

CHRONIC ORAL TOXICITY OF APFO IN MONKEYS

TABLE 2
Hormones in Male Cynomolgus Monkeys Dosed Orally for 6 Months with Ammonium Perfluorooctanoate

		Treatment week (day)				
		-1 (-4)	5 (35)	10 (66)	14 (94)	27 (183)
	Thyroid stimulating hormone (mU/ml)					
14	Control	0.37 ± 0.36	0.23 ± 0.23	0.23 ± 0.34	0.54 ± 0.46	0.40 ± 0.23
8 ^b	3 mg/kg/day	0.53 ± 0.58 ^a	0.36 ± 0.53	0.19 ± 0.27	0.60 ± 0.55	0.65 ± 0.17
20	10 mg/kg/day	0.46 ± 0.57	0.26 ± 0.44	0.56 ± 1.07	0.38 ± 0.53	0.87 ± 1.09
28 ^c	30/20 mg/kg/day	0.29 ± 0.28	0.03 ± 0.04 ^c	0.22 ± 0.25 ^d	0.20 ± 0.11 ^e	0.39 ± 0.10
	Total thyroxine (μ g/dl)					
35	Control	5.13 ± 0.81	4.72 ± 0.95	4.65 ± 0.86	4.22 ± 0.90	3.84 ± 0.77
47	3 mg/kg/day	5.16 ± 1.28	4.02 ± 0.76	3.52 ± 0.53	3.55 ± 0.38	2.58 ± 0.17
31	10 mg/kg/day	4.17 ± 0.51	2.95 ± 0.46**	3.04 ± 0.46**	2.93 ± 0.42**	2.71 ± 0.35
16	30/20 mg/kg/day	4.51 ± 0.79	3.70 ± 0.29	3.27 ± 1.02**	3.76 ± 0.42	2.61 ± 0.25
	Free thyroxine (μ g/dl)					
9	Control	1.77 ± 0.29	1.60 ± 0.34	1.48 ± 0.26	1.49 ± 0.50	1.55 ± 0.43
24	3 mg/kg/day	1.72 ± 0.35	1.47 ± 0.16	1.34 ± 0.30	1.32 ± 0.28	1.04 ± 0.04
25	10 mg/kg/day	1.56 ± 0.18	1.09 ± 0.17**	1.08 ± 0.20**	1.06 ± 0.20	0.96 ± 0.13
40**	30/20 mg/kg/day	1.56 ± 0.26	1.23 ± 0.06**	1.08 ± 0.26	1.34 ± 0.27	0.90 ± 0.24
	Total triiodothyronine (ng/dl)					
191	Control	155 ± 18	171 ± 16	163 ± 19	162 ± 25	157 ± 15
290	3 mg/kg/day	150 ± 26	168 ± 30	170 ± 21*	177 ± 28*	134 ± 17
181	10 mg/kg/day	170 ± 23	152 ± 15	162 ± 10	157 ± 18	135 ± 23
261	30/20 mg/kg/day	148 ± 16	110 ± 39**	90 ± 51**	120 ± 35	104 ± 33*
	Free triiodothyronine (ng/dl)					
16	Control	6.39 ± 0.63	5.49 ± 0.70	5.71 ± 1.14	5.02 ± 0.73	5.62 ± 0.89
6	3 mg/kg/day	6.06 ± 0.63	5.58 ± 0.65	6.23 ± 0.59	5.28 ± 0.34	4.87 ± 0.12
27	10 mg/kg/day	6.16 ± 0.44	5.13 ± 0.41	5.31 ± 0.54	4.98 ± 0.89	4.67 ± 0.64
8	30/20 mg/kg/day	6.00 ± 0.88	3.78 ± 1.18**	3.01 ± 1.96**	4.46 ± 0.76	3.39 ± 1.54
	Testosterone (ng/ml)					
0.1*	Control	3.76 ± 3.46	2.22 ± 2.63	4.76 ± 3.45	4.63 ± 4.31	7.49 ± 4.62
0.2	3 mg/kg/day	6.67 ± 6.55	3.03 ± 2.99	3.68 ± 2.26	7.36 ± 2.66	7.81 ± 4.27
0.2	10 mg/kg/day	2.47 ± 2.42	2.00 ± 2.02	5.15 ± 3.92	2.89 ± 2.06	7.83 ± 3.69
0.4	30/20 mg/kg/day	3.97 ± 3.21	0.81 ± 0.49	2.76 ± 3.01	1.25 ± 0.09	1.74 ± 0.44
ontrol	Estradiol (pg/ml)					
	Control	24.9 ± 6.3	7.6 ± 7.0	15.0 ± 12.5	13.5 ± 10.1	10.8 ± 17.0
	3 mg/kg/day	35.1 ± 9.7	14.7 ± 12.7	18.3 ± 11.5	7.7 ± 7.8	13.6 ± 11.1
	10 mg/kg/day	30.2 ± 7.4	11.2 ± 7.4	19.8 ± 10.1	6.4 ± 7.9	7.8 ± 6.2
	30/20 mg/kg/day	27.7 ± 6.7	4.6 ± 7.1	2.1 ± 4.2	0.0 ± 0.0	0.0 ± 0.0
	Cholecystokinin (Fmol/mR)					
	Control	1.76 ± 0.55	3.15 ± 0.86*	3.07 ± 1.52*	1.79 ± 0.59	2.43 ± 0.84
	3 mg/kg/day	1.81 ± 0.82	3.02 ± 1.28*	3.90 ± 2.69	1.38 ± 0.73 ^f	3.03 ± 1.42
	10 mg/kg/day	1.53 ± 0.62	3.10 ± 1.18*	2.74 ± 1.30	1.43 ± 0.23 ^g	2.31 ± 0.83
	30/20 mg/kg/day	1.88 ± 1.07	2.55 ± 0.39	2.44 ± 1.10	1.90 ± 0.14	1.80 ± 1.10

Note. Group means ± SD. Statistics reflect only those animals receiving treatment when blood was drawn, including comparisons to prestudy values. Control group, $n = 6$; 3 mg/kg/day group, $n = 4$, unless otherwise noted; 10 mg/kg/day and 30/20 mg/kg/day groups, $n = 6$, unless otherwise noted.

*Monkey 5721 was added to study in Week 3 (Day 17) to replace a monkey (5723).

^a $n = 3$. Monkey 5721 was sacrificed in moribund condition in Week 20 (Day 137).

^b $n = 5$. Monkey 5724 was sacrificed in moribund condition in Week 5 (Day 29).

^c $n = 4$. Dosing of monkey 5711 was suspended in Week 7 (Day 43).

^d $n = 2$. Dosing of monkeys 5722 and 5703 was suspended in Weeks 10 (Day 66) and 12 (Day 81), respectively.

^e $n = 3$. Technical problems were encountered with extraction of sample from Monkey 5706.

^f $n = 5$. Technical problems were encountered with extraction of sample from Monkey 5710.

^g*Significantly different from pretreatment values (Week -1) by a two-tailed, paired Student's *t*-test ($p < 0.05$).

**Significantly different from time-related control using Dunnett's *t*-test ($p < 0.05$, 2 tailed).

PFOA concentrations from 10 mg/kg dose-group monkeys sacrificed at the end of the recovery period or from the three 30/20 dose-group monkeys that were removed from dosing by

Day 81 and sacrificed on Day 183 ranged from 0.08 to 1.41 PFOA/g tissue. At the recovery sacrifice of the 10 mg/kg monkeys, liver PFOA concentrations had returned to normal.