26-Week Capsule Toxicity Study with Perfluorooctanesulfonic Acid Potassium Salt (PFOS) in Cynomolgus Monkeys

Current Summary as of May 4, 2000

The purpose of this study was to identify the earliest clinically measurable biological response from repeated daily exposure to potassium perfluorooctane sulfonate (PFOS) and to correlate this response to serum concentrations for purposes of risk assessment and medical monitoring of exposed populations. Groups of male and female Cynomolgus monkeys received daily doses of 0 (six per sex), 0.03 (four per sex), 0.15 (six per sex), or 0.75 (six per sex) mg/kg/day potassium perfluorooctane sulfonate for 26 weeks by capsule via gastric intubation. Two males and two females in each of the 0, 0.15 and 0.75 mg/kg/day dosed groups were followed for one year after cessation of dosing to observe depuration of compound and reversibility of effects. There were no recovery animals in the 0.03 mg/kg/day dose group. This report covers the 26 weeks of dosing. A separate report will detail the findings from 52 weeks of recovery. Effects occuring in the 0.75 mg/kg/day dose group which are believed to be compound related include: 1) severe illness of two males which died or were sacrificed *in extremis* within the last month of treatment; 2) lower body weight in males and females; 3) increased liver weight and hepatocellular hypertrophy and vacuolation in animals; 4) lowering of serum cholesterol in correlation to increasing serum PFOS levels during treatment; 5) lowered triiodothryonine (T3) values in both males and females; 6) lowered estradiol (E2) levels in males. No significant compound-related effects were observed in monkeys treated with 0.03 or 0.15 mg/kg/day over 26 weeks. Serum PFOS values increased linearly to an average of 18 and 90 in the 0.03 and 0.15 mg/kg/day dose groups, respectively. The increase in serum PFOS in the 0.75 mg/kg/day dose group was not linear during the dosing period and reached an average of 215 ppm after 26 weeks of dosing. Liver PFOS levels averaged 25, 80 and 415 ppm for 0.03, 0.15, and 0.75 mg/kg/day dose groups, respectively. Cholesterol values returned to pre-dose levels within 36 days of recovery, without correlation to serum PFOS. Serum PFOS had an apparent elimination half-life of 275 and 128 days over the first six-months of recovery in the 0.15 and 0.75 mg/kg/day dose groups, respectively. The decrease in total serum cholesterol observed in high-dose animals was confirmed as the earliest measurable clinical response. The lowering of total serum cholesterol occurred only at serum PFOS concentrations greater than 100 ppm. The biological responses observed in this study are consistent with prior rodent and monkey studies with the exception that hepatocellular peroxisome proliferation, as observed in rodents, was not observed in this study. Health effects have not been observed from years of medical monitoring of 3M chemical workers with occupational exposure resulting in average serum concentrations of approximately one to two ppm, and generally less than six ppm (Olsen et al., JOEM Sept., 1999). Therefore, non-occupationally exposed populations with pooled average serum PFOS concentrations that are one to two orders of magnitude lower than average worker serum concentrations (3M, "Perfluorooctane Sulfonate: Current Summary of Human Sera, Health and Toxicology Data", January 21, 1999) have a margin of safety of 10^3 to 10^4 with respect to the first clinically measurable biological response to perfluorooctane sulfonate exposure, cholesterol lowering.