKusick on 7/18 to review the data in References 1 and 2.

Meeting with 3M Company - A meeting is planned* with 3M Company (the C-8 manufacturer) on 7/20 to review any new 3M data and results from blood tests run at Chambers Works. It was agreed that B. C. McKusick would report Washington Works' blood data as results of a preliminary study; process data will not be given. McKusick will report to PP&R any findings from the meeting that are significant regarding plans outlined below.

Further Blood Sampling at WW - It was agreed that additional blood samples should be taken at WW to meet the following objectives:

- Check all individuals currently exposed to C-8 in the semiworks (total 8), FEP polykettle operator (total 13) and TFE polykettle operator (total 13).
- Verify that fluorine in blood levels is due to C-8 exposure rather than from other fluorochemicals. About 4 samples should be taken from "Teflon" Monomer operators (or other personnel from the "Teflon" area) with no potential for C-8 exposure for at least 10 years.

EID107194

*Meeting was arranged May 1979.

- Define the biological decay, or buildup, rates of fluorine in blood. WW should develop a program to define decay rates or buildup of fluorine in blood by a careful review of work histories and blood sampling of certain individuals selected from list described below. We should attempt to determine if fluorine in blood levels increases with increasing lengths (years) of exposure in the jobs with C-8 exposure. We should also sample a few individuals who have left jobs with C-8 exposure for different lengths of time (years). Development of such a program will require careful planning and we would like to review it as soon as practical.

CD&P has agreed to continue to analyze samples for PP&R.

To help meet the above objectives, lists should be prepared of all jobs (including mechanics) and personnel assigned these jobs who would have been routinely potentially exposed to C-8 for a significant period for the past 10 years.

Communication with Washington Works' Employees - Present status should be communicated to affected employees at an appropriate time. Public Affairs (C. Perry) is working with information in Reference 1 and 2 to assist in statements to employees. The statements should be cleared with J. W. Raines before being used.

Medical Follow-up - Dr. B. Karrh will review data summarized in Reference 2 directly with Dr. Power and request additional medical analyses as needed.

Dordrecht and Spruance (Textile Fibers) - We agreed to defer sampling Dordrecht until further sampling has been completed at WW. McKusick is advising Textile Fibers Department of our present status. Some sampling of affected Spruance employees is indicated.

"Teflon" Customers - Any communication will be deferred until plant studies are more complete.

Notification of EPA (Section 8(e) - Toxic Substances Control Act) - The "Substantial Risk" Committee will review next week to decide if a report under 8(e) is required. This will also be discussed with 3M.

LFP:ldb

EID107195

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E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

WILMINGTON, DELAWARE 19898
CENTRAL RESEARCH & DEVELOPMENT DEPARTMENT

HASKELL LABORATORY
FOR
TOXICOLOGY AND INDUSTRIAL MEDICINE

Copies to:

- S. N. Boyd, Jr., CD&P, B-16234
- B. W. Karrh, M.D., ERD, N-11400
- A. A. Wright, Fibrs, N-4522
- J. W. Raines, PP&R, D-12017
- F. J. Marascia/R. D. Richardson/R. E. Read, CD&P
- H. E. Simmons/M. S. Sadler, CR&D, D-6032
- C. F. Reinhardt/G. L. Kennedy, CR&D, Haskell

*file - fluorochemical on
fluorochemical. Here a file
July 23, 1979*

C O N F I D E N T I A L

MEMO TO: F. E. FRENCH, JR.
CD&P, B-17249

FROM : B. C. MC KUSICK

B. C. McKusick

RECEIVED
JUL 24 1979
BRUCE W. KARRH, M.D.

DISCUSSION OF FLUORO-CHEMICALS WITH 3M

On July 20, S. N. Boyd, G. L. Kennedy, F. J. Marascia, B. C. McKusick, R. E. Read, and R. D. Richardson of Du Pont met in Chicago with F. D. Griffith, L. C. Krogh, R. A. Prokop, and F. A. Ubel of 3M.

Richardson described measurements of organic fluorochemicals in blood of fluorosurfactant production employees at Chambers Works*. In contrast to experience at 3M, concentrations are normal. A retroactive study of medical records found no adverse health effects. The blood analysis program has been discontinued.

Kennedy described Haskell's subacute toxicity studies of CD&P fluorochemicals*. They are consistent with 3M animal data.

Prokop of 3M described a gas chromatographic method to determine per-fluorooctanoic acid (FC-143) in blood, urine, liver, and other biological materials. It can measure as little as 1.5 ppb. A paper has been prepared (copy attached) that should appear in about six months.

Ubel, the 3M medical director, said that no adverse liver effects or other health effects have been found among employees in FC-143 operations. Blood levels of organofluorine in employees have changed little despite steps to lessen exposure. Blood levels of employees moved to locations outside the fluorochemical area have dropped only slightly, although measurable amounts of organic fluorine is excreted. This was illustrated by data on an employee who had been in the fluorochemical area for 15 years and had the highest blood level of any (Table I).

EID107173

(*Transparencies attached to copies of French, Simmons, & Reinhardt.)

July 23, 1979

TABLE IORGANOFLUORINE IN ONE EMPLOYEE

<u>Date</u>	<u>Blood Concentration, ppm</u>			<u>Urine Conc., µg/24 hr.</u>
	<u>RF</u>	<u>F-</u>	<u>FC-143</u>	<u>RF</u>
July 76:	39	0.05		
Oct 77	40	.03		
Apr 78	71		53	
May 78	67			
(At this point, he was transferred to another area)				
June 6, 78	66			484
June 13, 78	71			272
July 78	66			160
Aug 78	55			175
Oct 78	59			160
Jan 79	45			220
Apr 79	47			

3M got blood samples from 8 peasants in a Chinese village 30 miles from Canton. The organic fluorine was significantly lower (0.004-0.017 ppm), than values found in developed countries (e.g., 3M found 0.002-0.13 in 106 members of the general U.S. population).

Ubel said that a University of Minnesota professor is doing an epidemiology study of 4000-5000 employees who have worked at the oldest and biggest 3M plant manufacturing fluorochemicals. Nothing noteworthy has shown up, but the study has a long way to go.

A year ago all employees in fluorochemical manufacture were told the results of the blood study. 3M recently told them about it again. About 60 employees in the fluorochemical area have had blood organic fluorine measured. All who have been found to have elevated organic fluorine blood levels have been informed of the fact and told that 3M does not know what it means, but that no adverse health effects have been related to it. The employees have taken the information calmly.

Griffith, 3M manager of toxicology, reported data on 90-day studies of FC-143 in rats and monkeys (see attachment). The effects were similar to what Du Pont saw with similar materials. Thus, the liver was the main target organ.

There was no significant difference in effects between male and female rats, but males retained about 100 times more FC-143! Griffith said he would send me details on this.

EID107174

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MEMO TO: F. E. FRENCH, JR.

-3-

July 23, 1979

3M will start a metabolism study of radiolabeled $C_7F_{15}C^*O_2H$ in rats soon. This may show where FC-143 is being stored in the body.

Studies of FC-143 dust on animal skin indicates it does not penetrate the skin easily.

3M indicated interest in another review in about a year, or whenever one company has interesting results.

BCM/bjd

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AR 226 - 1460



E. I. DU PONT DE NEMOURS & COMPANY
WILMINGTON, DELAWARE 19898

PLASTIC PRODUCTS AND RESINS DEPARTMENT

CC: J. R. MUNDA
B. C. MC KUSICK - CR&D
B. W. KARRH - ER
P. M. NORLING - ADMIN.
S. N. BOYD - CD&P
A. A. WRIGHT

PERSONAL & CONFIDENTIAL

July 25, 1979

RECEIVED
JUL 26 1979
PRICE W. KARRH, M.D.

TO: R. L. RICHARDS

FROM: J. W. RAINES *JWR*

ORGANIC FLUOROCOMPOUNDS IN BLOOD

Published Article

Organic Fluorocompounds in Human Plasma: Prevalence and Characterization, by W. S. Guy, D. R. Traves, and W. S. Brey, Jr., was published by the American Chemical Society in 1976. They reported organic fluorine in blood plasma obtained from blood banks in 5 U.S. cities, determined by subtracting inorganic fluorine from total fluorine.

3M Company

May 30, 1978, informed Du Pont of elevated organic fluorine (1-71 ppm) in blood of employees exposed to long chain perfluoro surfactants such as the ammonium salt of perfluoro-octanoic acid (FC-143) which they supply to Du Pont. Control group was less than 1 ppm.

July 20, 1979, advised Du Pont:

- No adverse health effects.
- Decay rate after removal from exposure relatively slow (71 ppm - 47 ppm in one year).
- Fluorine in urine also decayed slowly (484 micrograms per 24 hours to 220 micrograms per 24 hours in 10 months).
- FC-143 not adsorbed through skin of rabbits.
- University of Minnesota professor is doing an epidemiology study on 4,000 - 5,000 employees who worked at 3M's oldest and biggest fluorochemical plant.

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- Eight Chinese peasants had significantly lower (0.004 - 0.017 ppm) blood levels than general U.S. population (0.002 - 0.13 ppm).

CD&P

Analyzed blood of 55 employees at Chambers Works. Average .15 ppm, range 0 - .37 ppm. Discontinued blood sampling. Exposure is not to same family of chemicals as that at Washington Works (WW) and 3M.

PP&R

- Analyzed blood of 8 employees potentially exposed to C-8 (FC-143) at WW.

2 Laboratorians	.4 - .5 ppm
2 FEP Polymerization Operators	2.2 - 3.5 ppm
4 TFE Dispersion Polymerization Operators	9.5 - 21.1 ppm

- No adverse health effects attributable to C-8.
- Decided not to report to EPA under 8(e) of TOSCA because fluorine in blood per se was disclosed in 1976 article and because no adverse health effect is known, therefore, no substantial risk.

Program

- Obtain raw medical data from WW employees and study by Corporate Medical to confirm that liver function and other medical analyses are normal.
- Identify personnel in all jobs with potential exposure to C-8 for the past 10 years at WW.
- Analyze blood samples (Jackson Lab will do) of selected additional employees at WW to:
 - Check all employees currently exposed to C-8.
 - Verify that fluorine levels in blood are due to C-8 exposure rather than other fluoro-compounds.
 - Define the decay rate (confirm that found by 3M).

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- (Cont'd)
 - Communicate results of latest tests to WW employees before additional blood samples are taken.
- Defer blood sampling at Dordrecht until additional results are in from WW.
- Textile Fibers will decide by August 3 about sampling blood of employees at Spruance where they produce fibers from poly TFE dispersion containing .3% C-8.

JWR:ldb

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AR 226-1461



E. I. DU PONT DE NEMOURS & COMPANY
WILMINGTON, DELAWARE 19898

LEGAL DEPARTMENT

cc: P. M. Norling, Adm.
S. N. Boyd, Jr., CD&P Dept.
B. W. Karrh, M.D., Empl. Rel. Dept.
E. D. Champney, Jr., PP&R Dept.
J. W. Raines, PP&R Dept.
R. M. Shepherd, PP&R Dept.
A. A. Wright, Textile Fibers Dept.
B. C. McKusick, CR&D Dept., Hasht

RECEIVED

AUG 01 1979

BRUCE W. KARRH, M.D.

July 30, 1979

TO: FILE

FROM: EUGENE BERMAN

Eugene Berman

FLUORINE BLOOD LEVELS

A meeting, attended by the above individuals, was held on July 23, 1979 to review additional PP&R information related to its use of ammonium perfluoro octanoate (3M's product FC-143). The discussion included a review of (1) data provided by 3M Company, including fluorine levels in blood and urine measured in 3M employees exposed to FC-143 and data on fluorine blood levels in the general population, (2) fluorine blood levels measured in eight PP&R Washington Works employees, as well as levels measured in 55 CD&P Chambers Works employees, and (3) available health data.

Based upon this review, it was concluded that the information did not reasonably support a conclusion that a substantial risk was presented, primarily based upon the absence of any known adverse health effects related to fluorine in blood. Accordingly, it was concluded that no reporting under TSCA Section 8(e) was required. Corporate Medical Division will continue its review of the Washington Works employees' medical data to confirm that there are no adverse health effects.

On July 26, 1979, I advised Robert Prokop of 3M of our above conclusions with regard to Section 8(e) and our general practice of reporting or otherwise publicizing relevant findings even if they are not required to be reported under Section 8(e). I asked Prokop to clarify what plans 3M had with regard to publicizing this fluorine blood level information and/or directly advising the relevant health agency of this information. Prokop indicated that he believed 3M was favorably disposed toward disclosing this information and promised a more definitive response next week after reviewing the matter with Lester Krogh (3M's Division Vice President).

EB/caw

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AR 226-1462

x



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

WILMINGTON, DELAWARE 19898

EMPLOYEE RELATIONS DEPARTMENT

CC: B. W. Karrh, M.D.
V. A. Brewster, M.D.
S. Pell
W. A. Bower-PP&R-Parkersburg
R. Dyer-PP&R-Parkersburg
G. A. Ploeger-PP&R-Parkersburg
R. M. Shepherd-PP&R-D-120

JOHN DOUGHTY-B-1

PERSONAL & CONFIDENTIAL

August 28, 1979

Y. L. POWER, M.D.
MEDICAL SUPERINTENDENT
PP&R DEPARTMENT
PARKERSBURG, W. VA.

STATUS REPORT ON WASHINGTON WORKS LIVER FUNCTION SURVEY AND
CORONARY HEART DISEASE MORTALITY STUDY

B. W. Karrh asked me to look into the liver function test results for workers with C-8 exposure, and Y. L. Power asked me to examine myocardial infarction cases and deaths at the Plant. S. Pell and R. M. Shepherd agreed that these items should be investigated.

End of October
My preliminary results suggest that C-8 exposed workers may possibly have positive liver function tests more often than the plant population as a whole, and that the number of active wage roll employees having myocardial infarctions from 1974 through 1977 was somewhat higher than was expected based on Company-wide experience. As a consequence of these preliminary findings, the following steps are being taken:

(1) Liver function survey

- Y. L. Power is having every tenth active employee's most recent SMA-12 test results photocopied and sent to me. Included on each worker's SMA-12 sheet will be name, the date the blood chemistries were done and the worker's age. *OK*

copy
- G. A. Ploeger is gathering exposure history records for every worker selected by Y. L. Power above (over 220 workers). These exposure histories will contain the worker's name, social security number, birth date, sex, payroll class, date hired, dates in and out of the Teflon area, and the job titles held during each period spent in Teflon area.

