Table 7

In this guide

Table 7. Repeated dose toxicity studies for PFCAs - PFBA

*Derived by contractor; ** calculated according to EFSA. (2012); NR – not reported; NA – not applicable.

Substance / CAS no. / purity / reference	Strain & species / sex / no. of animals	Dose (mg/kg bw/day) / vehicle / route of admin / duration / Guideline (GL) study / Good Laboratory Practice (GLP) status	PFAS concentration (µg/mL / µg/g)	Observed effects at LOAEL (controls vs treated groups). Recovery (controls vs treated groups).	Published NOAEL / LOAEL (mg/kg bw/day)	Study author comments

PFBA (ammonium salt) CAS No. not given 28.9% solution in distilled water. Butenhoff et al. (2012a)	Sprague-Dawley rats Male and female 10/sex/dose. Recovery group: Male and female 10/sex/dose.	0, 6, 30 or 150 (actual dose 0, 5.3, 25.4 or 130.2). Milli-Q or Milli-U water Gavage, 28 days, Non-GL study, GLP not stated. Recovery group: 0, 6, 30 or	Treatment: Males (mean ± SD): At 6 mg/kg bw/day Serum: 24.65 ± 17.63 Liver: 7.49 ± 4.46. At 30 mg/kg bw/day Serum: 38.40 ± 23.15 Liver: 14.72 ± 8.15. Females: At 150 mg/lg bw/day: 10.30 ± 4.50. Recovery: Males: At 150 mg/kg	Males (mean ± SD): ↑ absolute liver weight (g): 8.08 ± 0.73 vs 10.26 ± 1.43, ↑ ALP (IU): 234 ± 51 vs 320 ± 67. ↓ cholesterol (mmol/L): 1.37 ± 0.27 vs 1.09 ± 0.20. ↑ mRNA of Acox, Ugt 1A1 and CYP4A1 in liver (data only reported in figures). ↓ mRNA for Cyp1A1, Ugt 1A6 and Ugt 2A in liver (data only reported in figures). Females: No adverse effects reported (NOAEL is highest dose tested). Recovery: Males (mean	Males: 6 / 30. Female: 150 / NA. Recovery: Males: 30 / 150*. Females: 150 / NA*.	Male rats appeared more sensitive than female rats in both the 28-day and 90-day studies. The observed reduced sensitivity of females likely is a result, in part, of the greater elimination rate of PFBA in female rats as compared to males. Liver hypertrophy was observed in the absence of either clinical or microscopic evidence of liver injury and was fully reversible on cessation of treatment. The lowering

PFBA (ammonium salt) CAS No. not given 28.9%	Sprague-Dawley rats Male and female 10/sex/dose. Recovery group:	0, 1.2, 6 or 30 (actual dose 0, 1.4, 6.9 or 32.4). Milli-Q or Milli-U water. Gavage, 90 days,	At 6 mg/kg bw/day in males after treatment (mean ± SD): Serum: 13.63 ± 9.12 Liver: 3.07 ± 2.03. At 30 mg/kg bw/day in males after treatment Serum: 52.22 ± 24.89 Liver: 16.09 ± 9.06. At 30 mg/kg bw/day in females after treatment	Males (mean ± SD): ↑ absolute liver weight (g): 10.92 ± 1.17 vs 13.41 ± 2.01. ↑ ALP (IU): 146 ± 38 vs 193 ± 55. ↓ TP (g/L): 71.4 ± 3.0 vs.67.8 ± 3.0. ↓ bilirubin (µmol/L): 2.8 ± 0. 3 vs 2.2 ± 0.3. ↑ hepatocellular hypertrophy (0 vs 9; 5 minimum and 4 slight). ↑ mRNA of Acox, UGT1A1, CYP4A1, malic enzyme and Por (data only reported in figures). ↓ mRNA for Cyp1A1 in liver (data only reported in figures).	Males: 6 / 30. Female: 30 / NA. Recovery:	Male rats appeared more sensitive than female rats in both the 28-day and 90-day studies. The observed reduced sensitivity of females likely is a result, in part, of the greater elimination rate of PFBA in female rats

PFBA CAS No. not given Purity not given. Foreman et al. (2009)	SV/129 mice (WT, PPAR-α null and humanised. PPAR-α) Male, 10/dose.	0, 35, 175 or 350, Water, Gavage, 28 days, Non-GL study, GLP not stated.	Data only reported in figures.	WT (mean ± SEM) ↑ relative liver weight (Data only reported in figures). ↑ Hepatocyte hypertrophy (total): 0 vs 10. ↑ ALT (U/L): 5.29 ± 3.38. ↑ hepatic replicative DNA. synthesis: 1.8 ± 0.6 vs 19.1 ± 11.7. ↑ mRNA of Cyp4A10 (Data only reported in figures). ↑ mRNA of ACO (Data only reported in figures). Recovery not assessed.	Males: NA / 35*	Administration of PFBA caused a PPAR-α –dependent increase in average liver weight and hepatocyte hypertrophy because these changes were found in wild-type mice but not in similarly treated PPAR-α null mice. The relative increase in liver weight and hepatocyte hypertrophy was also observed in humanized PPAR-α mice.