

and urinary bladder. The adrenals, liver, pancreas, spleen, and testes from each animal were embedded in paraffin, sectioned, stained with hematoxylin and eosin and examined microscopically.

All animals survived to scheduled sacrifice. There were no clinical signs of toxicity in the treated groups and there was no effect on body weight. Low or no food consumption was observed for one animal given 20 mg/kg/day. No food consumption was noted for this animal on day 12 and low food consumption was noted on days 5, 7, 11, 14, 17, and 24, respectively. For this animal, decreased food consumption is in all likelihood related to APFO administration.

There were no effects on estradiol, estriol, thyroid stimulating hormone, total and free triiodothyronine, and total and free thyroxine. Estrone levels were notably lower for males given 2 and 20 mg/kg/day APFO. There was no evidence of peroxisome proliferation or cell proliferation in the liver, testes or pancreas of treated monkeys. No adverse effects were noted in either gross or clinical pathology studies.

In the 26-week study, male cynomolgus monkeys were administered APFO by oral capsule at doses of 0, 3, 10 or 30 mg/kg/day for 26 weeks (Thomford, 2001b; Butenhoff et al., 2002). At study initiation the monkeys weighed 3.2 to 4.5 kg. There were 4 monkeys in the 3 mg/kg/day group and 6 monkeys in each of the other groups. 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. At the end of the 26-week treatment period, 2 animals in the control and 10 mg/kg/day groups were observed for a 13-week recovery period.

Animals were observed twice daily for mortality and moribundity and were examined at least once daily for signs of poor health or abnormal behavior; food consumption was assessed qualitatively. Ophthalmic examinations were done before initiation of treatment and during weeks 26 and 40. Body weight data were recorded weekly before the start of treatment, on day 1 of treatment and weekly thereafter. Blood and urine samples were collected for clinical hematology, clinical chemistry, and urinalysis before the start of treatment and on days 11, 31, 63, 91, 182, 217, 245 and 275. Blood samples were also taken for hormone determinations; samples were analyzed for estradiol, estrone, estriol, thyroid stimulating hormone, total and free triiodothyronine, total and free thyroxine, and testosterone. Blood, urine and feces were collected during week 2 and every 2 weeks thereafter during treatment and recovery for PFOA concentration analyses. The animals were not fasted before collections.

At scheduled necropsy, liver samples were taken for determination of PFOA levels. The right lateral lobe of the liver was collected from each animal for palmitoyl CoA oxidase activity analyses, and representative samples of liver, right and left testes, and pancreas were collected from each animal for cell proliferation evaluation using proliferation cell nuclear antigen. All available bile was collected for bile acid determination. The following organs were weighed at scheduled and unscheduled sacrifices; paired organs were weighed separately: adrenal (2), brain, epididymis (2), kidney (2), liver, pancreas, testis (2), and thyroid (2) with parathyroid. Organ to body weight percentages and organ to brain weight ratios were calculated. The following tissues