EID080214

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- Ploeger and Power will construct a list of everyone who is currently potentially exposed to C-8. SMA-12's and exposure histories for these workers will be sent to me. Ploeger and Power estimate that it will be two to three weeks before all SMA-12's and exposure histories can be supplied.

(2) Coronary heart disease mortality

- R. Dyer is seeing if it is possible to construct a list of pensioners who were receiving a pension in 1957. If he can make such a list, he should also be able to make lists for the years 1958-1978, in which case we could study coronary heart disease mortality among active and pensioned employees.

*work of
9/24*

MEDICAL DIVISION

W. E. Fayerweather

W. E. Fayerweather
Epidemiologist

WEF:msd

AJP001400

EID080215

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WORK HISTORY of 220 EMPLOYEES

Date Hired	ASD	Name	SS#	Birth Date	Jobs worked in TFF	
					Dates In	Dates
3/19/79	3/10/79	6		3-10-50	-	-
4/20/55	4/20/55	6		4-24-32	-	-
5/14/65	5/14/65	6		8-4-43		
				Polym. Proc.	5-23-65	6-26-
				Thiost. Mill Oper.	4-26/65	11-14-
				Finish. Oper.	11-14-65	11-28-
				HEP Serv. Oper.	11-28-65	2-10-
				Ref. Pol. "A" Oper.	2-10-74	Presen
4-30-59	4-30-59	6		12-8-36		
				P&E Polymer Proc.	3-7-60	4-11-
5-2-77	5-2-77	6		7-8-54	-	-
2-27-59	2-28-61	6		1-1-40		
				P&E Serv. Oper.	10-29-78	11-20-
				Refin. Polymerization Oper.	11-20-78	Presen
12-15-58	12-15-58	6		3-4-32		
				P&E Poly. Proc.	6-15-59	2-27-
				P&E Drier Oper.	2-29-60	6-1-
				P&E Poly. Proc.	6-13-60	4-17-
				Refin. Poly. Proc "C" (Op)	12-27-61	11-5-
				P&E Finishing Oper.	11-5-62	2-1-
				" " " " " S	5-4-69	5-2-
				Refin. HEP Serv. Oper.	5-25-69	6-15-
				Refin. Polymerization Oper.	6-15-69	10-2-
				Refin. Poly. Proc. Oper.	10-28-69	Presen
11-4-58	11-4-58	6		9-19-39	-	-
3-19-79	3-19-79	6		6-17-52	-	-
6-23-50	6-12-50	6		3-26-19	-	-
3-19-59	3-19-59	6		7-20-38	-	-

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EID080216

WORK HISTORY - ~~CONFIDENTIAL~~

Date Hired	ASD	Name	SS#	Birth Date	Jobs worked in TEF	
					Dates In	Dates
2/23/61	2/23/61	h E		3-6-41		
				Yellow Iron. Oper.	3-3-62	9-29-
				White Poly. Processor	9-29-63	10-6-
				White Poly. Oper.	12-16-66	5-18-6
				Yellow Poly. Oper.	5-18-69	12-14-
				Yellow Poly. Oper.	12-14-69	7-19-70
				Yellow Post Finishing Oper.	7-19-70	10-11-
				Yellow H.P. Machine Oper.	10-11-70	12-7-
				Yellow Finishing Oper.	12-7-70	1-2-7
				Yellow Poly. H.P. Oper.	1-2-72	1-12-7
				Yellow H.P. Machine Oper.	1-12-75	
12/15/58	12/15/58	"		3-4-32		
				White Poly. Processor	6-15-59	2-29-6
				White Poly. Oper.	2-29-60	6-13-6
				White Poly. Oper.	6-13-60	4-17-6
				Yellow Poly. Proc. "C"	12-27-61	11-5-6
				White Finishing Oper.	11-5-62	2-10-6
				" " " 5	5-4-69	5-25-
				Yellow H.P. Machine Oper.	5-25-69	6-15-6
				Yellow Finishing Oper.	6-15-69	10-28-
				Yellow Poly. H.P. Oper.	10-28-69	
7/26/76	7/26/76			3-26-52		
				White Iron. Oper.	9-12-76	4-16-7
				Yellow Machine Oper.	4-16-79	?
				White Iron. Oper.	4-16-79	

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EID080217

000169

ALP001402

AR 226-1463



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INCORPORATED
P. O. Box 1217
PARKERSBURG, W. VA. 26101

CC: J. W. Raines - Wilm.
C. H. Foshee
W. A. Bower/R. J. Burger
C. R. Campbell
J. L. Granquist
Y. L. Power
P. Thistleton

PLASTIC PRODUCTS AND RESINS DEPARTMENT

October 1, 1979

PERSONAL AND CONFIDENTIAL

TO: R. M. SHEPHERD
ENERGY AND ENVIRONMENTAL AFFAIRS
WILMINGTON

FROM: J. F. DOUGHTY
WASHINGTON WORKS
J. F. Doughty

ORGANIC FLUORIDES IN BLOOD ANALYSES

A table is attached showing the results we have obtained to date. We plan to update the table when the remainder of the blood results are available. Please destroy the previous letter dated September 20, 1979. All of the organic fluoride results shown were incorrect because the inorganic fluoride was not subtracted from the total nonvolatile fluoride.

JFD:sah
Attachment

EID080255

000170

AJP001440

ORGANIC FLUORIDES IN BLOOD SAMPLES

NAME	P.R. NO.	ZONE	ORGANIC FLUORIDE PPM	COMMENTS
<u>GRANULAR OPERATORS</u>				
<u>Polymerization</u>				
	REDACTED	6	0.47	4/60-6/71, 12/72 to present
r	REDACTED	6	2.33	Exposure since 1968 ⁶ , granular polymerization since 2/74.
	REDACTED	6F	0.52	Special job. Relief on granular polymerization about 1 day/week. 2/69 to present
	REDACTED	6	3.54	FEP dispersion 8/70-12/71
	REDACTED	6	5.61	5/60 to 3/62, 4/67 polymerization 9/68 to 1/69, polymerization 2/74 to present
	REDACTED	6	3.91	4/68 to present, other jobs since 65
1	REDACTED	6	6.84	F.P. 9/55 to 12/72, polymerization 4/73 to present
.....	REDACTED	6	2.53	3/76 to present
<u>Finishing</u>				
	REDACTED	4	2.06	Disp. P.O. 4/71 to 4/72, relief to polymerization 4/73 to present
	REDACTED	4	0.69	Detailed to polymerization 10 days in past 5 months
	REDACTED	4	0.72	Detailed to granular polymerization 8 of last 10 weeks as of 9/13/79.
<u>FINE POWDER/DISPERSION OPERATOR</u>				
<u>Polymerization</u>				
	REDACTED	6	4.39	F.P. Dispersion and Disp. P.O. 9/75 to 4/77, polymerization 4/79 to present
	REDACTED	6	(22.17) 21.22	Special operator jobs 6/66 to 4/68, relief since 2/63
	REDACTED	6	0.17	5/76 to present
	REDACTED	6	(9.53) 9.25	4/57 to present, other jobs previous because
	REDACTED	6	1.52	F.P. P.O. and Dryer 6/66 to 1/72, polymerization 2/74 to present.

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() Previous blood samples taken in June.

000171

EID080256

AJP001411

NAME	P.R. NO.	ZONE	ORGANIC FLUORIDE PPM	COMMENTS
<u>Polymerization (Cont.)</u>				
st	REDACTED	6F	0.59	3/63 to present, <i>polymerization</i> 10/77 - 4/79
		6	00.81	1960 to present.
		6F	(10.56) 8.70	11/75 to present
		6	(15.02) 13.75	4/68 to present. Service operator jobs previous 4 years
		6	1.60	11/75 to present.
		6	3.55	3/76 to 5/75 F.P. dryer, <i>polymerization</i> 4/75 to present
		6	5.90	6/65 to present, Service operator jobs previous 4 years
		6	0.38	3/79 to present.
		6	6.91	4/77 to present, Service operator jobs previous 4 years
		6	16.52	12/75 to 11/76, <i>polymerization</i> 8/75 to present
		6	0.98	F.P. dryer and P.O. 2/75-5/76, some granular polymerization. F.P./disp. polymerization 4/79 to present.
		6	3.51	Service operator jobs 1/72 - 1/77, <i>polymerization</i> 11/77 to present
		6	3.23	5/76 to present
		<u>Service Operator</u>		
m	REDACTED	4	4.97	F.P. dryer and P.O. 6/66 to 12/69, <i>polymerization</i> 10/75 to 12/75 Warehouse, detailed to other jobs.
		4	1.98	F.P. dryer since 11/78.
		4	4.54	F.P. dryer and Disp. RO. 9/76 to present
		4F	2.24	Service operator jobs 5/59 to present
		4	1.03	F.P. dryer since 11/78
		4	2.92	12/78 to present, <i>polymerization</i> 11/78 to present
		4	0.50	3/79 to present all 3 jobs.
4	1.04			
4	1.80	F.P. packout.		

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() Previous blood samples taken in June.

EID080257

000172

AJP001442

NAME	P.R. NO.	ZONE	ORGANIC FLUORIDE PPM	COMMENTS
<u>Service Operator (Cont.)</u>				
[REDACTED]		4	2.97	F.P. Dyeer 12 years, F.P. P.O. before, other 3 years.
		4	3.89	12/72 to present F.P. Dyeer and P.O.
		4	2.30	Details to polymerization 1/79 to present Dyeer and polymerization
		4	1.78	F.P. packout.
		4	1.18 1.91	F.P. P.O. 11/76 to present, initially to polymerization.
<u>MONOMER OPERATORS</u>				
		7	0.35	
		7	0.39	
		7	0.08	
		6F	0.54	
		7	0.17	
		7	0.37	
		7	0.52	
<u>FEP OPERATORS</u>				
<u>Polymerization</u>				
		6	(1.36) 0.99	1976 to present. <i>additional exposure in 1976</i>
		6F	1.72	1976 to present. <i>additional exposure in 1976</i>
		6	2.71	Disp. 1964-1971; polymerization 1976 to present.
		6	0.91	1976 to present.
		6	2.10	1976 to present.
		6	4.64	Disp. 10/60-11/63; polymerization 1976 to present.
		6	3.70	1976 to present. <i>additional exposure in 1976</i>
		6	(3.61) 1.99	1976 to present.

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() Previous blood samples taken in June.

NAME	P.R. NO.	ZONE	ORGANIC FLUORIDE PPM	COMMENTS
<u>Polymerization (Cont.)</u>				
	REDACTED	6	1.95	1976 to present.
		6	1.47	1976 to present.
		6	4.96	1976 to present. <i>additional exposure in long polymer</i>
		6	4.52	10/77 to present. <i>additional exposure in long polymer</i>
		6	4.14	12/76 to present. <i>additional exposure in long polymer</i>
<u>Dispersion</u>				
		4	1.31	6/75 to present
<u>RESEARCH</u>				
<u>Research Chemists</u>				
			0.43	
			0.45	
<u>Semiworks Laboratorians</u>				
		6	0.44	5/70 to present.
		6	1.50	8/77 to present, <i>similar concs 9/68 to 11/69, possibly additional exposure in production. Service operator 5/72 to 7/72, long polymer 7/72 to 7/75, 7/75.</i>
		6F	0.24	4/77 to present. <i>11/75</i>
		6	0.70	2/75 to present.
		6	(0.46) 0.26	4/77 to present.
		6	0.30	7/69 to 10/72, 5/79 to present.
		6F	0.24	8/77 to present. <i>Service operator 6/73 to 7/73</i>
		6	(0.72) 0.59	10/72 to present. <i>Service operator 3/63 to 2/65</i>
<u>MONOMER OPERATORS WITH PAST FINE POWDER/DISP. POLYMERIZATION EXPOSURE</u>				
		7	6.66	<i>Polymerization 1/62 to 12/75 Monomer operator 11 months</i>

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d

() Previous blood samples taken in June.

EID080259

000174

ALP001444

NAME	P.R. NO.	ZONE	ORGANIC FLUORIDE PPM	COMMENTS
<u>MONOMER OPERATORS WITH PAST FINE POWDER/DISP. POLYMERIZATION EXPOSURE</u> (Cont.)				
	REDACTED	7	5.29	Exposure 5/62 to 5/77 Monomer operator 28 months all jobs.
		7	5.64	Exposure 1/62 to 11/77 Monomer operator 22 months
<u>FOREMAN VOLUNTEER</u>				0.69

JFDoughty:sah
10/1/79

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AJP001445

000175

EID080260



ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

P. O. Box 1217
PARKERSBURG, W. VA. 26101

PLASTIC PRODUCTS AND RESINS DEPARTMENT

CC: J. W. Raines - Wilm.
C. H. Foshee
W. A. Bower/R. J. Burger
C. R. Campbell
J. L. Granquist
Y. L. Power
P. Thistleton

October 10, 1979

PERSONAL AND CONFIDENTIAL

TO: R. M. SHEPHERD
ENERGY AND ENVIRONMENTAL AFFAIRS
WILMINGTON

FROM: J. F. DOUGHTY
WASHINGTON WORKS

ORGANIC FLUORIDES IN BLOOD ANALYSES

A table is attached showing the results we have obtained. We plan to update the table when additional work history information is available on the monomer operators.

