- RESTRICTED -

DRAFT

# HEALTH HAZARD SUMMARY OF PERFLUOROOCTANE SULFONIC ACID, POTASSIUM SALT AS REPRESENTED BY FC-95

## Identity and Composition

| | |
|---|---|
| **Material Names** | 1-Octanesulfonic acid, heptadecafluoro-, potassium salt; FC-95 FLUORAD Brand Fluorochemical Surfactant; L-1159 |
| **Folder Numbers** | 12234, T-2014, T-3351, T-4979, T-5142, T-1117, T-1389, T-2306 |
| CAS Number | 2759-39-3 |
| Formula | $C_8F_{17}OSO_2^-K^+$ |
| Purity (of FC-95) | 82-86% [1] |
| Impurities (in FC-95) [1] | Potassium perfluorohexane sulfonate [3871-99-6] 3-8%<br>Potassium perfluorobutane sulfonate [29420-49-3] 3-7%<br>Potassium perfluoropentane sulfonate [60270-55-5] 2-6%<br>Potassium perfluoroheptane sulfonate [3872-25-1] 1-3% |

## Exposure and Use

| | |
|---|---|
| **Primary Uses** | Wetting and foaming agent [18] |
| **Production Volume** | No data found |
| **Where made/used** | Cottage Grove, Decatur |
| **Workers Exposed** | No data found |
| Air Monitoring Data | Long-term breathing zone samples of 2 Cottage Grove workers in 1993 showed FC-95 concentrations of 1.42 and 0.45 $mg/m^3$, respectively. An area sample in the Cottage Grove mixing and milling area indicated a concentration of 0.04 $mg/m^3$ [26]. |
| Biol. Monitoring | Serum samples from 5 Decatur employees were found to contain perfluorohexane sulfonate (~ 0.57 ppm), perfluoro-octane sulfonate (~ 5.35 ppm) and perfluorooctanoate (~1.79 ppm) [17]. |
| Customer Exposure | No data found |
| Exposure Limits | 0.1 mg/m3 (skin) 8-hr TWA [1] |

Exhibit 1418
State of Minnesota v. 3M Co., Court File No. 27-CV-10-28862

## Physicochemical Properties

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|---|---|
| **Physical State** | Free-flowing powder, light colored [1] |
| **Particle Size** | No data found |
| **Melting Point** | ca. 240°C [23]; decomposes at 390°C [18] |
| **Boiling Point** | Not applicable |
| **Specific Gravity** | ca. 0.6 [1] |
| **Molecular Weight** | 538.1 (for the $C_8$ salt) |
| **Vapor Pressure** | No data found |
| **Water Solubility** | 0.2 g/100 g [18] |
| **Lipid Solubility** | No data found |
| **Other Solubility** | < 0.1 g/100 g in 37% HCl, 40% $HNO_3$, 50% $H_2SO_4$ and 10% NaOH [18] |
| Octanol:Water Partition Coefficient | 10 [23] |
| **Dissoc. Constant** | $pK_a < 1$ [24] |
| **pH in water** | 7.0 - 8.0 (0.1% aq. soln.) [1] |
| **Reactivity** | No data found |
| **Conversion Factor** | Not determined |

## Toxicokinetics

**Absorption:** At least 95% of a single oral dose of [$^{14}$C]FC-95 administered to male rats was absorbed within 24 h [15]. The radiochemical purity of the [$^{14}$C]FC-95 used in this and the other radiolabel studies listed below was ≥ 99% [19].

After a single, 24-hour occluded dermal exposure to FC-95 at a dose of 5000 mg/kg, total serum fluorine concentrations were 0.9 and 10.3 ppm, respectively, for female and male albino rabbits. Serum concentrations 28 days after dosing had risen to 128.0 and 130.2 ppm for females and males, respectively [5].

**Distribution:** Single i.v. doses (mean 4.2 mg/kg) of [$^{14}$C]FC-95 in 0.9% NaCl were administered to male rats. At 89 days after dosing, mean tissue $^{14}$C concentrations (expressed as μg FC-95 equivalents/g tissue) were: liver, 20.56; plasma, 2.21; kidney, 1.09; lung, 1.06; spleen, 0.51; bone marrow, 0.46; RBC, 0.45; adrenals, 0.41; testes, 0.36; skin, 0.35; muscle, 0.29; subcutaneous fat, 0.20; eye, 0.16; abdominal fat, ≤ 0.08; and brain, < 0.05 [7].

