serum and liver levels did not reveal a gender difference in monkeys, but the sample size was very small (N=2). In a 6-month study of male cynomolgus monkeys, dosing of animals in the 30 mg/kg/day dose group was stopped from days 11–21 because of toxicity. When dosing was resumed on day 22, animals received 20 mg/kg/day and this group was designated the 30/20 mg/kg/day group. This treatment was also not tolerated and treatment was stopped for 3/6 monkeys. Mortality was observed in one monkey at 3 mg/kg/day and at 30/20 mg/kg/day. There were no consistent effects on hormone levels. Increased absolute and relative liver weights were noted at 3, 10 and 30/20 mg/kg/day. While there was no evidence of peroxisome proliferation, there was evidence of mitochondrial proliferation suggesting a different mode of action than observed in rats. The serum levels were highly variable and should be treated with caution. On day 9 of treatment, the serum levels were 126 ± 36.1 µg/mL in the 3 mg/kg/day group and 1597 ± 2392 µg/mL in the 30/20 mg/kg/day group, and during weeks 26/27, the serum levels were 52.5 ± 9.14 µg/mL in the 3 mg/kg/day group and 51.5 ± 77.6 µg/mL in the 30/20 mg/kg/day group. The LOAEL for this study was 3 mg/kg/day and a NOAEL was not established.

PFOA is immunotoxic in mice. Feeding C57Bl/6 mice a diet containing 0.02% PFOA resulted in adverse effects to both the thymus and spleen. In addition, this feeding regimen resulted in suppression of the specific humoral immune response to horse red blood cells, and suppression of splenic lymphocyte proliferation in response to LPS and ConA. The suppressed mice recovered their ability to generate a humoral immune response when they were fed a diet devoid of PFOA. Studies using transgenic mice showed that the peroxisome proliferator-activated receptor alpha was involved in causing the adverse effects to the immune system.

Prenatal developmental toxicity studies in rats resulted in death and reduced body weight in dams exposed to oral doses of 100 mg/kg/day or by inhalation to 25 mg/m^3 APFO. There was no evidence of developmental toxicity after oral exposure to doses as high as 150 mg/kg/day, while inhalation exposure to 25 mg/m^3 resulted in reduced fetal body weights. In a rabbit oral developmental toxicity study there was a significant increase in skeletal variations after exposure to 50 mg/kg/day APFO. There was no evidence of maternal toxicity at 50 mg/kg/day, the highest dose tested.

In a two-generation reproductive toxicity study in rats exposed to 0, 1, 3, 10, and 30 mg/kg/day APFO, significant increases in absolute and relative liver and kidney weights were observed in F0 males at 1 mg/kg/day, while significant reductions in absolute and relative kidney weights were observed in F0 females at 30 mg/kg/day. Reproductive indices were not affected in the F0 animals. Serum levels of the 10 and 30 mg/kg/day groups were measured for F0 males after mating and F0 females at weaning of the F1 pups. In F0 males, the serum levels were 51.1$\pm$9.30 and 45.3$\pm$12.6 ug/l, respectively for the 10 and 30 mg/kg/day groups, and in F0 females, the serum levels were 0.37$\pm$0.0805 and 1.02$\pm$0.425 ug/l, respectively for the 10 and 30 mg/kg/day groups. In F1 females, there was a significant increase in post weaning mortality, a significant decrease in mean body weight, and a significant delay in sexual maturation at 30 mg/kg/day. In F1 males, significant decreases in body weights and body weight gains, and significant changes in absolute liver and spleen weights and in the ratios of liver, kidney, and spleen weights-to-