Attachments to Letter to C. Auer dated May 4, 2000
Perfluoroctane Sulfonate Studies

Pharmacokinetic Studies

1) Skin Absorption Studies on Surfactants (1983)

   a) Report from W. C. McCormick to D. R. Ricker, dated September 26, 1983 summarizing data

   b) 28 Day Percutaneous Absorption Study in Rabbits with FC-95, Safety Evaluation Laboratory, Riker Laboratories, Inc., Experiment No. 0979AB0632 (FC-95)

   c) 28 Day Percutaneous Absorption Study in Rabbits with FC-99, Safety Evaluation Laboratory, Riker Laboratories, Inc., Experiment No. 0979AB0633, 3M Reference No. T-3988.1 (FC-99, diethanolamine salt of perfluorooctanesulfonate, assumed to be 25 % in water)

2) Single-Dose Intravenous Pharmacokinetic Study of T-6053 in Rabbits, 3M Environmental Laboratory (FC-99, diethanolamine salt of perfluorooctanesulfonate in water Lot 130, Unit 177. 0.04 % FC solids in water), November 16, 1995. Final Report - Analytical Study, which includes copy of *in vivo* Study No. AMDT-010495.1, Hazleton Wisconsin, Inc., Project No. HWI 6329-136, 3M Reference No. T-6053.1

3) Single-Dose Dermal Absorption / Toxicity Study of T-6053 in Rabbits, 3M Environmental Laboratory, Study No. AMDT-022195.1 (FC-99, diethanolamine salt of perfluorooctanesulfonate in water Lot 130, Unit 177. 0.04 % FC solids in water), November 22, 1995. Final Report - Analytical Study, includes *in vivo* Study Hazleton Wisconsin, Inc., Project No. HWI 6329-137, 3M Reference No. T-6053.2

4) Fluorochemical (FC) Levels in Naïve Rats, 3M Medical Department, Toxciology Services, Study No. T-6316.9, DT21, Draft Report for Objective 3, May 14, 1999.

5) Analytical Data submitted to Dr. Jennifer Seed, USEPA, by letter dated May 3, 2000, including serum measurements from two in-life studies:

   a) Analytical data from Advanced Bioanalytical Services Study No. FACT-TOX-111, with respect to Oral (Gavage) Pharmacokinetic Recovery Study of Perfluorooctane Sulfonate in Rats, Argus Laboratories Protocol No. 418-015, 3M Reference T-6295.14.

b) Analytical data from Advanced Bioanalytical Services Study No. FACT-TOX-110., with respect to Oral (Gavage) Pharmacokinetic Study of Perfluorooctane Sulfonate in Rats, Argus Laboratories Protocol No. 418-013, 3M Reference T-6295.12.

6) In Vitro Comparative Metabolism Study in Rat and Human Hepatocytes with Various Fluorochemicals, 3M Reference T-6295.1, study of T-6292 (N-ethyl FOSE), T-6293 (N-ethyl FOSE monophosphate ester), T-6294 (N-ethyl perfluorooctane sulfonamide), and T-6295 (Perfluorooctane Sulfonate)

a) Range-finding Cytotocity Assay, SRI International Toxicology Laboratory, Study No. B010-95 – protocol and faxed results dated Oct. 26, 1995, Dec.12, 1995, and Jan. 16, 1996

b) Metabolism of T-6292, T-6293 , T-6294, T-6295 by Rat and Human Hepatocytes, SRI International Toxicology Laboratory, Study No. B011-95

c) Advanced Bioanalytical Services, Inc., Analytical Report, Additional Characterization of Metabolites of T-6292, T-6293 and T-6294 from Rat and Human Hepatocytes by TurboIonSpray LC/MS and LC/MS/MS. Semi-Quantitative Analysis of T-6295 in Rat and Human Hepatocytes Incubated with T-6292, T-6293 and T-6294 by LC/MS/MS, January 28, 1998, Report 98AGKP01.3M

d) Working Interpretation of Results, chart entitled Perfluorosulfonamide Metabolism in Rat vs. Human Hepatocytes, updated Feb. 5, 1998 based on ABS Jan. 1998 report

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To: D. R. RICKER - COMMERCIAL CHEMICALS DIVISION - 236-2B-01

From: W. C. MC CORMICK - MEDICAL, TOXICOLOGY SERVICES - 220-2E-02

Subject: Skin Absorption Studies on Surfactants

Date: September 26, 1983

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Attached are the final reports from Riker Safety Evaluation Laboratory on the dermal toxicity and absorption studies conducted on FC-95, FC-98, FC-99, FC-128, FC-129, FC-134 and FC-135.

Each study was conducted in the following manner. Following a range finder study from which doses were selected, ten male and ten female rabbits were clipped free of hair and the test article was place on 40% of the total body surface area. An impervious plastic sheet occluded the skin for 24 hours after which time the test article was removed. Animals were maintained and observed for a 28 day period. Blood samples were obtained on days 1, 7, 14 and 28. Analysis of day 1 and 28 fluorine levels were made for a single male and female for each compound. Initial, 7, 14 and 28 day body weights were recorded. Surviving animals were sacrificed and necropsied on day 28.