Liver, plasma and RBC $^{14}C$ levels were markedly reduced in male rats administered cholestyramine (~ 2.7 g/kg/d) in their diet following single i.v. doses of [$^{14}C$]FC-95 [8].

**Metabolism:** Preliminary data from analysis of urine, feces and tissues of rats as well as the inherent stability of perfluorinated anions suggest that FC-95 is not metabolized [24].

**Excretion:** Single i.v. doses (mean 4.2 mg/kg) of [$^{14}C$]FC-95 in 0.9% NaCl were administered to male rats. By 89 days after dosing, 30.2% of the administered $^{14}C$ had been excreted in the urine and 12.6% had been excreted in the feces [7].

Fecal and total excretion of $^{14}C$ were markedly increased in male rats administered cholestyramine (~ 2.7 g/kg/d) in their diet following single i.v. doses of [$^{14}C$]FC-95. The results suggest that there was significant enterohepatic circulation of FC-95 [8, 24].

Biological Half-life: The plasma elimination half-life of $^{14}C$ following single oral administration of [$^{14}C$]FC-95 (mean dose 4.2 mg/kg) to male rats was 7.5 days [15].

## Acute Toxicity

**Oral:** LD50, rat: 1.25 - 2.5 g/kg (aqueous suspension of FC-95, T-1389) [3].

LD50, rat: 251 mg/kg (20:80 acetone:corn oil suspension of FC-95, Lot 640). Clinical signs included diarrhea, hypoactivity, decreased limb tone, ataxia, corneal opacity, high carriage, ptosis, piloerection, prostration and tremors [4].

Single 250 mg/kg doses of an aqueous suspension of FC-95 (Lot 640) were administered by oral gavage to 6 male and 6 female rats. Two animals of each sex were sacrificed and necropsied at 4, 24 and 48 hours after dosing. Blood, urine, feces, liver, kidney, brain and bone marrow samples were collected and returned to the sponsor for analysis. No deaths or gross lesions were observed [16]. (The samples were reportedly sent to Jon Belisle but results of the sample analyses were not found.)

**Dermal:** LD50, rabbit > 5000 mg/kg (aqueous suspension of FC-95, Lot 646). No deaths occurred during the 28-day observation period. Hyperactivity in 5/10 males was observed on day 6. Body weights were lower at 7 days but increased thereafter. No visible lesions were noted on necropsy. Total serum fluorine concentrations were 0.9 and 10.3 ppm, respectively, for females and males 1 day after dosing and 128.0 and 130.2 ppm, respectively, 28 days after dosing [5].

**Inhalation:** 1-Hour LC50, rats: 5.2 mg/L (FC-95, T-2306CoC). Clinical signs included red nasal discharge, dry rales, breathing difficulty, hypoactivity, lacrimation, salivation, hair loss, loss of righting reflex, sensitivity to touch, cold extremi-

ties, ataxia, convulsions, tremors and seisures. Weight losses occurred prior to death and weight loss or reduced weight gain occurred in all surviving animals. Lung and liver discoloration were the most frequent necropsy findings. The respirable fraction or size distribution of the sample was not reported [6].

**Other:** No data found

## Primary Irritation

**Ocular:** FC-95 (T-1117) was minimally irritating to the eyes in a standard Draize test in rabbits. The maximum primary eye irritation score was 9.3 out of a possible 110.0. Effects were limited to the conjunctivae [2].

**Dermal:** FC-95 (T-1117) was non-irritating to intact or abraded skin sites in a standard Draize test in rabbits. The primary skin irritation score 0.0 out of a possible 8.0 at each observation time [2].

**Respiratory:** No data found

## Sensitization

**Dermal:** No data found

**Respiratory:** No data found

## Genotoxicity

**Gene Mutation:** FC-95 (T-2014CoC) was not muagenic in *Salmonella typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98, TA-100 or in *Saccharomyces cerevisiae* strain D4 in a standard plate incorporation assay with or without metabolic activation [9].

