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August 9, 2004

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EPA East -- Room 6428 Attention: Section 8(e) Docket
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N. W.
Washington, D. C. 20460

Contain No CBI

Re: TSCA Section 8(e) Supplemental Notice on
Perfluorooctanesulfonate Docket Nos. 8EHQ-1180-374

Dear Sir and Madam:

3M has received final reports for two studies addressing the metabolism of perfluorooctane sulfonyl fluoride (POSF)-based compounds. POSF-based compounds were included in 3M's commercial production phase-out of perfluorooctanyl chemistries completed in 2002. In prior submissions to the Agency, 3M has provided data and other information on the metabolic pathways of the POSF-based compounds that 3M no longer produces for commercial sale.[1] As EPA has recognized based on these submissions, perfluorooctanesulfonate (PFOS) is the "ultimate degradation product" under certain conditions for many of the POSF-derived

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[1] See, e.g., EPA OPPT Docket Nos. 8EHQ-1180-374: Absorption and Biotransformation of N-ethyl FOSE and Tissue Distribution and Elimination of Carbon 14 after Administration of N-ethyl FOSE14C in Feed (N-EtFOSE) (1/19/83); Single Dose Intravenous Pharamacokinetic Study of T-6246 in Rabbits. 3M Environmental Laboratory Study #AMDT-042095.1 (K PFOS) (11/11/95); Repeated Dermal Contact Absorption/Toxicology Study in Rats By Fraunhofer Institute of Toxicology (Draft Report 12/2/02). See also EPA OPPT Docket AR-226: Sulfonated Perfluorochemicals in the Environment: Sources, Dispersion, Fate and Effects (Mar. 1, 2000) (AR-226-0620); The Science of Organic Fluorochemistry (Feb. 5, 2000) (AR-226-0547); Perfluorooctane Sulfonate: Current Summary of Human Sera, Health and Toxicology Data (Jan. 21, 1999) (AR-226-0548).

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chemicals.[2] In addition, a number of published sources also report that POSF and its derivative substances will degrade to PFOS under certain conditions.[3]

The two enclosed studies add to this body of knowledge and are briefly described below:

- *Adipate (T-7211) Metabolite Identification in Rats*. In this study, a single five mg/kg dose was administered via oral gavage to two male and two female Sprague Dawley rats. The following fluorochemicals were quantified in the liver and serum: PFOS, perfluorooctanesulfonamide (FOSA), perfluorooctanesulfonamido acetate (FOSAA or M556), N-methyl perfluorooctanesulfonamido acetate (M570), and N-methyl-perfluorooctanesulfonamido ethanol (N-MeFOSE). These quantification data indicate that cumulative amounts of PFOS, FOSA, M556, M570 and N-MeFOSE in the rat liver and serum exceeded the cumulative amounts of these monomers present in the dose. These data support the conclusion that the administered adipate polymer was metabolized by the rat to N-MeFOSE in the liver and that further metabolism occurred to M570, M556, FOSA, and PFOS. These data suggest that the adipate polymer was metabolized after a single oral dose, but a definitive conclusion in this regard cannot be drawn based on these data alone.

- *Comparative Molecular Biology of Perfluorooctanesulfonate (PFOS, T-6295), N-ethyl perfluorooctanesulfonamido ethanol (N-EtFOSE, T-6316), N-Ethyl perfluorooctanesulfonamide (N-EtFOSA, T-6868), Perfluorooctanesulfonamido acetate (FOSAA, T-7071), and/or Perfluorooctanesulfonamide (FOSA, T-7132) in Rats and Guinea Pigs following Oral Dosing*. The purpose of this study was to evaluate the potential for peroxisome proliferation in rats and guinea pigs after dosing with PFOS, N-EtFOSE, FOSAA, and FOSA. Adult male and female Sprague Dawley rats and Harlan guinea pigs received oral gavage doses of vehicle control (2% Tween, 80), 40 mg/kg/d (PFOS, either 40 or 60 mg/kg/d N-EtFOSE, or 40 mg/kg/d N-EtFOSA for four days with sacrifice on the fifth day. Male Sprague-Dawley rats received oral gavage doses of vehicle

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2 Perfluoroalkyl Sulfonates; Significant New Use Rule; Final Rule and Proposed Supplemental Rule, 67 Fed. Reg. 11007, 11010 (Mar. 11, 2002); Perfluorooctyl Sulfonates; Proposed Significant New Use Rule, 65 Fed. Reg. 62319, 62325 (Oct. 18, 2000).

