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Document Processing Center
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Office of Pollution Prevention and Toxics
US EPA
1200 Pennsylvania Avenue NW
Washington DC 20460-0001

RE: TSCA 8(E) SUPPLEMENTAL SUBMISSION:
Docket No. 8EHQ-06-16638

To Whom It May Concern:

In October of 2006 3M notified the EPA that data had been received from a 28-day repeat dose oral toxicity study (gastric lavage) in Sprague Dawley rats conducted on ammonium perfluorobutanoate (PFBA; CASRN 10495-86-0).[1] Ammonium perfluorooctanoate (PFOA; CASRN 3825-26-1) at 30 mg/kg, was included as a positive control/reference material. PFBA was given to male and female rats (20/sex/group) at nominal doses of 0, 6, 30 and 150 mg/kg/day for 28 days. Half of the rats in each group were allowed to recover for 21 days. Endpoints evaluated were: clinical chemistry; hematology; body and organ weights; food consumption; gross and microscopic histology; and functional observations.

As communicated in the October 2006 submission, all tested males receiving the highest dose of PFBA (150 mg/kg-d), and all tested males receiving the positive control dose of 30 mg/kg-d of PFOA demonstrated an absence of pupillary reflex to light stimulation in both eyes.

This supplemental notification relates to histopathological data that are now available. Males receiving 150 mg ammonium PFBA/kg-d experienced an increase in hepatocellular hypertrophy. Males dosed at 30 and 150 mg ammonium PFBA/kg-d also experienced an increased incidence and/or severity of hypertrophy/hyperplasia of the follicular epithelium of the thyroid glands. These effects were not observed at the 6 mg/kg/day dose. The observations had resolved in rats allowed to recover for three weeks.

The hepatocellular hypertrophy and increased incidence and/or severity of thyroid follicular epithelial cell hypertrophy/hyperplasia were also present in both sexes of rats dosed with 30 mg ammonium PFOA/kg-d, but to a slightly higher degree with respect to incidence and severity. In some males treated with PFOA, coagulative necrosis of the liver was present.

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[1] The October 2006 letter mistakenly referred to PFBA as a research and development chemical. Although 3M produced ammonium PFBA as a commercial product historically, such manufacture no longer occurs.

These histological findings were still present in male rats dosed with PFOA after three weeks of recovery.

The hypertrophy/hyperplasia of the follicular epithelium of the thyroid glands most likely reflects an increase in the thyroxine-producing follicular cells in response to feedback mechanisms from putative increased turn-over of thyroxine by the hypertrophic hepatocytes.

By way of further background on this study, we provide the following information. Primary treatment-related effects for PFBA (males only) included increased liver weights and decreases in cholesterol (30 and 150 mg/kg-d), and increased serum K+ and inorganic PO4++ (150 mg/kg-d). These effects did not occur at 6 mg/kg/day, which was the study NOEL.

Effects in male rats receiving PFOA included, reductions in RBC parameters (slight), body weight, weight gain, absolute food consumption (first week), total serum protein, and physical activity and health, and increases in relative feed consumption (2nd week through recovery), albumin, ALT, BUN, ALP, liver weights, and platelets. Females receiving PFOA had increased ALT, albumin, and liver weight, and reduced physical activity and health.

During recovery, liver weight and cholesterol effects in PFBA-treated males resolved, as did the liver weight effects for the PFOA-treated males and females, and PFOA treated rats no longer showed signs of stress. The slight effects on RBCs in PFOA-treated males persisted.

Major differences between male rats given PFBA and PFOA were that PFBA did not affect body weight and did lower cholesterol; whereas, PFOA caused body-weight reduction, reduced physical activity and stress, and slight reductions in RBC-related parameters (likely not adverse).

Preliminary BMDL10 estimates for PFBA-induced liver-weight increase and cholesterol decrease in male rats were 10.5 and 3.4 mg/kg/d, respectively, based on nominal doses. Based on linear low-dose extrapolation of the low dose serum PFBA concentration for males (24,630 ppb), the serum concentration at 3.4 mg/kg-day (BMDL10 for cholesterol decrease in male rats) is estimated at 14,000 ppb. Due to the non-linearity below the low dose, this is likely to be a conservative estimate. Based on linear interpolation between the low-dose and mid-dose serum PFBA concentrations (24,630 ppb and 38,040 ppb) in males, the PFBA serum concentration at 10.5 mg/kg-day (BMDL10 for liver-weight increase in male rats) is estimated to be 32,000 ppb.

The study is on-going at NOTOX Safety and Environmental Research Laboratory. Upon receipt, 3M will forward a copy of the final report to the EPA.

Please contact Deanna Luebker at 651-737-1374 if you have any questions or if we can provide additional information.

Sincerely,

Katherine E. Reed

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