**Chromosomal Effects:** No data found

**Other:** No data found

## Subchronic Toxicity

**90-Day Oral Toxicity in Rats**

FC-95 was administered in the diet for 90 days to groups consisting of 5 male and 5 female Sprague Dawley rats. Doses were 0 (control), 30, 100, 300, 1000 and 3000 ppm. All animals in the 300, 1000 and 3000 ppm dose groups and 3 animals

in the 100 ppm dose group died during the study. Significant treatment-related effects (and LOELs) included: weight loss, elevated plasma glutamate-pyruvate transaminase, elevated plasma glutamate-oxalacetate transaminase and liver discoloration (30 ppm); increased sensitivity to external stimuli, red material around the eyes or mouth, decreased food consumption, elevated plasma creatinine phosphokinase, alkaline phosphatase, blood glucose and blood urea nitrogen, decreased hemoglobin, hematocrit, erythrocyte count, reticulocyte count (in females) and leucocyte count, liver enlargement, necrosis and hepatocellular hypertrophy and stomach discoloration and hemorrhage (100 ppm); emaciation, convulsions, stomach mucosal hyperkeratosis, bone marrow hypocellularity, thymic follicular atrophy, splenic lymphoid follicular atrophy, atrophy of mesenteric lymph nodes, atrophy of villi in small intestines, skeletal muscle atrophy and dermal acanthosis and hyperkeratosis (300 ppm); hunched posture (1000) and hypoactivity (3000). Liver effects were more prevalent in males. A NOAEL was not identified in this study [13]. (1978)

**Repeated Dose Oral Toxicity in Monkeys**

FC-95 was administered daily by oral gavage to groups consisting of 2 male and 2 female rhesus monkeys. Doses were 0 (control), 10, 30, 100 and 300 mg/kg/day. All animals receiving FC-95 died by day 20. Clinical signs included anorexia, hypoactivity, emesis and occasional diarrhea. Just prior to death the animals exhibited general body trembling, twitching, convulsions and prostration [20]. (1978)

**90-Day Oral Toxicity in Monkeys**

FC-95 suspended in water was administered daily for 90 days by oral gavage to groups consisting of 2 male and 2 female rhesus monkeys. Doses were 0 (control), 0.5, 1.5 and 4.5 mg/kg/day. All animals in the highest dose group died or were sacrificed *in extremis* by week 7. Significant treatment-related effects (and LOELs) included: anorexia, emesis, diarrhea and decreased serum alkaline phosphatase (0.5 mg/kg/day); hypoactivity, trembling and weight loss (1.5 mg/kg/day); black or bloody stool, dehydration, rigidity, convulsions, prostration, decreased serum cholesterol, diffuse lipid depletion of adrenals, atrophy of pancreatic exocrine cells and atrophy of submandibular salivary gland serous alveolar cells (4.5 mg/kg/day). No gross lesions were noted at necropsy and there were no significant organ weight variations from controls. A NOAEL was not identified in this study [14]. (1978)

## Chronic Toxicity and Carcinogenicity

No data found

## Reproductive and Developmental Toxicity

**Oral Developmental Toxicity in Rats (Pilot Study)**

FC-95 (T-3551) in corn oil was administered by oral gavage to groups of 6-7 pregnant rats on days 6-15 of gestation. Doses were 0 (control), 1, 5, 10 and 20

mg/kg/day. Maternal body weights and food consumption in the two highest dose groups were significantly reduced compared to controls. All dams in the high dose group died before day 20. Clinical signs in surviving dams included hunching, rough haircoat, tremors, convulsions, prostration and anorexia. No consistant treatment-related teratogenic or embryotoxic effects were observed [11].