JFD:mps
Attachment

000176

EID080732

AP001331

ORGANIC FLUORIDES IN BLOOD SAMPLES

<u>NAME</u>	<u>P.R. NO.</u>	<u>ZONE</u>	<u>ORGANIC FLUORIDE PPM</u>	<u>COMMENTS</u>	
GRANULAR OPERATORS					
<u>Polymerization</u>					
	REDACTED	6	0.47	8/60-6/71, 12/72 to present	
		6	2.33	Exposure since 1968, granular polymerization since 2/74.	
		6F	0.52	Special job. Relief on granular polymerization about 1 day/week 2/69 to present.	
		6	3.54	F.P. P.O. 8/62 to 3/69, FEP polymerization 8/69 to 7/70, polymerization 12/71 to present	
		6	5.61	12/72 to present, others jobs since 5/55	
		6	3.91	9/71 to present.	
		6	6.84	FP, P.O. 9/65 to 12/72, polymerization 9/73 to present	
		6	2.23	3/76 to present.	
<u>Finishing</u>					
			4	2.06	Disp. P.O. 9/71 to 7/72, details to polymerization 5/76 to present.
		4	0.69	Detailed to polymerization 65 days in past 5 months.	
		4	0.72	Detailed to granular polymerization 8 of last 10 weeks as of 9/13/79.	
<u>FINE POWDER/DISPERSION OPERATOR</u>					
<u>Polymerization</u>					
		6	4.39	F.P. Dryers and Disp. P.O. 9/76 to 4/79, Polymerization 4/79 to present.	
		6(22.17)	21.22	Service operator jobs 6/56 to 6/60, polymerization since 2/63.	

() Previous blood samples taken in June.

000177

EID080733

NAME	P.R. NO.	ZONE	ORGANIC FLUORIDE PPM	COMMENTS
<u>Polymerization (Cont.)</u>				
	REDACTED	6	0.17	8/76 to present.
		6	(9.53) 8.25 -	4/62 to present, others job previous 6 years.
		6	1.52	F.P. P.O. and Dryer 6/66 to 3/72, polymerization 2/74 to present.
		6F	0.59	3/63 to present, except monomer operator 10/77-4/79.
		6	20.81 -	1960 to present.
		6F	(10.56) 8.70 -	11/75 to present.
		6	(15.02) 13.75 -	4/62 to present. Service operator jobs previous 4 years.
		6	1.60	11/75 to present.
st		6	3.55	3/76 to 8/78 F.P. dryer, polymerization 8/78 to present.
		6	5.90	5/65 to present, service operator jobs additional 5 years.
		6	0.38	3/79 to present.
		6	6.91 -	4/77 to present, FEP service operator 2/75 to 4/77
		6	16.89 -	F.P. dryer 10/75 to 4/77, polymerization 8/78 to present.
		6	0.98	F.P. dryer and P.O. 2/75-5/76, some granular polymerization. F.P./disp. polymerization 4/79 to present.
		6	3.81	Service operator jobs 9/72-11/77. Polymerization 11/77 to present.
		6	3.23	8/76 to present

() Previous blood samples taken in June.

0-1 4
 1-5 5
 5-10 4
 10-15 1
 15-20 1
 20-25 1

EID080734

000178

AJP001333

<u>NAME</u>	<u>P.R. NO.</u>	<u>ZONE</u>	<u>ORGANIC FLUORIDE PPM</u>	<u>COMMENTS</u>
<u>Service Operator</u>				
	REDACTED	4	4.97	F.P. dryer and P.O. 6/66 to 12/69 Polymerization 10/77 to 10/78.
r		4	1.98	F.P. Dryer since 11/78.
am		4	4.84	F.P. Dryer and Disp. P.O. 9/76 to present.
		4F	2.24	Service Operator jobs 5/57 to present.
		4	1.03	
		4	2.92	12/78 to present F.P. Dryer, detailed to polymerization.
		4	0.50	3/79 to present all 3 jobs.
		4	1.04	
		4	1.80	F.P. packout.
		4	2.97	F.P. Dryer 12 years, F.P. P.O 8 years, other 3 years.
		4	3.89	12/72 to present F.P. Dryer and P.O.
		4	2.30	1/79 to present Disp. and Polymerization.
		4	1.78	F.P. packout.
		4	1.81	F.P. P.O. 11/76 to present, Details to polymerization.
<u>MONOMER OPERATORS</u>				
		7	0.35	
		7	0.39	
		7	0.08	
		6E	0.54	
		7	0.17	
		7	0.37	
		7	0.52	

c-1 B
1-5 D

000179

EID080735

<u>NAME</u>	<u>P.R. NO.</u>	<u>ZONE</u>	<u>ORGANIC FLUORIDE PPM</u>	<u>COMMENTS</u>
<u>Semiworks Laboratorians</u>				
	REDACTED	6	0.44	5/70 to present.
		6	1.50	8/77 to present. Finishing operator 9/68 to 11/69, service operator 5/72 to 12/72, homopoly service operator 12/72 to 7/74, 8/75 to 11/75
		6F	0.24	4/77 to present.
		6	0.70	2/75 to present.
		6	(0.46) 0.26	4/77 to present.
		6	0.30	7/69 to 10/72, 5/79 to present.
		6F	0.24	8/77 to present. Service operator 2/75 to 9/75.
		6	(0.72) 0.59	10/72 to present. Teflon exposure 9/59-4/62, service operator 3/63-2/69

MONOMER OPERATORS WITH
FAST FINE POWDER/DISP.
POLYMERIZATION EXPOSURE

7	6.66	Polymerization 1/62 to 10/78 Monomer operator 11 months.
7	5.29	Exposure 5/62 to 5/77. Monomer operator 28 months.
7	5.64	Exposure 9/62 to 11/77. Monomer operator 22 months.

$$\bar{x} = 5.86$$

FOREMAN VOLUNTEER

0.69	Various jobs with C-8 10/56 to 3/63. Monomer operator 3/63 to 2/69. Foreman 2/69 to present.
------	--

Total 12

() Previous blood samples taken in June.

0 - 1 8
1 - 5 1
5 - 12 3
10 - 15
15 - 20

000181



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

PLASTIC PRODUCTS AND RESINS DEPARTMENT

CC: B. W. KARRH - ER
H. E. SERENBETZ - ELAS
R. L. RHODES - TF
R. E. JACKSON

October 16, 1979

TO: B. C. MC KUSICK - HASKELL
G. L. KENNEDY - HASKELL
V. A. BREWSTER - MEDICAL, ERD
W. E. FAYERWEATHER - MEDICAL, ERD
F. E. FRENCH - CD&P
S. N. BOYD - CD&P
H. A. SMITH - ELAS
E. E. SWAIN - F&F
A. C. HAVEN - INTERNATIONAL
A. A. WRIGHT - TF

E. D. CHAMPNEY - PP&R
E. E. LEWIS - PP&R
J. B. ARMITAGE - PP&R
J. W. RAINES - PP&R
L. F. PERCIVAL - PP&R
J. F. DOUGHTY - WASH. WKS.
P. THISTLETON - WASH. WKS.

FROM: R. M. SHEPHERD *Shep*

*> F & < C → less active as
not tested for as sensitization*

C-8 (FC-143) - AMMONIUM PERFLUOROOCCTANOATE

You are invited to a meeting this Friday, October 19, 1979 at 1:15 p.m. in our Conference Room, D-12015 for an update on our occupational health studies concerning the above chemical. The agenda is as follows.

- Introduction - Shepherd
- Organic Fluorides in Blood - Thistleton
- Haskell Laboratory Report - Kennedy
Skin tests; 3M Co. liaison
- Medical Studies - Status and Schedule - Fayerweather
- Plant Program - Status and Plans - Thistleton
Handling Practices; Sampling
- Other Items - All

RMS:ldb

EID107158

RL001725

C-8 (FC-143) - AMMONIUM PERFLUOROCTANOATE

CHRONOLOGICAL SUMMARY OF REPORTS

<u>Month/Year</u>	<u>Sources</u>	<u>No. of People</u>	<u>No. of Samples</u>	<u>Organic Fluorides in Blood</u>	
				<u>Aver. (ppm)</u>	<u>Range (ppm)</u>
June 1978	3M Co. discussion	130	?		up to 70
May 1979	CD&P/Haskell review				
	<u>3M Data</u>				
	General Population	106	?	0.02	0.002-0.13
	Plant Office Worker				0.01-0.06
	Plant Worker General				0.13-1.18
	Plant Worker - F/C Area - newer plant -				0.9-9.1
	- older plant -				5.9-71
	<u>Du Pont Data</u>				
	Wilmington Control Group	25	23	0.094	0-0.38
	Chambers Works Group	55 (of 199)	54	0.15	0-0.37
July 1979	<u>Du Pont Data</u>				
	Initial Wash. Wks.	8	8	8.2	0.6-22
August 1979	<u>3M Data</u>				
	C-8 Packaging - 1 year service -				5-10
	15-20 yrs. service - typical				10-20
	Top levels				30-70
	F1-Sulfonic Acid Area				1-4
Oct. 1979	<u>Du Pont Data</u>				
	Washington Works	78	86		0.1-22

RL001726

RMS:ldb
10/18/79

EID107159

000183

A G E N D A

C-8 (FC-143) - AMMONIUM PERFLUOROCTANOATE

- Introduction - Shepherd
- Organic Fluorides in Blood - Thistleton
- Haskell Laboratory Report - Kennedy
Skin Tests; 3M Co. Liaison
- Medical Studies - Status and Schedule - Fayerweather
- Plant Program - Status and Plans - Thistleton
Handling Practices; Sampling
- Other Items - All

EID107160

RL001727

000184

AR 226 - 1464

BB

CC: J. F. Doughty
Dr. Y. L. Power
C. R. Campbell
J. L. Granquist
L. W. Goin
J. J. Hegenbarth

January 17, 1980

TO: C. A. ROBINSON
FROM: PAUL THISTLETON *PT*

BLOOD ANALYSES

I obtained the following data from Erik Kissa, Jackson Lab, 1/16 and 1/17.

<u>NAME</u>	<u>ORGANIC FLUORIDE</u> <u>ppm</u>	
	0.72	10/17/79 0.78
	0.60	0.65
	0.83	0.40
	0.58	0.63
	0.55	0.60
AVERAGE	0.66	0.72
<i>Powell</i> <i>Stewart</i>		0.53

These values are low and do not support wider sampling of mechanics.

Seven long service Monomer Operators had 0.1 to 0.5 ppm organic fluoride (average 0.35 ppm). Eight semiworks laboratorians had 0.2 to 1.5 ppm organic fluoride (average 0.56 ppm). These results were obtained from samples taken in August, 1979.

PT/nsw

AR226-1465

cc



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

EMPLOYEE RELATIONS DEPARTMENT

cc: W. E. Feyerweather
B. W. Karrh, M.D.
R. N. Ligo, M.D.
S. Pell

January 28, 1980

J. W. RAINES - PP&R
R. M. SHEPHERD - PP&R
P. THISTLETON - PP&R

LIVER ENZYME STUDY OF WORKERS EXPOSED
TO C-8 AT PARKERSBURG

The following is a summary of conclusions reached at our meeting 1/25/80 to discuss the above study.

- Based on the above study there is no conclusive evidence of an occupationally related health problem among workers exposed to C-8.
- Nearly all individual blood enzyme levels are in an acceptable range. However the mean SGOT* in the TFE process operator group and the mean AP** in the FEP process group are elevated when compared to other plant groups. Those elevations do not indicate conclusive evidence of a health problem but they do justify further follow-up.
- There were no significant differences of the mean bilirubin and mean LDH*** blood levels of the cohorts when compared to other plant groups.
- Based on available data we are unable to explain why only the mean SGOT would be elevated in one group and only the mean AP would be elevated in another group. Normally we would expect better correlation of all liver studies when compared to each other.
- After comparing the local laboratory liver enzyme results with the results from Upjohn on the same employees there appears to be a local laboratory problem resulting in consistently higher SGOT readings. Therefore we recommend that either a different technique or a different laboratory be considered for routine medical examinations on all employees at the Parkersburg plant.

* Serum glutamic oxalacetic transaminase
**Alkaline phosphatase
***Lactic dehydrogenase

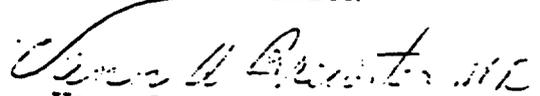
EID099433

BIR000090

- For epidemiological reasons, we recommend that duplicate SMA-12's be obtained on employees in the exposed cohorts and control cohort using the present technique and present laboratory.
- There were conflicting data in our attempt to correlate organic fluoride levels with liver enzyme levels. We recommend continuation of biological monitoring of blood organic fluorides as follows:
 1. Get fluoride levels on those employees not yet tested but in cohort jobs.*
 2. Get fluoride levels in a year or less on employees in cohort jobs* and already sampled.
 3. In a year or less reassess the need for and/or frequency of additional samples.
- We recommend that the plant continue transmittal to the Medical Division SMA-12's, relevant medical data, and relevant work history data on all employees now in the study and employees newly assigned to cohort jobs. This includes non-Teflon® area employees in the control group.

A report of the above study results from Bill Fayerweather will follow in the near future.

MEDICAL DIVISION



Vann A. Brewster, M.D.
Asst. Medical Director

* TFE Polymerization Process Operator, TFE Service Operator,
FEP Polymerization Process Operator, FEP Service Operator,
Monomer Operator

VAB/kcs

BJR000091

EID099434

000187

AR226-1466

DD

F&F DEPARTMENT
 FC-143 DATA
 FEBRUARY, 1980

SITE NAME	Weeks Exposure (approx.)	Blood Analysis		Workplace* Conc. FC-143 mg/m ³
		Total F (ppm)	Organic F (ppm)	
Toledo • Lead, mix dispensing • Sample • Lead finished product introduced • Ambient temp.	190	2.	1.92	.0022
	292	1.08	0.98	<.0011
	15	0.82	0.74	.0033
				oven → .001 room
Philadelphia, PE • Handle Pk/year	200	0.46	0.36	0.00038
	50	1.15	1.07	<.00016
Philadelphia, Plant Quality Control Technician Process Operator Relief Operator	100	0.6	0.5	0.0027
	250	1.02	0.92	.002
	16**	0.46	0.37	
Marshall Lab Rm 432	250***	<u>1.12</u>	<u>1.02</u>	< 0.0001
		Mean 0.97	0.88	
Fairfield Process Operator Coated glass fabric	56	> 28.	> 28. (bomb) 900. (torch)	.005 .007

* Area samples, not personal samples

** Relief worker

*** Sprays every 2 weeks

./bjm
 2/28/80

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AR 226-1467

EE



ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

SPRUANCE PLANT
P.O. Box 27001
RICHMOND, VIRGINIA 23261

TEXTILE FIBERS DEPARTMENT

cc: M. R. Warden - A. A. Wright - T.F. - Wi
 R. L. Rhodes - T.F. - Wilm.
 R. J. Shepherd - PP&R - Wilm.
 E. E. French - CD&P - Wilm.
 A. A. Brewster, M. D. - E.R. - Wilm.
 B. C. McKusick - J. F. Morgan -
 Haskell Lab.
 G. B. Faigle, Jr. - J. W. Williams
 R. L. Cook
 G. R. Anderson
 D. O. Inslee, M. D.
 P. S. Calvo, Jr.
 H. J. Sampson
 File: TE-1

*To: Parkersburg / Fayetteville
 for info & disc card*

February 25, 1980

RECEIVED

FEB 28 1980

YANN A. BREWSTER, M.D.