FC-95: Two doses were used in the rangefinder study: 5,000 mg/kg and 1,000 mg/kg. No deaths or pharmacotoxic signs were observed at either dose. The higher dose level was chosen for the full study. FC-95 was applied as a suspension in water at 5,000 mg/kg. Hyperactivity was noted in 5/10 males only at day 6. All animals recovered by day 7 and remained asymptomatic throughout the study period. Weight gains were observed for all rabbits. No visible lesions were noted at necropsy.

Analysis of day 1 and day 28 blood fluorine (total) levels showed:

	Total F, ppm	
	Day 1	Day 28
Male	10.3	130.2
Female	0.9	128.0

FC-95 appears to be absorbed through the skin but is not toxic at high dermal doses. FC-95 can be considered practically non-toxic dermally.

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FC-98: Two doses, 5,000 and 1,000 mg/kg were used in the rangefinder study. The compound was dosed as a suspension in water. No pharmacotoxic signs were noted. In the full study the 5,000 mg/kg dose was used. No pharmacotoxic signs were observed. One female died as a results of a technician handling error. At necropsy, no gross lesions were noted. Blood fluorine levels were:

	Total F, ppm	
	Day 1	Day 28
Male	271.9	94.3
Female	226.4	93.1

FC-98 appears to be absorbed and eliminated to some extent. The acute dermal LD_{50} is greater than 5 g/kg. FC-98 can be considered practically non-toxic dermally.

FC-99: Three doses were used in a rangefinder study for FC-99, 5000-, 2000- and 1000 mg/kg. No adverse signs were seen at any dose level. The 5,000 mg/kg dose was used in the full study. FC-99 is a liquid and was applied undiluted to the skin. No significant reactions or pharmacotoxic signs were noted. There were no deaths. Weight gains were normal. At necropsy no observable lesions were noted. Total blood fluorine levels were:

	Total F, ppm	
	Day 1	Day 28
Male	129.1	73.5
Female	42.5	111.5

FC-99 appeared to have been slightly absorbed without apparent toxic effects. The acute dermal LD_{50} is greater than 5 g/kg. FC-99 is considered practically non-toxic dermally.

FC-128: Three dose levels were used on the rangefinder, 5,000-, 2,000- and 1,000 mg/kg with 0/4, 1/4, and 0/4 deaths respectively. Because of the death at 2,000 mg/kg it was chosen as the dose level for the full study. The material was applied as a suspension in water. No pharmacotoxic signs were observed. There were no deaths. Weight gains were noted in all males but 3/10 females lost weight over the study period. No visible lesions were noted at necropsy. Blood fluorine levels were:

	Total F, ppm	
	Day 1	Day 28
Males	1.6	10.5
Females	4.4	16.5

FC-128 appears to be relatively poorly absorbed and is non-toxic at 2,000 mg/kg. The acute dermal LD_{50} is greater than 2 g/kg.

FC-129: Three dose levels were used in the rangefinder, 5,000-, 2,000- and 1,000 mg/kg. The 5,000 mg/kg dose was used in the full study. The material was applied undiluted. The dose elicited a variety of pharmacotoxic signs: lethargy, prostration and hypoactivity. Five female rabbits died within 3 days of dosing. One male died after 2 days. Necropsies of those dying acutely revealed pale mottled livers and blood in the urine in the bladder. In general, survivors showed no lesions at necropsy (one rabbit had an atrophic spleen). Blood Fluorine levels were:

	Total F, ppm	
	Day 1	Day 28
Male	11.4	23.3
Female	26.1	69.6

Given the obvious toxic response of those animals to FC-129 the blood fluorine levels are not particularly revealing. The acute dermal LD_{50} (female rabbits) is 5 g/kg. For males it is greater than 5 g/kg. FC-129 can be considered slightly toxic dermally.

FC-134: Three doses were used in the rangefinder: 5,000-, 2,000- and 1,000 mg/kg. The material was applied as a suspension in water. There were no deaths or pharmacotoxic signs at any dose. The full study used the 5,000 mg/kg application. As with the rangefinder no pharmacotoxic signs were observed. One death occurred as a result of a technician handling error. Weight gains were noted for all animals. No visible lesions were noted at necropsy. Blood fluorine levels:

	Total F, ppm	
	Day 1	Day 28
Males	18.8	23.9
Females	0.2	18.1

FC-134 seems poorly absorbed through the skin. The acute dermal LD_{50} is greater than 5 g/kg. FC-134 can be considered non-toxic

dermally.

FC-135: Three dose levels were used in the rangefinder, 5,000-, 2,000- and 1,000 mg/kg. The material was applied undiluted to the skin. No pharmacotoxic signs were observed at any dose. 5,000 mg/kg was used in the full study. No pharmacotoxic signs or deaths were seen. Weight gains were noted for all females and 8/10 males. Two males lost weight during the first week after dosing and failed to gain back to their initial weight. At necropsy no visible lesions were observed. Blood fluorine levels were:

	Total F, ppm	
	Day 1	Day 28
Male	2.3	7.6
Female	6.9	20.8

FC-135 seems relatively poorly absorbed dermally. The acute dermal LD_{50} is greater than 5 g/kg. FC-135 can be considered practically non-toxic dermally.

Bill McCormick

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Attachments