**Oral Developmental Toxicity in Rats**
FC-95 (T-3351) in corn oil was administered by oral gavage to groups of 25 pregnant rats on days 6-15 of gestation. Doses were 0 (control), 1, 5, and 10 mg/kg/day. Maternal body weights and food consumption in the two highest dose groups were significantly reduced compared to controls. Two dams in the high dose group died before day 20. Clinical signs in surviving dams included hunching, thinness, alopecia, rough haircoat, anorexia. Gastrointestinal lesions were noted in the high-dose dams. Treatment-related fetal effects included: increased resorptions and fetal death, decreased fetal body weight, delayed skeletal ossification, cleft palate, subcutaneous edema and cryptorchism (undescended testicles). These effects occurred primarily in the high-dose group. The maternal and fetal NOAELs for this study were both 1mg/kg/day [12]. (1983)

**Oral Developmental Toxicity in Rats**
FC-95 in corn oil was administered by oral gavage to groups of pregnant rats on days 6-15 of gestation. Doses were 0 (control), 1, 5 and 10 mg/kg/day. Animals were sacrificed on day 20. Maternal body weights in the high dose group were significantly reduced compared to controls. No significant treatment-related teratogenic or embryotoxic effects were observed. Observed fetal lens abnormalities were subsequently interpreted to be artifacts of the tissue sectioning procedure [10].

## Mechanistic Studies

Perfluorooctane sulfonic acid has been demonstrated to cause hepatic peroxisome proliferation in the rat [22].

Male mice administered perfluorooctane sulfonic acid at a concentration of 0.05% w/w in their diet for 5 days exhibited weight loss and increases in each of the following hepatic parameters: relative liver weight (slight), mitochondrial and microsomal protein, palmitoyl-CoA oxidation, catalase in mitochondrial and cytosolic fractions, glutathione transferase, epoxide hydrolase, DT-diaphorase, Ω- and Ω-1-hydroxylation [21].

Treatment of male rats with perfluorooctanesulfonic acid (0.02% in the diet for 7-14 days) caused decreased body weight, increased liver weight, increased liver triacylglycerol, increased liver free cholesterol, decreased liver cholesterol ester, decreased serum cholesterol and triacylglycerols. Hepatocytes isolated from treated rats showed reduced synthesis of cholesterol from acetate, pyruvate and hydroxymethylglutarate but not from mevalonate, increased oxidation of palmitate and reduced fatty acid synthesis. Activities of liver hydroxymethyl glutaric acid-

CoA reductase and acyl-CoA:cholesterol acyltransferase were reduced. These results suggest that the hypolipemic effect of perfluorooctanesulfonic acid may be due to impaired production of lipoprotein particles due to reduced synthesis and esterification of cholesterol together with enhanced oxidation of fatty acids in the liver [25].

## Human Health Effects

No data found

## References


1. 3M Industrial Chemical Products Division. 1992. FC-95 FLUORAD Brand Fluorochemical Surfactant. Material Safety Data Sheet, Document 10-3796-9, St. Paul, MN.
2. Biesemeier, J.A. and Harris, D.L. 1974. Report T-1117. WARF No. 4102871, WARF Institute, Inc., Madison, WI.
3. Gabriel, K.L. 1976. [Acute oral toxicity in rats of T-1389]. Biosearch, Inc., Philadelphia, PA.
4. Dean, W.P., Jessup, D.C., Thompson, G., Romig, G. and Powell, D. 1978. Fluorad® Fluorochemical Surfactant FC-95 acute oral toxicity (LD50) study in rats. Report No. 137-083. International Research and Development Corporation, Mattawan, MI.
5. O'Malley, K.D. and Ebbens, K.L. 1980. 28 Day percutaneous absorption study with FC-95 in albino rabbits. Expt. No. 0979AB0632. Riker Laboratories, Inc., St. Paul, MN.
6. Rusch, G.M. and Rinehart, W.E. 1979. An acute inhalation toxicity study of T-2306CoC in the rat. Project No. 78-7185, Bio/dynamics, Inc.
7. Johnson, J.D., Gibson, S.J. and Ober, R.E. 1979. Extent and route of excretion and tissue distribution of total carbon-14 in rats after a single i.v. dose of FC-95-$^{14}$C. Project No. 8900310200, Riker Laboratories, Inc., St. Paul, MN.
8. Johnson, J.D., Gibson, S.J. and Ober, R.E. 1980. Enhanced elimination of FC-95-$^{14}$C and FC-143-$^{14}$C in rats with cholestyramine treatment. Project No. 8900310200, Riker Laboratories, Inc., St. Paul, MN.
9. Jagannath, D.R. and Brusic, D. 1978. Mutagenicity evaluation of T-2014CoC in the Ames Salmonella/microsome plate test. LBI Project No. 20838, Litton Bionetics, Inc., Kensington, MD.
10. Gortner, E.G., Lamprecht, E.G. and Case, M.T. 1980. Oral teratology study of FC-95 in rats. Expt. No. 0680TR0008, Riker Laboratories, Inc., St. Paul, MN.
11. Wetzel, L.T., Burdock, G.A., Durloo, R.S. and Mistrella, L.H. 1983. Pilot teratology study in rats. Project No. 154-158, Hazleton Laboratories America, Inc., Vienna, VA.
12. Wetzel, L.T., Burdock, G.A., Durloo, R.S. and Colpean, B.R. 1983. Rat teratology study. Project No. 154-160, Hazleton Laboratories America, Inc., Vienna, VA.
13. Goldenthal, E.I., Jessup, D.C., Geil, R.G., Jefferson, N.D. and Arceo, R.J. 1978. Ninety-day subacute rat study. Study No. 137-085, International Research and Development Corporation, Mattawan, MI.