PERSONAL & CONFIDENTIAL

TO: G. L. WATTS

FROM: E. R. PURCHASE *ERP*

FC-143 FLUOROSURFACTANT

(Ref.: Letter, A. A. Wright to M. R. Warden, same subject, 10/29/79)

The reference letter reviews information on FC-143, a 3M Company product, used at Parkersburg in Teflon® dispersion which in turn is used in Teflon® operations at Spruance. Blood tests on employees who work with FC-143 showed up to 70 ppm of organic fluorine in 3M employees and up to 22 ppm in Parkersburg employees compared to a general background level of less than 1 ppm. No adverse health effect has been detected in any of the exposed people. Tests at Haskell Laboratory revealed that FC-143 readily penetrates the skin of animals and causes liver damage and in heavy doses may cause death. In view of this information, a decision was made to analyze blood samples from a small group of Spruance employees with potential FC-143 exposure in Spinning and Finishing and a control group.

The analyses of blood samples were carried out at Jackson Laboratory by the same group that analyzed samples from Parkersburg. The results are shown below:

<u>Employee</u>	<u>Age</u>	<u>Area</u>	<u>Fluorine, ppm</u>		
			<u>Total (1)</u>	<u>Inorganic</u>	<u>Organic (2)</u>
	37	Spin.	0.34	0.21	0.13
	58	Spin.	0.41	0.12	0.29
	25	Spin.	0.18	0.11	0.07
	28	Spin.	0.23	0.15	0.08
	37	Fin.	0.35	0.15	0.20
	32	Fin.	0.18	0.18	0.00
	31	Control	0.21	0.20	0.01
	24	Control	0.18	0.14	0.04
	35	Control	0.18	0.15	0.03

- (1) Non-volatile
- (2) By difference

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RL001722

These results indicate that there is no significant exposure to FC-143. This view is supported by personnel from Haskell Laboratory, Jackson Laboratory and the Parkersburg plant, who consider that blood levels of organic fluorine below 1 ppm are not significant. Therefore, we plan no further analysis of blood samples from Spruance employees.

To ensure continued protection of personnel against exposure to FC-143, operating procedures will continue to be based on no skin contact with Teflon® dispersion. No special precautions are required for yarn handling. In routine periodic audits of operating area conditions and practices, special attention will be given to those factors which protect employees against exposure to FC-143.

ERP:fsg

EID107156

RL001723

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AR226 - 1468

C-O-N-F-I-D-E-N-T-I-A-L

SUMMARY

ORGANIC FLUORIDES IN BLOOD SAMPLES

<u>Location</u>	<u>Job Group</u>	<u>Number Sampled</u>	<u>Range ppm</u>	<u>Average ppm</u>
Washington Works	Process Operators - TFE	26	0.2-21.7	5.79
	Process Operators - FEP	13	0.9-5.0	2.83
	Service Operators	18	0.5-5.0	2.14
	Mechanics	5	0.55-0.83	0.66
	Semi Works Laboratorians	8	0.2-1.5	0.56
	Monomer Operators*	7	0.1-0.5	0.35
	(*no service in polymer)			
Wilmington	Background Group	25	0.0-0.78	0.13
Chambers Works	CD&P Operators (Fluoro Products)	55	0.0-0.37	0.15
Chambers Works - PPD	"Kalrez" Operators	14	0.02-0.21	0.12
Experimental Sta.-PPD	"Kalrez"	4	0.15-0.86	0.57
Spruance - TF	"Teflon" Fiber Process Operators	6	0.0-0.29	0.13
Finishes Plants (F&F)		9	0.36-1.92	0.89
Fabrics Plant (F&F)	(one sample - recheck and more samples recommended.)			

R:S/is
3/3/30

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RJZ009056

AR226 - 1469



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

cc: B. W. Karrh/ J. C. Bonnett
 R. N. Ligo/ S. Pell ←
 W. E. Fayerweather/File

EMPLOYEE RELATIONS DEPARTMENT

June 9, 1980

L. F. PERCIVAL
 POLYMER PRODUCTS DEPARTMENT
 WT 642

YOUR MEMO, JUNE 4, REQUESTING COMMENTS ON THE
 WASHINGTON WORKS COMMUNICATION DRAFT "FLURO-
 SURFACTANTS IN BLOOD"

I am concerned that the "Draft" implies that the Medical Division will not continue the study of liver tests on those employees potentially exposed to C-8. Even though we have found no "conclusive evidence of an occupationally related health problem," we still cannot explain why the mean SGOT was significantly higher among TFE process workers and that the mean AP was significantly higher among FEP process and service workers.

Therefore, I recommend the following changes to the Draft:

- At the end of the second paragraph, page 1, add:
 "However, it was recommended that the study of liver tests continue."
- At the bottom of page 2, add a fourth item:
 "Continue to evaluate the liver tests of employees with potential exposure to C-8."

Because of Bill Fayerweather's involvement, I would appreciate your copying him in on any communication relating to the evaluation of workers exposed to C-8. He will be sending you and Dick the second draft of his epidemiological study within the next few days.

MEDICAL DIVISION

VANN A. BREWSTER, M. D.
 ASSISTANT MEDICAL DIRECTOR

VAB:mjk

EID102477

WEF000044

AR226 - 1470

CC: R. J. Burger
C. R. Campbell
J. R. Broadway
J. L. Granquist
R. J. Zipfel
P. Thistleton
G. H. Stoltz
C. A. Robinson
K. G. Kronberg
J. F. Doughty

C-8 COMMUNICATIONS MEETING

OUTLINE, TALK & CHARTS

C. E. STEINER
7/31/80

PERSONAL & CONFIDENTIAL

EID079399

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AJP002552

INTRODUCTION

- C-8's desirable process qualities
- Short C-8 history in TFE & FEP Manufacture

TOXICITY

- Oral toxicity - slightly toxic
 - Compare to other compounds
- Skin contact - slightly to moderately toxic
- Inhalation toxicity - highly toxic
 - Compare to other compounds
 - Concentrations found in area are lower

INITIAL BLOOD TESTS

- 3M Data
- Our Results

RECOGNIZING EXPECTED OPERATOR QUESTIONS - A transition

- Some disbelieve based on past experience
- Short history of chemicals in industry showing why we are careful

MEDICAL RECORD STUDIES

- No evidence of health problem
- Studies thorough

PROVISIONAL AEL

- AEL committee has set provisional AEL of 0.55 mpb
- Not yet firm AEL
- This very low number is to protect people who work with C-8 every day
- The low provisional AEL and goal to reduce blood fluorine is the reason we are making changes in equipment and procedures.

EQUIPMENT IMPROVEMENTS

- Goal to reduce exposure to solid C-8, airborne C-8 and C-8 solutions
- Ingredients addition hood and stack
- Eliminate Weighing Citric Acid in C-8 hood
- Raising Dryer Air supply Inlets
- Seal Dryer Leaks
- Additional Dryer Windows
- Increase Ventillation During Outages
- Removing C-8 from Dryer Exhausts

PROTECTIVE EQUIPMENT

Clothing and Gloves

- Needs to be disposable to prevent secondary contamination.
- An EOD is being prepared to evaluate clothing.
- Different protection levels for 3 exposure classes

Breathing

- Equipment improvements will reduce airborne C-8 but high C-8 concentrations will still remain in some areas.
- Breathing air will be installed - ultimate solution.
- Comfo II air respirator with GMAH cartridge acceptable.

TESTING

Personal Air Samples

- Will Resample.

Blood Samples

- Blood sampling will be resumed.
- Frequent sampling is not necessary.

Area Air Samples

- Will continue to define progress.
- Often exceed provisional AEL before improvements.

SUMMARY

- C-8 is toxic but can be handled safely.
 - People working with C-8 generally accumulate organic fluorine in the blood, and levels generally correlate with job exposure potential.
 - Although this has caused no health effects continued exposure is not tolerable.
 - Our basic goals are to reduce exposures to below the provisional AEL, and to reduce organic fluorine levels in blood of exposed workers and prevent accumulation in new workers.
 - This will require equipment changes that are being done.
 - It will also require use of disposable protective clothing and use of breathing air or respirators for certain jobs.
- One other ingredient is needed -- your cooperation in controlling this hazard.

CES
6/3/80

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C-8 COMMUNICATION MEETING

The purpose of this meeting is to bring everyone up to date on our findings regarding C-8, our immediate program, and our long term plans.

Most of you know that C-8 is a fluorochemical surfactant that is used for producing fine powder, dispersion, granular and FEP. It has unique properties that allow it to wet Teflon's surface, shorten reaction cycle time, stabilize dispersions and provide sites for reactions. It has been used for Teflon® manufacture for over 25 years. Other chemicals have been tested but none match C-8's properties. Four years ago it was introduced in FEP manufacture where it was a manufacturing improvement.

Let's look over the highlights of the Technical history of C-8. In 1965 tests showed that C-8 was slightly toxic when swallowed. This was not surprising. There is a dose level where almost every chemical becomes poisonous, even water. (Chart 1). This chart shows the oral toxicity of C-8 relative to some common chemicals. These tests were done on animals, and represent what dose would kill 50% of the animals tested. I've scaled up the dose from test data to animal weights comparable to an operator's weight. You can see that C-8 is not as toxic as acetone. It has a lower toxicity like table salt.

C-8, like table salt, can also be absorbed through the skin where it is about as toxic as it is orally. But, based on this low toxicity, no change in our safety program was necessary.

EID079402

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In 1969 it was found that C-8 was more toxic by inhalation, Chart 2. This second chart shows the approximate concentration that will kill test animals in a 4 hour period. This approximate lethal concentration for rats exceeds anything we have measured in the plant. The highest level ever measured in the plant is about 1/4 of that level -- and that a 1.1mpm leak at the feed end of No. 3 dryer which has been repaired. The other C-8 concentrations are generally about 1,000 to 10,000 times lower than this so people working in the area see no immediate effect. (.004-.04 mpm)

However, since 3M informed us in 1978 of organic fluorine being detected in the blood of their employees who worked with C-8, we have been reviewing and expanding our C-8 program. We have concluded that personnel routinely exposed to C-8 will absorb it in their body. Tests at Washington Works show that blood fluorine levels which indicate C-8 levels generally correlate with potential job exposure.

Repeated exposures can result in accumulation of C-8 in the blood. One of the things that we are studying with the blood samples is the rate that C-8 is eliminated from the body.

Some of the old timers remember when C-8 was treated with less respect and they wonder "Why is it suddenly harmful now?"

EID079403

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Throughout the chemical industries over the last 50 years this story has been repeated with the same disbelief but often with more drastic consequences.

For example, carbon tetrachloride was used to clean auto parts and as a fire extinguisher for years, and now it is known to cause damage in some people and is used with care. The same story has been repeated several times for things like chloroform (which was used in cough suryp), methyl alcohol and other chemicals.

The difference between the ending of the C-8 story and the others is that Du Pont is reacting while C-8 levels in the blood are low and before any damage is done in the body.

The medical data show that no one has been injured by C-8 (Chart 4). The Medical Division after a thorough study has concluded that ". . .there is no conclusive evidence of an occupationally related health problem among workers exposed to C-8." All that was noted was a small increase in two liver enzyme levels. After 25 years of handling C-8 we see no damage among the workers. However, the potential is there -- C-8 has accumulated in the blood. Because of this accumulation we have decided to undertake programs to minimize accumulation of C-8 in the blood of new workers.

EID079404

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The AEL Committee of Haskell Laboratories has set a provisional Allowable Exposure Limit or "AEL" at 0.55 mpb of C-8 in air. This very low proposal is based on a safety factor of 800 below the level where reversible liver effects were observed. An AEL is the same thing as a TLV or EGL -- it is a safe concentration in the air of a working environment.

In order to meet the expected low AEL, equipment changes are necessary to protect from solid, liquid and airborne C-8.

The next transparencies show the changes that have been made recently to protect against C-8 exposure. To date we have:

- Modified the Fine Powder/Dispersion ingredients addition hood to reduce C-8 emissions and bring the mixing operations into the hood. C-8 tools will also be stored in the hood where possible.
- Improved the C-8 addition hood exhaust stack. The hood exhaust stack was close to an H & V inlet on the roof.
- Removed operations that don't have to be done in the C-8 hood -- like citric acid weighing. This has reduced exposure of concentration to the operators.

The dryers have been improved also:

- Air supply inlets have been raised to remove C-8 rich air from the ceiling.

EID079405

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- Seals of No. 3 dryer doors and seams have been improved.
- Inspection windows have been added to reduce need to open dryer doors.

We have also put guards inside the dryer that will permit using the exhaust fans to remove C-8 when dryers are being cleaned. This has reduced some C-8 concentrations, but more work is to be done; for example, we plan to cover injection pump tanks, seal openings in floor and vent oscillating feeder compartments, sealing No. 3 dryer fans.

The next chart shows the three different protection levels required for three exposure classes: Low dry exposure, high dry exposure and wet exposure. A disposable garments of the appropriate design, gloves and air protection are recommended for each of these exposure classes. Sample garments have been selected and an EOD will be run to evaluate this clothing. Tyvek® was selected over cloth or paper garments because it is light fairly resistant to tearing, a good filter and disposable. Disposability is required to prevent secondary contamination when laundering. During this EOD, sample garments will be tried and evaluated by operators and mechanics.

C-8 will permeate all glove materials over a period of time. New flock lined latex gloves will be used in jobs where C-8 exposure is likely. Even these gloves will be permeated by C-8 over a period of time, so these gloves will be disposed of after each shift.

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Breathing protection is very important to reducing C-8 exposures. Equipment improvements will reduce airborne C-8 in most areas but there will still be areas where exposure is possible. A COMFO II air respirator with a special GMAH cartridge is required as a minimum. Breathing air is better and will be available soon. The yellow 3M masks are not acceptable.