3 E.g., Serum Perfluorooctante Sulfonate and Hepatic and Lipid Clinical Chemistry Tests in Fluorochemical Production Employees, 41:9 JOEM (Sept. 1999); Epidemiologic Assessment of Worker Serum Perfluorooctanesulfonate (PFOS) and Perfluorooctanote (PFOA) Concentrations and Medical Surveillance Examinations, 10.1097/01.JOM.000052958_59271.10; Human Donor Liver and Serum Concentrations of Perfluorooctanesulfonate and Other Perfluorochemicals, Vo. xx, No. xx Environmental Science and Technology; Prenatal Window of Susceptibility of Perfluorooctane Sulfonate-Induced Neonatal Mortality in the Sprague-Dawley Rat, Birth Defects Research (Part B) 68:465-471 (2003); Mortality of Employees of a Perfluorooctanesulfphonyl Fluoride Manufacturing Facility, Occup. Environ Med 2003: 60:722-29; Perfluorooctanesulfonate and Other Fluorochemicals in the Serum of American Red Cross Adult Blood Donors, 111: 16 Environmental Health Perspectives (Dec. 2003); Serum Concentrations of Perfluorooctanesulfonate and Other Fluorochemicals in an Elderly Population from Seattle, Washington, Chemosphere 54 (2004) 1599-1611; Biotransformation of N-Ethyl-N-(2-hydroxyethyl)perfluorooctanesulfonamide by Rat Liver Microsomes, Cytosol, and Slices and by Expressed Rat and Human Cytochromes P450. Chem Res Toxicol 17:767-75 (June, 2004).

control (propylene glycol), 160 mg/kg/d FOSAA, or 40 mg/kg/d FOSA for four days with sacrifice on the fifth day. PFOS, N-EtFOSE, FOSA and FOSAA all caused indications of peroxisome proliferation in rats, but not in guinea pigs[4]. Because the observed peroxisome proliferation could be due to parent compound, metabolites, or both, the study also produced analytical data on metabolism. FOSA was determined in the livers of all PFOS-treated animals, including those instances in which group controls had no measurable background PFOS or FOSA. Because FOSA would not be expected to form as a metabolite of PFOS based on the known chemistry of PFOS and the fact that there were several instances of high background levels of FOSA in controls, the potential for metabolism of PFOS to FOSA must be interpreted carefully and after additional study to confirm that FOSA is or is not a metabolite of PFOS. Regardless of origin, FOSA was further metabolized to by formation of the glucuronide conjugate (FOSA N-glucuronide). The analytical data also indicated that N-EtFOSE alcohol gives rise to a range of major and minor metabolites, including N-2-hydroxyethyl-perfluorooctanesulfonamide, N-EtFOSAA, FOSAA, FOSA, FOSA N-glucuronide, and PFOS.

Please contact Andrew Seacat (651-575-3161) if you have any technical questions or if we can provide additional information. For any other assistance, please do not hesitate to contact the undersigned (651-778-4331).

Sincerely,

Katherine E. Reed (9.#.)

Katherine E. Reed
Staff Vice President, Environmental Health and Safety Operations

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[4] For completeness, 3M also is enclosing a related, prior study -- Inter-Species Comparison of Mechanisms Fluorochemical Toxicity Following Interperitoneal Dosing of Perfluorooctanesulfonate (PFOS, T-6295) or Ammonium Perfluorooctaneoate (APFO, T-6889) in Rats and Guinea Pigs and Oral Dosing of N-Ethyl Perfluorooctanesulfonamido Ethanol (N-EtFOSE, T-6316) in Rats – also aimed at addressing the mechanisms by which some fluorochemicals initiate peroxisomal proliferation in rats. This related, prior study indicated that interperitoneal dosing was not the appropriate route of administration and that subsequent studies should be conducted following oral administration.