14. Goldenthal, E.I., Jessup, D.C., Geil, R.G. and Mehring, J.S. 1978. Ninety-day subacute rhesus monkey toxicity study. Study No. 137-092, International Research and Development Corporation, Mattawan, MI.

15. Johnson, J.D. and Ober, R.E. 1979. Absorption of FC-95-$^{14}$C in rats after a single oral dose. Project No. 8900310200, Riker Laboratories, Inc., St. Paul, MN.

16. Goldenthal, E.I., Jessup, D.C., Geil, R.G. and Jefferson, N.D. 1979. Metabolism study with FC-95 in rats. Study No. 137-093, International Research and Development Corporation, Mattawan, MI.

17. Anon. 1979. Analysis of selected Decatur employee serum for sulfonic and carboxylic fluorochemicals. Tech. Report No. 723Q, 3M Central Analytical Laboratory, St. Paul, MN.

18. 3M Commercial Chemicals Division. 19xx. Fluorad® Brand Fluorochemical Surfactants FC-95 and FC-98. Technical Information, 3M Company, St. Paul, MN.

19. Johnson, J.D. and Behr, F.E. 1979. Synthesis and characterization of FC-95-$^{14}$C. Project No. 8900310200, Riker Laboratories, Inc., St. Paul, MN.

20. Goldenthal E.I. 1978. Letter to J.E. Long regarding IRDC Study No. 137-087. International Research and Development Corp., Mattawan, MI.

21. Sohlenius, A-K., Eriksson, A.M., Högström, C., Kimland, M. and DePierre, J.W. 1993. Perfluorooctane sulfonic acid is a potent inducer of peroxisomal fatty acid β-oxidation and other activities known to be affected by peroxisome proliferators in mouse liver. *Pharmacol. Toxicol.* 72, 90-93.

22. Ikeda, T., Fukuda, K., Mori, I., Enomoto, M., Komai, T. and Suga, T. 1987. Induction of cytochrome P-450 and peroxisome proliferation in rat liver by perfluorinated octanesulfonic acid. In: *Peroxisomes in Biology and Medicine*, H.D. Fahimi and H. Sies, Eds. Springer Verlag, New York, 304-308.

23. Armstrong, K.E. 1990. Personal communication to M. Hron.

24. Johnson, J.D., Gibson, S.J. and Ober, R.E. 1984. Cholestramine-enhanced fecal elimination of carbon-14 in rats after administration of ammonium [$^{14}$C]perfluorooctanoate or potassium [$^{14}$C]perfluorooctanesulfonate. *Fund. Appl. Toxicol.* 4, 972-976.

25. Haughom, B. and Øystein, S. 1992. The mechanism underlying the hypolipemic effect of perfluorooctanoic acid (PFOA), perfluorooctane sulphonic acid (PFOSA) and clofibric acid. *Biochim. Biophys. Acta* 1128, 65-72.

26. Industrial Hygiene Information System. 1994. 3M Industrial Hygiene Services, St. Paul, MN.

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