I've had some questions on future C-8 air samples and blood samples. We now have our baseline data and have mapped out the problem areas. The procedures are modified and equipment improved so C-8 exposures will be reduced.

Blood sampling will probably be done on an annual basis in the future to define the real improvements in C-8 control.

Let me summarize the items covered:

- C-8 is toxic, but it can be used and controlled below the proposed toxic limit.
- In the past, people working with C-8 have accumulated organic fluorine in the blood and levels generally correlate with job exposure potential.
- Although this has caused no health effects, continued exposure should be minimized with controls.
- Our objective is to reduce exposures to below the provisional AEL, and to reduce organic fluorine levels in blood of exposed workers and to limit accumulation in new workers.

EID079407

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- This will require equipment changes that are partially complete
- It will also require use of disposable protective clothing and use of breathing air or respirators for certain jobs.
- One other ingredient is needed -- Total Division cooperation in controlling this material.

CHART 1

ORAL TOXICITY

(DOSES LETHAL TO ABOUT 50% OF ANIMALS)

	<u>Oz./150 LB. ANIMAL</u>	
ACETONE	0.2	(DOG)
C-8	1.0	(DOG)
TABLE SALT	7.2	(RAT)
METHYLENE CHLORIDE	7.2	(RAT)

000203

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ALP002562

CHART 2

INHALATION TOXICITY

(APPROXIMATE LETHAL CONCENTRATIONS FOR 4-HOUR EXPOSURES WITH RATS)

	<u>MPM*</u>
C-8	41
METHANOL	300

* MPM = MOLES PER MILLION -- SAME AS PARTS PER MILLION BY VOLUME.

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CHART 4

MEDICAL STUDIES

- MEDICAL DIVISION 1/25/80 STATEMENT BASED ON LIVER ENZYME STUDY -- " . . . THERE IS NO CONCLUSIVE EVIDENCE OF AN OCCUPATIONALLY RELATED HEALTH PROBLEM AMONG WORKERS EXPOSED TO C-8."
- 3M MEDICAL DIRECTOR IN 3/14/80 MEETING WITH DU PONT STATED THAT THEY HAVE NOT IDENTIFIED ANY SIGNIFICANT INDUSTRIAL DISEASE RELATED TO C-8 EXPOSURE.
- NO EVIDENCE OF HEALTH PROBLEMS IN MORE THAN 25 YEARS USE OF C-8. HANDLING PRACTICES IN EARLIER YEARS HAD GREATER EXPOSURE POTENTIAL THAN RECENT OPERATIONS.

CONCLUSION

- NO CONCLUSIVE EVIDENCE OF HEALTH PROBLEMS RELATED TO C-8 EXPOSURE.

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C-8 EXPOSURE CLASS
AND PROTECTIVE CLOTHING SUMMARY

<u>Class 1</u>	<u>Class 2</u>	<u>Class 3</u>
<u>DRY LOW EXPOSURE</u> <ul style="list-style-type: none">● Disposable TYVEK® coat or smock ● Disposable latex gloves (or orange rubber gloves if yellow latex is unavailable)	<u>DRY HIGH EXPOSURE</u> <ul style="list-style-type: none">● Disposable TYVEK® coveralls with hood or cap ● Disposable latex gloves● Black rubber boots	<u>WET EXPOSURE</u> <ul style="list-style-type: none">● Disposable coated TYVEK® coveralls with hood or coated smock and coated pants ● Disposable latex gloves● Black rubber boots

NOTE: Breathing air or COMFO II respirator with GMAH cartridge is also recommended for all exposures, but are not included as part of this test.

CES/ikm
5/13/80

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AIPO0206

SUMMARY

- C-8 IS TOXIC
- PEOPLE ACCUMULATE C-8
- NO HEALTH EFFECTS AT PRESENT LOW LEVELS
- GOALS:
 - TO REDUCE EXPOSURE BELOW AEL
 - TO REDUCE ORGANIC FLUORINE IN BLOOD
- REQUIRES:
 - EQUIPMENT CHANGES
 - DISPOSABLE PROTECTIVE CLOTHING AND GLOVES
 - BREATHING AIR OR COMFO II
 - COOPERATION

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EID079418

AJP002571



ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY

INCORPORATED

P. O. Box 1217

PARKERSBURG, W. VA. 26101

CC: E. D. Champney, Jr. - Wilm.
D. K. Duncan - Wilm.
J. W. Raines/R. M. Shepherd-Wil
R. J. Burger
R. E. Putnam

POLYMER PRODUCTS DEPARTMENT

September 30, 1980

PERSONAL AND CONFIDENTIAL

TO: T. F. JORDAN
TOKYO

J. S. LINDELL
DORDRECHT

FROM: PAUL THISTLETON
WASHINGTON WORKS



TEFLON® DIVISIONS - C-8 (FC-143) CONTROL

Attached is a copy of the "Status and Program" that was reviewed at our Teflon® Divisions' C-8 meeting on Sept. 25, 1980.

Please let me know if you have comments or questions.

Attachment

PT/nsw

EID077237

TEFLON® DIVISIONS C-8 (FC-143) CONTROL

STATUS AND PROGRAM

<u>SECTION</u>	<u>PAGE</u>
A. COMMUNICATION MEETINGS	2
B. EPIDEMIOLOGY STUDIES	2
C. BLOOD ANALYSES	3 & 4
D. TOXICITY TESTS AND EXPOSURE LIMITS	4 & 5
E. C-8 SUPPLY	5
F. C-8 REPLACEMENT	6
G. AIR MONITORING	7
H. AIR MONITORING PROCEDURE	7
I. ENGINEERING CONTROLS - FEP	8, 9, 10, 11
J. ENGINEERING CONTROLS - FINE POWDER/DISPERSION	12
K. PROTECTIVE EQUIPMENT - RESPIRATORS	13
L. PROTECTIVE EQUIPMENT - CLOTHING	14

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A. COMMUNICATION MEETINGS

JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MARCH
 1981

(1) August - Nine shift meetings held for Mechanics, Operators and Research Seminars Operators. Kronberg and Steiner reviewed C-8 toxicity, discussed engineering controls, protective equipment, etc.

(2) Oct. - Meeting(s) will be held for laboratorians.

B. EPIDEMIOLOGY STUDIES

(1) 1/25 - Medical Division Statement based on liver enzyme study - ". . . there is no conclusive evidence of an occupationally related health problem among workers exposed to C-8." (report expected in Oct.).

(2) July - Teflon® area workers had no significant excess of heart attacks compared with rest of plant.

(3) July - Teflon® area workers had no significant difference in blood pressure from a control group with no Teflon® (or C-8) exposure (adjusted for age, smoking, etc)

(4) August - 3M Medical Dept. published a paper, "Health status of plant workers exposed to fluorochemicals - a preliminary report." in the American Industrial Hygiene Association Journal.

X

X

X

X

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JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MAR.

C. BLOOD ANALYSES

- (1) May - Comparison at Jackson Lab showed good agreement of 3M (Bomb) and Du Pont (Torch) methods at low levels (0.3 and 1.2 ppm fluorine).
- (2) May - C-8 Specific method demonstrated at ESL (improved 3M method).
- (3) 8/1 - Letter detailing blood sampling program issued. Includes comparison of analytical methods and discussion of data interpretation.
- (4) 8/4 - Release of employee communication "Fluoro-surfactants in Blood" started. It described blood sampling plans and summarized overall program.
- (5) August - ESL established for C-8 Specific blood analyses.
- (6) August - Sampling started for comparison of test methods.

X
X
X

X
X

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C. BLOOD ANALYSES - (continued)

- (7) 9/2 - Comparison of C-8 Specific and Torch methods started at ESL. About 25 samples from MW Teflon® workers will be tested.
- (8) Nov. - Decide which method should be used for routine analyses.
- (9) Nov. - Start routine sampling as outlined in 8/1/80 letter.

D. TOXICITY TESTS AND EXPOSURE LIMITS

- (1) 2/11- -- Inhalation subacute test
 2/29 exposure period.
- (2) 2/22 - Blood analyses finished for skin subacute tests.
- (3) August - Haskell Lab ingestion studies showed no significant sex differences in lethal doses for guinea pigs, mice and rats. Tests made by 3M showed that female rats eliminate C-8 much faster than males.
- (4) Oct. - Initial blood results from inhalation subacute tests.

	<u>JULY</u>	<u>AUG.</u>	<u>SEPT.</u>	<u>OCT.</u>	<u>NOV.</u>	<u>DEC.</u>	<u>JAN.</u>	<u>FEB.</u>	<u>MAR.</u>
(7)			X						
(8)					X				
(9)					X				
(1)									
(2)									
(3)				X					
(4)				X					

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D. TOXICITY TESTS AND EXPOSURE LIMITS - (continued)

(5) Sept. - Haskell Lab report on skin subacute tests to be issued.

(6) Jan '81 - AEL Committee Review

E. C-8 SUPPLY

(1) 7/31 - 3M representatives visited WW to promote rapid conversion from current solid C-8 (from ribbon dryer) to spray dried C-8. Change in dryer eliminates many of their environmental problems. Activity on C-8 solution terminated (at least temporarily).

(2) August - 450 lb. spray dried C-8 C-8 received from 3M for evaluation.

(3) Sept. - Fine powder, granular and FEP made using spray dried C-8 in BOD tests. Dispersion polymerization reaction rate 10 - 15% below normal. Granular polymer thermal stability below normal. May be a problem with operator acceptance because C-8 is very fine and clings to scoops.

(4) 9/17 - 3M representatives visited WW to review spray dried C-8 evaluation. More semiworks evaluation of samples will be made before plant tests.

JULY

AUG.

SEPT.

OCT.

NOV.

DEC.

JAN.

FEB.

MARCH

X

X

X

X

X

X

EID077242

000213

STATUS AND PROGRAM

1981

JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MARCH

F. C-8 REPLACEMENT

- (1) 3/4 - Evaluation of "in-situ" surfactant recommended. (Morgan/Thistleton letter)
- (2) May - Semiworks products made with three fluorinated surfactants appear to yield satisfactory end product. Evaluation continues.
- (3) 5/8 - PMN* testing program reviewed at Haskell Lab. Tests will include monitoring blood fluoride levels.
- (4) August- Tests authorized. Timing depends on availability of material. X
- (5) ** - FEP Plant Test.

* Premanufacture notice as required by TOSCA.
 ** Timing depends on toxicity testing and plant availability.

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EID077243

I. ENGINEERING CONTROLS - FEP

	<u>JULY</u>	<u>AUG.</u>	<u>SEPT.</u>	<u>OCT.</u>	<u>NOV.</u>	<u>DEC.</u>	<u>JAN.</u>	<u>FEB.</u>	<u>MARCH</u>
(1) Sept. - Completed COD TY-077 Eliminate free falling streams in clean room by installing eductors under V-Disc press and Torus Disc dryer scrubber. --- (\$32,000)			X						
(2) Coagulator to fluff bin seal.									
July - Drafting request.	X								
Oct. - COD issue.				X					
Dec. - Installed on one coagulator						X			
(3) New recycle tank to return recycle tank fluff to fluff blender instead of manual dipping.									
Sept. - COD circulating (\$36,000)			X						
Feb. - New tank installed.								X	
(4) Eliminate the once/shift dumping of coagulator bag filter.									
Aug. - COD TY-127 approved (\$7800).		X							
Nov. - Installed					X				
(5) Provide means to vacuum sump rather than scoop polymer - COD TY-085 (\$5900)									
Sept. - Equipment due.			X						
Oct. - In use.				X					

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I. ENGINEERING CONTROLS - FEB - (continued)

	<u>JULY</u>	<u>AUG.</u>	<u>SEPT.</u>	<u>OCT.</u>	<u>NOV.</u>	<u>DEC.</u>	<u>JAN.</u>	<u>FEB.</u>	<u>MARCH</u>
(6) Engineering controls at trayout.									
July - Rec'd recommendations from Fernandes, ESD Consultant, on dust control and ventilation.	X								
Aug. - Drafting request.		X							
Nov. - COD issue - (\$40,000)					X				
May '81 - Installation.									
(7) Eliminate polymer exhaust from coagulation bag filter.									
Sept - Receive bags from vendor for evaluation.			X						
Nov. - Install first set.					X				
Dec. - Install second set, if necessary.						X			
Jan. - Install third set, if necessary.							X		
Feb. - Determine final effluent concentration and determine necessary stack height.								X	
(8) Eliminate the manual dumping of the central vacuum system.									
Oct. - COD issue - (\$17,750).				X					
March '81 - Installed.									X

000216

I. ENGINEERING CONTROLS - FEP - (continued)

	<u>JULY</u>	<u>AUG.</u>	<u>SEPT.</u>	<u>OCT.</u>	<u>NOV.</u>	<u>DEC.</u>	<u>JAN.</u>	<u>FEB.</u>	<u>MARCH</u>
(9) Raise exhaust stacks of coagulation and wet finishing bag filters.									
March - Determine final concentration after bag test.									
April - Contact Wevodau for height needed.									
May - COD issue.									
(10) Investigate shoe cleaner.									
July - Installed but removed from service twice due to decanter overflows.			X						
(11) Determine effect of Torus Disc product temperature on C-8 concentration.									
Sept. - Asked ADG to set up bench scale work because too much plant penalty.			X						
Nov. - Complete bench scale work and issue findings.					X				
(12) Prevent hot steams containing polymer/C-8 from flowing through surps.									
Sept. - COD TY-183 (\$4700).			X						
Dec. - Installation						X			

X
000217

STATUS AND PROGRAM

1981

JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MARCH

I. ENGINEERING CONTROLS - FEP (continued)

(13) Monitoring of equipment with RAM (Real-time Aerosol Monitor) to determine effectiveness of seals.

Jan. - Restart program.

(14) Improve ventilation in clean room through use of diamond plate on top of grating.

OOD on hold pending outcome of educator OOD.

X

000218

J. ENGINEERING CONTROLS-FINE POWDER/DISPERSION

- (1) May - completed COD TY-586 - Raise Fine Powder dryer air supply inlets to exhaust additional airborne C-8 (\$1,200).
- (2) May - completed COD TY-047 - Internal Fine Powder dryer fan guards to exhaust airborne C-8 during outages - (\$8,500).
- (3) May - completed COD TY-048 - Additional inspection windows for Fine Powder dryers (\$2,500).
- (4) May - completed COD TY-061 - Improve dispersion ingredients hood and its exhaust stack - (\$5,000).
- (5) May - Improved sealing of Fine Powder Dryers - included better door seals and sealing between dryer sections.
- (6) Oct. - Further improvements to be made in dryer sealing.
- (7) Reduce Fine Powder Dryer Exhaust Stacks' C-8 emissions - (\$100,000).
Nov. - COD approval
- May '81 - Installation
- (8) Oct. - Seal holes in floor above Fine Powder Dryers to reduce C-8 concentration upstairs.
- (9) Increase exhaust capacity from #2 Dryer.
Oct. - COD issue.
Feb. - Installation

	<u>JULY</u>	<u>AUG.</u>	<u>SEPT.</u>	<u>OCT.</u>	<u>NOV.</u>	<u>DEC.</u>	<u>JAN.</u>	<u>FEB.</u>	<u>MARCH</u>
(1)									
(2)									
(3)									
(4)									
(5)									
(6)				X					
(7)					X				
May '81 - Installation									
(8)				X					
(9)				X				X	

000219

TEFLON® DIVISIONS C-8 (FC-143) CONTROL
STATUS AND PROGRAM

<u>SECTION</u>	<u>PAGE</u>
A. COMMUNICATION MEETINGS	2
B. EPIDEMIOLOGY STUDIES	2
C. BLOOD ANALYSES	3 & 4
D. TOXICITY TESTS AND EXPOSURE LIMITS	4 & 5
E. C-8 SUPPLY	5
F. C-8 REPLACEMENT	6
G. AIR MONITORING	7
H. AIR MONITORING PROCEDURE	7
I. ENGINEERING CONTROLS - FEP	8, 9, 10, 11
J. ENGINEERING CONTROLS - FINE POWDER/DISPERSION	12
K. PROTECTIVE EQUIPMENT - RESPIRATORS	13
L. PROTECTIVE EQUIPMENT - CLOTHING	14

EID077249

I28E00DJV

A. COMMUNICATION MEETINGS

(1) August - Nine shift meetings held for Mechanics, Operators and Research Seminars Operators.

X

Kronberg and Steiner reviewed C-8 toxicity, discussed engineering controls, protective equipment, etc.

(2) Oct. - Meeting(s) will be held for laboratorians.

X

BEST COPY AVAILABLE

B. EPIDEMIOLOGY STUDIES

(1) 1/25 - Medical Division Statement based on liver enzyme study - ". . . there is no conclusive evidence of an occupationally related health problem among workers exposed to C-8." (report expected in Oct.).

(2) July - Teflon® area workers had no significant excess of heart attacks compared with rest of plant.

X

(3) July - Teflon® area workers had no significant difference in blood pressure from a control group with no Teflon® (or C-8) exposure (adjusted for age, smoking, etc)

X

(4) August - 3M Medical Dept. published a paper, "Health status of plant workers exposed to fluorochemicals - a preliminary report." in the American Industrial Hygiene Association Journal.

X

1/8 of Teflon area workers are on antihypertensive drugs whereas 3/8 C-8 workers are on antihypertensive drugs. However, a sample of 8 persons - can't really say it's statistically significant, only took one set of blood pressure readings - these very somewhat by the each person taking them I should take a set of 2 or 3 readings.

W. J. [Signature]

EID077250

STATUS AND PROGRAM

1981

JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MAR.

C. BLOOD ANALYSES

- ~~(1) May - Comparison at Jackson Lab showed good agreement of 3M (Bomb) and Du Pont (Torch) methods at low levels (0.3 and 1.2 ppm fluorine).~~
- ~~(2) May - C-8 Specific method demonstrated at ESL (improved 3M method).~~
- (3) 8/1 - Letter detailing blood sampling program issued. Includes comparison of analytical methods and discussion of data interpretation.
- ~~(4) 8/4 - Release of employee communication "Fluoro-surfactants in Blood" started. It described blood sampling plans and summarized overall program.~~
- (5) August - ESL established for C-8 Specific blood analyses. X
- (6) August - Sampling started for comparison of test methods. X

000222

EID077251

5785001111

C. BLOOD ANALYSES - (continued)

- (7) 9/2 - Comparison of C-8 Specific (GC) and Torch methods started at ESL. ~~About 29~~ samples from WW Teflon® workers ~~will be tested.~~ X
- (8) Nov. - ~~Decide which method should be used for routine analyses.~~ *c-8/GC method recommended* X
- (9) ~~Dec~~ *Dec* - ~~Start routine sampling as outlined in 8/1/80 letter.~~ *Use of c-8/GC method approved by Mumps & Emery Division* X

000223

D. TOXICITY TESTS AND EXPOSURE LIMITS

- (1) 2/11 - Inhalation subacute test *2/29 exposure period.*
- (2) 2/22 - Blood analyses finished for skin subacute tests.
- (3) August - Haskell Lab ingestion studies showed no significant sex differences in lethal doses for guinea pigs, mice and rats. Tests made by 3M showed that female rats eliminate C-8 much faster than males. X
- (4) Oct. - Initial blood results from inhalation subacute tests. X

EID077252

4728300DJV

JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MARCH

D. TOXICITY TESTS AND EXPOSURE LIMITS - (continued)

(5) Sept. - Haskell Lab report on skin subacute tests ~~to~~ ^{be} issued.

(6) ~~Jan 1981~~ ^{April} - AEL Committee Review

E. C-8 SUPPLY

(1) 7/31/80 3M representatives visited WW to promote rapid conversion from current solid C-8 (from ribbon dryer) to spray dried C-8. Change in dryer eliminates many of their environmental problems. Activity on C-8 solution terminated (at least temporarily). X

(2) August ~~80~~ 450 lb. spray dried C-8 C-8 received from 3M for evaluation. X

(3) Sept. ~~80~~ Fine powder, granular and FEP made using spray dried C-8 in BOD tests. Dispersion polymerization reaction rate 10 - 15% below normal. Granular polymer thermal stability below normal. May be a problem with operator acceptance because C-8 is very fine and clings to sooops. X

(4) 9/17/80 3M representatives visited WW to review spray dried C-8 evaluation. More semisworks evaluation of samples will be made before plant starts. X

EID077253

C700001JRV

G. AIR MONITORING

(1) April - 7 day personal sampling program for Fine Powder & FEP Wet Finishing Operators showed 60 to 80% above 0.6 mpb limit.

(2) Sept. - 7 day personal samples for Fine Powder Dryer Operators had an average of 0.25 mpb with no values above limit.

(3) Sept. - 7 day personal samples for FEP Wet Finishing Operators had an average of 0.91 mpb. Personal samples in April had an average of 0.95 mpb.

(4) * - Repeat personal sampling for Fine Powder and Wet Finishing Operators and FEP operators.

H. AIR MONITORING PROCEDURE

- (1) May - Comparison of methylene blue and C-8 Specific methods (developed at ESL) using split sample shows excellent agreement.
- (2) May - Chloroform/Azure A Method developed from Dutch method by C. S. Cope.
- (3) 9/2 - C-8 Specific method available for review at WW.
- (4) Oct. - Recommend preferred method for routine use.

* Will depend on completion of Engineering Controls.

922000

EID077255

I. ENGINEERING CONTROLS - FEP

- (1) Sept. - Completed COD TY-077
Eliminate free falling streams in clean room by installing eductors under V-Disc press and Torus Disc dryer scrubber. -- (\$32,000)
- (2) Coagulator to fluff bin seal.
July - Drafting request. X
Oct: - COD issue.
Dec. - Installed on one coagulator
- (3) New recycle tank to return recycle tank fluff to fluff blender instead of manual dipping.
Sept. - COD circulating (\$36,000) X
July - ~~Feb~~ - New tank installed.
- (4) Eliminate the once/shift dumping of coagulator bag filter.
Aug. - COD TY-127 approved (\$7800). X
Nov. - Installed (*done*)
- (5) Provide means to vacuum sump rather than scoop polymer - COD TY-085 (\$5900)
Sept. - Equipment due. X
Oct. - In use.
Nov - Failed Trial Retest/Redesign

	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MARCH
(1)			X						
(2)	X			X			X		
(3)			X						
(4)						X			
(5)			X						

000227

PT 9/23/80

MARCH

I. ENGINEERING CONTROLS - FEP - (continued)

	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MARCH
(6) Engineering controls at trayout.									
July - Rec'd recommendations from Fernandes, ESD Consultant, on dust control and ventilation.	X								
Aug. - Drafting request. Proto type bins built for Prod/Mech. X									
Nov. - COD issue (\$40,000) Review COD TX 6/77									
Review Results on proto type (if successful)									
Installation. (if proto type acceptable)									
May '81 →									
(7) Eliminate polymer exhaust from coagulation bag filter.									
Sept - Receive bags from vendor for evaluation.			X						
Nov. - Install first set Substantial Improvement in Total Discharge					X				
Dec. - Install second set if necessary. Notice slight Dust Break thru but total discharge same as Nov.						X			
Jan. - Install third set if necessary. Plan to go with Teflon treated bags when we combine							X		
Feb. - Determine final effluent concentration and determine necessary stack height. Call T-100 system with good weather (late March/April).								X	
May - Determine final effluent concentration & determine height. necessary stack height									
(8) Eliminate the manual dumping of the central vacuum system.									
Oct. - COD issue - (\$17,750).				X					
March '81 - Installed.									X

822000

EID077257

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I. ENGINEERING CONTROLS - FEP - (continued)

JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MARCH

(9) Raise exhaust stacks of coagulation and wet finishing bag filters.

March - Determine final concentration after bag test.

April - Contact Wevodau for height ~~sum~~ needed.

May - OOD issue.

(10) Investigate Shoe cleaner.

July - Installed but removed from service twice due to decanter overflows.

JAN. - Re-installed at new location

(11) Determine effect of Torus Disc product temperature on C-8 concentration.

Sept. - Asked ADG to set up bench scale work because too much plant penalty.

Nov. - Complete bench scale work and issue findings.

(12) Prevent hot steams containing polymer/C-8 from flowing through sumps.

Sept. - COD TY-183 (\$4700).

Dec. - Installation (done)
JAN. -

	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MARCH
(9)									
(10)									
(11)			X				X		
(12)			X				X		

TESTLON DIVISIONS C. (FC-143) CONTROL
STATUS AND PROGRAM

1981

I. ENGINEERING CONTROLS - FEP (continued)

	<u>JULY</u>	<u>AUG.</u>	<u>SEPT.</u>	<u>OCT.</u>	<u>NOV.</u>	<u>DEC.</u>	<u>JAN.</u>	<u>FEB.</u>	<u>MARCH</u>
(13) Monitoring of equipment with RAM (Real-time Aerosol Monitor) to determine effectiveness of seals. <i>Fulcrum - Restart program.</i>							X		000230
(14) Improve ventilation in clean room through use of diamond plate on top of grating. COD on hold pending outcome of educator COD.									X
(15) From Additional Breathing Air Facilities - FEP (\$66.5m) Authorized COD - JAN Complete Installation - MAR <u>House Keeping Improvements</u>							X		X
(1) MASSA WINDMILL CLEANUP OF FEP BUILDING (5/m CONTRACT FOR TOTAL OF 4 CLEANUPS) Issued Purch Req - JAN 1st cleaning → FEP Monitor area for C-8 Decide timing for 2nd cleaning								X	X

PI 9/23/80 X

EID077259

AJP003831

J. ENGINEERING CONTROLS-FINE POWDER/DISPERSION

	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MARCH
(1) May - completed COD TY-586 - Raise Fine Powder dryer air supply inlets to exhaust additional airborne C-8 (\$1,200).									
		Complete 5/80							
(2) May - completed COD TY-047 - Internal Fine Powder dryer fan guards to exhaust airborne C-8 during outages - (\$8,500).									
		Complete 5/80							
(3) May - completed COD TY-048 - Additional inspection windows for Fine Powder dryers (\$2,500).									
		Comp 5/80							
(4) May - completed COD TY-061 - Improve dispersion ingredients hood and its exhaust stack - (\$5,000).									
		Comp 5/80							
(5) May - Improved sealing of Fine Powder Dryers - included better door seals and sealing between dryer sections.									
		Comp 5/80							
(6) Oct. - Further improvements to be made in dryer sealing.			X	X					
(7) Reduce Fine Powder Dryer Exhaust Stacks' C-8 emissions - (\$100,000). Nov. - COD approval May '81 - Installation									
(8) Oct. - Seal holes in floor above Fine Powder Dryers to reduce C-8 concentration upstairs.									
(9) Increase exhaust capacity from #2 Dryer. Oct. - COD issue. Feb. - Installation									

EID077260

000231

K. PROTECTIVE EQUIPMENT - RESPIRATORS

Comfo II

- (1) 3/5 - Use of GMA-H cartridges (combination high efficiency filter and activated charcoal) approved by R. F. Kinter, Chairman, Respiratory Protection Subcommittee.
- (2) March-June - GMA-H cartridges established for routine use.
- (3) May - GMA-H cartridge tested at Haskell Lab with 1 mg/m³ C-8 (100X proposed limit) feed. Capacity exceeds 40 hours.
- (4) 9/15 - Report on cartridge tests issued (HR 664-80). It should provide a basis to extend cartridge use to a month. This is under review.

Air Supplied Systems

- (5) May/June - Field tested 3M Hardcap system.
- (6) July - Recommended to Production to provide 3M Hardcap units for all Wet Finishing personnel. X
- (7) May - ^{Acc 80440} completed COD TY-045 (\$7290) for breathing air stations in FEP area.
- (8) Sept. - completed COD TY-082 (\$1,994) for breathing air station for weigh station. X
- (9) 3/11 - COD TY-051 (\$16,750) for breathing air stations in Polymers area authorized.
- Oct. - Breathing air stations in Service. X

10) Add'l BREATHING AIR FACILITIES - FEP

EID077261

1981

L. PROTECTIVE EQUIPMENT - CLOTHING

Disposable Clothing & Gloves

- (1) 8/28 - Started field test of protective clothing. X
- (2) Nov. - Start field test of protective clothing with more breathing capability. X
- (3) Feb ~~1980~~⁸⁰ - Stock approved protective clothing in Stores. X
- (4) May - Started routine use of #L-61 latex rubber gloves in Fine Powder/Dispersion and REP Areas.

	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MARCH
(1) 8/28 - Started field test of protective clothing.		X							
(2) Nov. - Start field test of protective clothing with more breathing capability.					X				
(3) Feb 1980 ⁸⁰ - Stock approved protective clothing in Stores.								X	
(4) May - Started routine use of #L-61 latex rubber gloves in Fine Powder/Dispersion and REP Areas.									

000233

EID077262

438300DJV

AR226 - 1471

3

November 24, 1980

TO: R. J. BURGER
C. R. CAMPBELL
D. A. ERDMAN

FROM: PAUL THISTLETON 

COMMUNICATING RESULTS OF BLOOD ANALYSES

Details of recent blood analyses are given in my 11/19/80 letter to R. J. Burger (copy attached). Results of August 1979 samples have been multiplied by 1.25 in Table I for comparison with August 1980 results obtained by the C-8/GC method (compare lined columns). We believe that this adjustment is required for proper comparison.

People sampled in 1979 were given results in Columns 1 and 2 using standard medical cards. We plan to report the C-8/GC results in column 6 in the same way. Some explanation of the increased values resulting from the C-8/GC analyses will be required. It appears that this can best be handled by Dr. Power on an individual basis. He may use the attached statement for background but it will not be distributed.

When the results in column 2 are multiplied by 1.25 (see column 3) there is generally good agreement with the recent C-8/GC results (column 6). Perhaps there is a significant increase for No. 16 (a fine powder dryer operator). The value reported for No. 17 in 1979 was recognized to be unusually low and may have been inaccurate. Three of the FEP people (Nos. 19, 23 and 24) show little change between the August 1979 (column 2) and August 1980 C-8/GC results (column 6).

Attachments

PT/nsw

AIPO01326

EID080726

000234

CC: R. J. Burger
J. F. Doughty
T. L. Schrenk

November 19, 1980

TO: DR. Y. L. POWER

FROM: PAUL THISTLETON 

RESULTS OF BLOOD ANALYSES

The blood sampling program proposed in my 8/1/80 letter is essentially complete. All samples have been analyzed by the C-8/GC method which was recommended for routine use in my 11/12/80 letter to R. J. Burger. Most of the samples have been analyzed by the Torch method at ESL and some have been measured by the Torch method at Jackson Laboratory (JL). Samples were sent to JL because of delays in demonstrating satisfactory Torch performance at ESL.

Results are given in Table I. It includes the 1979 data which was reported to the people sampled. Names of people sampled in 1980 and identification numbers used in Table I are given in the enclosed list (Dr. Y. L. Power, only). One person is omitted from Table I because results were variable and a resample is being requested.

The ESL and JL Torch results agree very well. The C-8/GC results are about 125% of the Torch results (see Figure 1 of my 11/12/80 letter). The difference may result from incomplete recovery in the Torch method and this is being checked at ESL and JL.

My 11/12/80 letter recommended that only C-8/GC results should be reported to employees. We believe that they are the best available measurements of organic fluorine in blood samples. The August, 1979, results given in Table I have been multiplied by 1.25 which is suggested as the basis for comparing these results with current C-8/GC results (see my 11/17/80 letter to R. J. Burger, copy attached). In most cases the numbers are very similar and it is doubtful if any of the apparent changes are statistically significant. This can be established when the total sampling program is completed and more 1979/1980 comparisons are possible.

ALP001327

000235

EID080727

NOVEMBER 19, 1980

In the meantime I conclude that there has been no significant decrease in organic fluorine in blood samples between August, 1979 and August, 1980. This may be because many of our corrective measures were functioning for only a small part of the year. Our 1980 data using the C-8/GC method, which is specific, should provide a good basis for comparing data to be obtained in 1981.

Attachment

PT/nsw

AJP001328

EID080728

000236

TABLE I

COMPARISON OF BLOOD ANALYSES

<u>IDENTIFICATION NUMBER</u>	<u>1979 SAMPLES BOMB ANALYSIS - JL (1)</u>			<u>AUGUST 1980 SAMPLES TORCH ANALYSIS - C-8/GC</u>		
	<u>ppm Organic Fluorine</u>			<u>ppm Organic Fluorine</u>		
	<u>JUNE</u>	<u>AUGUST</u>	<u>AUGUST X 1.25 (2)</u>	<u>ESL</u>	<u>JL</u>	<u>ESL</u>
	<u>-1-</u>	<u>-2-</u>	<u>-3-</u>	<u>-4-</u>	<u>-5-</u>	<u>-6-</u>
<u>No Direct Exposure</u>						
1		-	-	0.24		0.022
2		-	-	-		0.015
<u>Professionals</u>						
3		-	-	0.03		0.22
4		-	-	0.44		0.40
5		-	-	-		0.19
6		0.45	0.56		0.3	0.52
<u>Monomer Operators</u>						
7		0.39	0.49	0.8		0.78
8 (3)		5.3	6.6	5.2		6.4
9 (4)		6.7	8.4	6.5	6.7	8.2
<u>Fine Powder Dispersion</u>						
<u>Zone 6</u>						
10	22.2	21.2	26.5	20.3	21.0	24.0
12	10.6	8.7	10.9	9.7		13.0
13	15.0	13.8	17.3	16.5		21.0
14		20.8	26.0		22.9	29.0
15		1.8	2.3	3.3	3.8	4.6
<u>Zone 4</u>						
16		1.8	2.3	4.6	4.6	5.6
<u>Granular</u>						
<u>Zone 6</u>						
17		0.47	0.59	1.4	1.7	1.9

AJP001329

1979 SAMPLES
BOMB ANALYSIS - JL (1)

AUGUST 1980 SAMPLES
TORCH ANALYSIS - C-8/GC

IDENTIFICATION NUMBER	ppm Organic Fluorine			ppm Organic Fluorine		
	JUNE	AUGUST	AUGUST X 1.25 (2)	ESL	JL	ESL
	-1-	-2-	-3-	-4-	-5-	-6-
<u>FEP Polymerization</u>						
18	1.36	0.99	1.2	1.1		1.5
19		3.7	4.6	3.4		4.0
20	3.61	1.99	2.5	2.9	2.9	3.7
21		4.96	6.2	5.6		6.6
22		4.14	5.2	3.7		5.5
23		4.52	5.7	4.1		4.9
24		2.71	3.4	2.1		2.9
25		4.64	5.8	6.4		7.8
26		0.91	1.1	0.9, 1.1	0.87	1.2
<u>FEP Service</u>						
27				1.1		0.72
<u>Research Semiworks</u>						
28				0.5	0.32	0.26

- (1) JL = Jackson Laboratory
- (2) August, 1979 bomb results increased by 25%. This is the factor recommended to allow comparison of 1979 and 1980 results. ESL C-8/GC results are about 125% of ESL and JL Torch results for the August, 1980 samples. Equivalence of Torch and Bomb results was demonstrated in a study reported by Erik Kissa, Jackson Laboratory, 6/13/80.
- (3) Monomer Operator 21 months, 16 years Polymerization Service.
- (4) Monomer Operator 32 months, 15 years Polymerization Service.

PT
11/19/80

AJP001330

000238

EID080730

November 24, 1980

RESULTS OF BLOOD ANALYSES

A sample of your blood was taken in August for a test program to compare two analytical methods for measuring organic fluorine in blood. The Torch method burns the blood in a special torch and the combustion products are scrubbed and analyzed for fluorine. It measures organic fluorine plus inorganic fluorocompounds that burn in the torch. The C-8/GC method measures the C-8 by gas chromatography (GC) which separates the C-8 from other fluorocompounds.

We believe that C-8/GC results are the best measurements of organic fluorine in blood samples. We plan to use the C-8/GC method for analyzing blood samples because it measures C-8 and is less subject to interference than the Torch method.

We are reporting the C-8/GC measurement for your blood sample expressed as ppm organic fluorine. This method gives results about 25% higher than the method used for the 1979 samples. The difference may result from incomplete recovery of organic fluorine in the 1979 analyses.

If you have questions please contact Medical Division.

Y. L. POWER, M.D.

EID080731

000239

KK



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

W. C. Percival - 353
S. S. Stafford - 269
R. R. Twelves - 353
PRAL File
IC

POLYMER PRODUCTS DEPARTMENT
EXPERIMENTAL STATION

January 23, 1981

TO: PAUL THISTLETON - PPD, Washington Works

FROM: L. J. PAPA *LJP*
772-1765

COMMENTS ON VALIDITY OF 1979 FLUORINE IN BLOOD RESULTS

I have reviewed the 1979 blood fluorine results from Jackson Laboratory (JL) and investigated the entire situation to comment on the validity of the results. The situation is not simple because

1. The values reported were raw data and were not corrected for recovery. The data were obtained by the modified 3M bomb method (private communication with E. Kissa).
2. From data appearing in Kissa's report (CP-JL-80-14, p. 10) issued Sept. 1980, his recovery at that time appears to be ~94%.
3. 3M published a recovery of 92+5%. Belisle and Hagen, Anal. Bio. 87 545-555 (1978).
4. The bomb data correlated 1:1 with the torch data in Kissa's early work (CP-JL-80-14, p. 19-21B) - hence torch recoveries must have also been ~94%.
5. A reagent deteriorated in the modified bomb method causing the 8/79 values to be low by a factor of ~1.18 (Memos, E. Kissa to G. H. Patterson dated 10/30/79 and 11/29/79). This was not discovered and communicated to WW until after the results were given to our employees.
6. A recent study by Kissa shows the torch method, which is allegedly equivalent to the bomb method, gives 83% recovery and is 80% of the value by GC (Ref: my recent letter to you dated 1/23/81).

We are left with these facts

- A. All of the results from August 1979 sampling should have been corrected by a factor of 1.18 to compensate for the deteriorated reagent.

B. An additional correction is necessary to compensate for recovery. That factor is 1.06 if the 94% recovery of Kissa's early work is correct or 1.20 if the later 83% recovery is correct.

I have no way of judging which recovery number is correct. If fact, they both may be correct. He could have started with 94% recovery and drifted to 83% recovery. However, the numbers do allow us to set up boundaries. With the bad reagent and a 94% recovery, the correction factor is 1.25. With a bad reagent and an 83% recovery, the correction factor is 1.41. Results obtained from JL other than the August to October 1979 period do not suffer from the bad reagent contribution and the 1.18 correction factor is not applicable. However, they must still be corrected for recovery. The correction is 1.06 if you believe the 94% recovery, 1.09 if you believe the 92% recovery or 1.20 if you believe the 83% recovery.

I suggest you use the following set of corrections for any data you have in hand:

applies to June 79 samples

• Multiply by 1.09 for all data prior to August 1, 1979 - this uses 3M's recovery of 92% and was suggested by E. Kissa.

This probably covers element in the 79 samples

• For bomb data in the period of August 1, 1979 to October 30, 1979 use a factor of 1.28 - this assumes 92% recovery and corrects for the bad reagent. For torch data in this period use a factor of 1.09.

• For the period November 1, 1979 to early 1980 (1st quarter), assume the recovery was 92% and use a factor of 1.09. The rat dermal study blood analyses were performed in this time period.

• From early 1980 on, GC values or torch values corrected for 83% recovery are used so you have no corrections to make.

*1/0.83 = 1.2
but curve has 1.25 slope*

I hope this letter helps to end the confusion and does not create more. If you have questions please contact me.

fmt

Based on Kissa data

ADP001318

EID080718

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E. I. DU PONT DE NEMOURS & COMPANY

INCORPORATED

WILMINGTON, DELAWARE 19898

S. S. Stafford - 269

R. R. Twelves - 353

PRAL File

I.C.

POLYMER PRODUCTS DEPARTMENT
EXPERIMENTAL STATION

January 23, 1981

TO: PAUL THISTLETON - PPD, Washington Works

FROM: L. J. PAPA *LJP*

SPECIFIC DETERMINATION OF PERFLUOROOCTANOIC ACID IN BLOOD
BY GAS CHROMATOGRAPHY AND COMPARISON TO TORCH METHOD

S. S. Stafford has completed development and study of a gas chromatographic method to specifically determine perfluorooctanoic acid or its salts (including FC 143), hereby defined as C₈, in human or rat blood. The method is sensitive to 7 ppb fluorine and has a precision of $\pm 10\%$ throughout most of the concentration range of 7 ppb to 100 ppm although the precision falls off at the lower ppb range. The method gives comparable results to the Modified Wickbold Torch used by E. Kissa at Jackson Laboratory and duplicated at ESL by R. R. Twelves. The principle differences are the GC method is specific, easier to use, faster, cheaper and much more sensitive. You received a copy of this method on your last visit to our laboratory on January 8, 1981.

DISCUSSION

We compared the C₈-specific GC method to torch methods at ESL (Twelves) and at JL (Kissa) by analyzing 26 human blood samples obtained from Washington Works personnel. This allowed a simultaneous comparison of the two torch methods at ESL and JL. The data is listed in Table I and plotted in Figure 1. A least squares examination of this data (line shown in Figure 1) shows the two torch methods give comparable data and are 79% of the GC numbers. The GC numbers are corrected for recovery but a true recovery study had never been performed on the torch method.

I asked Kissa (JL) to perform a recovery study on this torch method. He later reported (by telephone) that he performed a 5 concentration calibration curve study in aqueous solution from 0.5 to 12.0 ppm fluorine. The slope of his line, or recovery, was 83%. He then spiked two blood samples with 10 ppm C₈ and obtained recoveries of 80 and 84%. I conclude from these data that his recovery is 83%. R. R. Twelves has never performed such a study but indications are that he has a similar recovery. Table II lists the GC data again and the JL torch values corrected for 83% recovery - the agreement is now very good.

AJP001319

S. S. Stafford later analyzed 7 rat blood samples from a Haskell Laboratory C₈ inhalation study that were also analyzed at Jackson Laboratory by the Torch Method (Kissa). These data are listed in Table III and again show good agreement.

These data show that the discussed methods can and did give equivalent results on real blood samples when all are calibrated to compensate for recovery. It should be remembered that interferences may be encountered in the future which could give erroneous answers by either method. This seems less likely with the C₈-specific GC method. For this reason as well as those mentioned in the first paragraph I think our decision to use the C₈-specific GC method is well founded.

Attachments
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TABLE I
Comparison of C₈-Specific GC Method to Torch Methods at ESL and Jackson Lab (JL)

<u>PRAL No.</u>	<u>ppm Fluorine</u>		<u>C₈/GC</u>
	<u>ESL</u>	<u>JL</u>	
80-63841	1.1	--	1.5
80-63838	20.3	21.0	24.
80-63837	1.4	1.7	1.9
80-62921	0.5	0.3	0.26
80-63834	0.03	--	0.22
80-63835	--	0.3	0.52
80-62916	2.1	2.6	2.9
80-62915	ND	0.2	0.015
80-63839	6.5	6.7	8.2
80-62912	0.8	--	0.78
80-62920	1.0	0.87	1.2
80-62919	6.4	6.4	7.8
80-63842	3.4	--	4.0
80-63843	2.9	2.9	3.7
80-63836	0.44	--	0.40
80-62922	3.3	3.8	4.6
80-62918	22.4	22.9	29.
80-63844	5.6	--	6.6
80-62910	9.7	10.3	13.
80-62913	16.5	14.8	21.
80-62911	4.1	--	4.9
80-62917	4.6	4.6	5.6
64330 80-63833 64329	0.24	--	0.022
80-63845	1.1	--	0.72
80-62914	5.2	5.0	6.4
80-63846	3.7	--	5.5

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TABLE II
Comparison of C₈-Specific GC Method to JL Torch - Corrected for 83% Recovery

PRAL No.	ppm Fluorine	
	JL Torch	C ₈ /GC
80-63841	----	1.5
80-63838	25.3	24.
80-63837	2.0	1.9
80-62921	0.4	0.26
80-63834	----	0.22
80-63835	0.4	0.52
80-62916	3.1	2.9
80-62915	0.2	0.015
80-63839	8.1	8.2
80-62912	----	0.78
80-62920	1.0	1.2
80-62919	7.7	7.8
80-63842	----	4.0
80-63843	3.5	3.7
80-63836	----	0.40
80-62922	4.6	4.6
80-62918	28.	29.
80-63844	----	6.6
80-62910	12.4	13.
80-62913	17.8	21.
80-62911	----	4.9
80-62917	5.5	5.6
⁶⁴³³⁰ 80-63833	----	0.022
⁸⁰⁻⁶⁴³²⁹ 80-63840	----	----
80-63845	----	0.72
80-62914	6.0	6.4
80-63846	----	5.5

* *triple*

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TABLE III
Comparison of C₈-Specific GC Method to Torch Method (JL) on Rat Blood

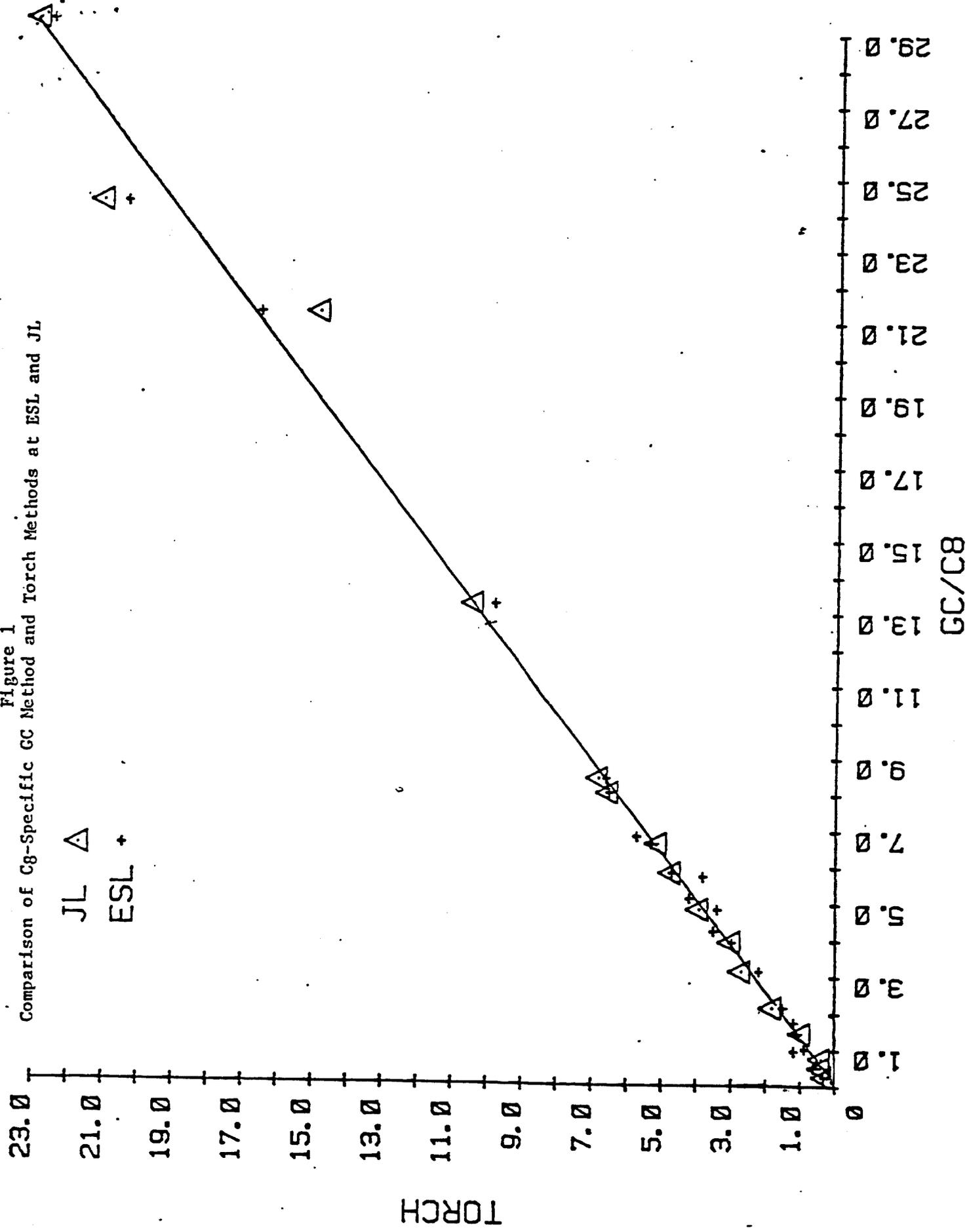
<u>PRAL No.</u>	<u>ppm Fluorine</u>		
	<u>Raw Data</u>	<u>Torch Jackson Lab</u>	
		<u>Corrected for 83% Recover</u>	
			<u>C₈/GC</u>
80-67461	6.9	8.3	7.7
80-67462	10.5	12.7	13.1
80-67752	9.5	11.4	11.4
80-67756	9.0	10.8	8.6
80-67481	1.8	2.2	1.3
80-67460	1.1	1.3	1.1
80-67484 (Blank)	0.76	0.92	<0.007

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Figure 1
Comparison of C8-Specific GC Method and Torch Methods at ESL and JL



- CC: E. D. Champney, Jr. - Wilm.
- A. J. Dahl - ESL
- D. K. Duncan - Wilm.
- L. J. Papa - ESL
- J. W. Raines - Wilm.
- R. J. Burger
- C. R. Campbell
- J. F. Doughty
- D. A. Erdman
- L. W. Goin
- J. G. Loschiavo
- T. L. Schrenk
- R. N. Taylor

February 17, 1981

TO: DR. Y. L. POWER

FROM: PAUL THISTLETON 

CORRECTION OF ORGANIC FLUORINE IN BLOOD RESULTS FOR RECOVERY

The recent comparison of Torch and C-8/GC results for 27 blood samples made at ESL indicated that C-8/GC results were about 25% above uncorrected Torch results. This led to a review of 1979 results (8 samples in June and 78 samples in August, 1979) which is reported in L. J. Papa's January 23, 1980, letter "Comments on Validity of 1979 Fluorine in Blood Results", (copy attached).

Following Papa's recommendations the results obtained by Bomb and Torch methods have been corrected for recovery as indicated below. Bomb data obtained for August, 1979 samples require an additional correction factor of 1.18 to compensate for deterioration of the reagent (#5 in Papa's letter), combining this with 92% recovery gives a correction factor of 1.28.

<u>Sampling Period</u>	<u>Analytical Method</u>	<u>Correction Factor</u>
June, 1979	Bomb	1.09
August, 1979	Bomb	1.28
December, 1979	Bomb	1.09
August, 1980	Torch	1.20

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DR. Y. L. POWER

- 2 -

FEBRUARY 17, 1981

Results are given in Table I. Only the 1979 samples that were repeated in 1980 are included.

There is good agreement between Torch results (Columns 5 and 6) and C-8/GC results (Column 7) which were obtained on the same samples. There is no obvious trend of results with time. A better comparison, including statistical analysis, will be possible when the rest of the 78 people sampled in 1979 have been tested. We expect that their blood will be analyzed only by the C-8/GC method. Their uncorrected 1979 results which were reported to them should be increased by 28% to allow comparison with C-8/GC results.

Attachment

PT/nsw

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ALP002520

TABLE I
COMPARISON OF BLOOD ANALYSES

IDENTIFICATION NUMBER	1979 SAMPLES BOMB ANALYSIS - JL (1)				AUGUST 1980 SAMPLES TORCH ANALYSIS C-8/GC		
	ppm Organic Fluorine				ppm Organic Fluorine		
	JUNE	JUNE X 1.09	AUGUST	AUGUST X 1.28	ESL (2)	JL	ESL
	-1-	-2-	-3-	(-4-)	-5-	-6-	(-7-)
<u>No Direct Exposure</u>							
1 ✓							
2 ✓					0.29		0.022
						0.2	0.015
<u>Professionals</u>							
3 ✓							
4 ✓					0.04		0.22
5 ✓					0.53		0.40
6 ✓			0.45	0.58		0.4	0.19
							0.52
<u>Monomer Operators</u>							
7 ✓							
8 ✓			0.39	0.50	1.0		0.78
9 ✓			5.3	6.8	6.2	6.0	6.4
			6.7	8.6	7.8	8.1	8.2
<u>Fine Powder Dispersion</u>							
<u>Zone 6</u>							
10 ✓	22.2	24.2	21.2	27.1	24.4	25.3	24.0
12 ✓	10.6	11.6	8.7	11.1	11.6	12.4	13.0
13 ✓	15.0	16.4	13.8	17.7	19.8	17.8	21.0
14 ✓			20.8	26.6		28.0	29.0
15 ✓			1.8	2.3	4.0	4.6	4.6
<u>Zone 4</u>							
16 ✓			1.8	2.3	5.5	5.5	5.6
<u>Granular</u>							
<u>Zone 6</u>							
17 ✓			0.47	0.60	1.7	2.0	1.9

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1979 SAMPLES
BOMB ANALYSIS - JL (1)

AUGUST 1980 SAMPLES
TORCH ANALYSIS C-8/GC

IDENTIFICATION NUMBER	ppm Organic Fluorine				ppm Organic Fluorine							
	JUNE	JUNE	AUGUST	AUGUST	ESL (2)	JL	ESL					
	-1-	X 1.09	-3-	X 1.28	-5-	-6-	-7-					
<u>FEP Polymerization</u>												
18 ✓	1.36	1.5	0.99	1.3	1.3	3.5	1.5					
19 ✓								3.7	4.7	4.0		
20 ✓								3.61	1.99	2.5	4.1	4.0
21 ✓								3.9	4.96	6.3	3.5	3.2
22 ✓									4.14	5.3	6.7	6.6
23 ✓									4.52	5.8	4.4	5.5
24 ✓									2.71	3.5	4.9	4.9
25 ✓									4.64	5.9	2.5	3.1
26 ✓		0.91	1.2	7.7	7.7	7.8						
<u>FEP Service</u>												
27 ✓					1.1		0.72					
<u>Research Semiworks</u>												
28 ✓					0.5	0.4	0.26					

- (1) JL = Jackson Laboratory
- (2) ESL = Experimental Station Laboratory

Notes on Columns

- 1- Part of first WW sampling (total of 8 samples). Data in this column is enclosed in a block to indicate that it should not be compared with corrected data.
- 2- Column -1- X 1.09 correction factor.
- 3- Part of second WW sampling (total of 78 samples, including resample of original 8 samples). Data in this column is enclosed in a block to indicate that it should not be compared with corrected data.
- 4- Column -3- X 1.28 correction factor.
- 5- August 1980 sampling for comparison of analytical methods (total of 28 samples)* analyzed by Torch method at ESL. Results corrected for 83% recovery demonstrated for Torch method by E. Kissa, Jackson Laboratory.
- 6- August 1980 sampling for comparison of analytical methods analyzed by Torch method at Jackson Laboratory. Results corrected for 83% recovery.
- 7- August 1980 sampling for comparison of analytical methods analyzed by C-8/GC method at ESL. 100% recovery assumed.

Correction factors and recovery are taken from L. J. Papa's letter "Comments on Validity of 1979 Fluorine in Blood Results", 1/23/81.

* Sample No. 11 is not reported because unusually large variation in results was found. Analysis will be made on a new sample.

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PT
2/17/81

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NN

CC: E. D. Champney, Jr. - Wil
A. J. Dahl - ESL
D. K. Duncan - Wilm
L. J. Papa - ESL
J. W. Raines - Wilm.
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C. R. Campbell
J. R. Doughty
D. A. Erdman
L. W. Goin
J. G. Loschiavo
T. L. Schrenk
R. N. Taylor

March 6, 1981

TO: DR. Y. L. POWER

FROM: PAUL THISTLETON *PT*

CORRECTION OF ORGANIC FLUORINE IN BLOOD RESULTS
FOR RECOVERY

Ref: Letter Thistleton to Power, same topic,
dated 2/17/81.

In the above referenced letter an error was made on page two of the attachment. Please let this letter serve to correct this error.

Attachment - Page Two - Notes on Columns - -7-

Note -7- should read as follows:

-7- August 1980 sampling for comparison of analytical methods analyzed by C-8/GC method at ESL. Correction for recovery is included in the method with an internal standard calculation giving 100 + or - 5% (relative standard deviation) for spiked samples.

NOTE: New or corrected information has been underlined for clarity.

PT/nsw

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