Table 19

In this guide

Table 19 Repeated dose toxicity studies for PFSAs – PFOS

*Derived by contractor; ** calculated according to EFSA. (2012); NR – not reported; NA – not applicable; # - no. of animals studied per endpoint differs to the no. of animals treated.

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 autho comm

Males (mean ± SD):

↓ body weight gain: data only reported in figures.

↑ absolute liver weight (g): 9.3 ± 1.2 vs 16.4 ± 1.6.

↑ relative liver weight: 0.031 ± 0.003 vs 0.057 ± 0.003.

↓ AST (U/L): 69 ± 7.2 vs 58 ± 3.8 on day 2; 89 ± 20.0 vs 64 ± 5.2 on day 9.

↓ ALT (U/L): 29 ± 4.0 vs 26 ± 3.0 on day 2; 32 ± 6.3 vs 28 ± 3.7 on day 9; 63 ± 8.2 vs 62 ± 7.2 on day 16.

↓ TGs (mg/dL): 120 ± 36.6 vs 71 ± 19.3 on day 16; 57 ± 9.3 vs 28 ± 6.3 on day 23.

				Males: ↑ liver weight: data only reported in figures. ↓ plasma TG: data only reported in figures. ↓ free cholesterol: data only reported in figures. ↓ non HDL cholesterol: data only reported in figures. ↓ HDL cholesterol: data only reported in figures. ↑ hepatic TG: data only reported in figures. ↓ bile acid excretion: data only reported in figures Altered gene expression related to transcription factors,		The po of PFAS affect lipopro metabo increas increas alkyl ch length.
PFOS (potassium salt) CAS. No. 2795-39-3 87.6%. Bijland et al. (2011)	APOE*3-Leiden.CETP mice. Male 6-8/dose.	0 or 0.003% in diet equivalent to 3 Diet (vehicle). Diet, 4-6 weeks, OECD 407, GLP not stated.	At 6 mg/kg bw/day at 4-6 weeks (mean ± SD) Serum: 85.6-124.7 ± 4.2-9.5.		Males: NA / 3*	The da sugges PFOS r plasma and tot cholest mainly impairi lipopro produc

PFOS (potassium salt) CAS no. Not given 86.9%. Butenhoff et al. (2012b)	Crl:CD®(SD) IGS BR rats. Male and Female, 60-70/sex /dose. Recovery group: 40/dose.	0, 0.5, 2, 5 or 20 ppm in diet equivalent to 0, 0.024, 0.098, 0.242, 0.984 (males) and 0, 0.029, 0.120, 0.299, 1.251 (females). Diet, 104 weeks, Non-GL study, GLP not stated. Recovery: 20 ppm in diet equivalent to 1.144 (males) or 1.385 (females) 52 weeks treatment	At 0.024 mg/kg bw/day in males at week 105 (mean ± SD) Serum: 1.31 ± 1.30 Liver: 7.83 ± 7.34. At 0.098 mg/kg bw/day in males at week 105 Serum: 7.60 ± 8.60 Liver: 26.40 ± 20.40. At 0.024 mg/kg bw/day in females at week 105 Serum: 4.35 ± 2.78 Liver: 12.9 ± 6.81. At 0.098 mg/kg bw/day in females at week 102	Males: ↑ hepatocellular centrilobular hypertrophy: 0/65 vs 4/55 #. ↑ cystic hepatocellular degeneration: 5/65 vs 19/55. Females: ↑ hepatocellular periportal vacuolation: 15/65 vs 22/55. ↓ serum total cholesterol at week 27: data only reported in figures. Recovery: Data not presented as animals only treated with	Males: 0.024 / 0.098. Females: 0.024 / 0.098. Increased liver tumour incidence BMDL10 (diet) 7.9 and 8.0 ppm in males and females respectively. BMDL10 (serum) 62 and 92 µg/mL in males and females respectively. Recovery Males: NA / 1.144.	Liver w princip target dietary exposu liver ef as evid by eith serum chemis micros observ were la limited centrilo finding hypertr eosinop hepato granule hepato pigmer hepato vacuola and an increas hepato adenor the hig dietary group. There w relative statisti signific otherw notable differer betwee control treated groups

PFOS (potassium salt) CAS No. 2795-39-3 98%. Chen et al. (2022)	C57BL/6 mice. Male 6/dose.	0 or 500 µg/l in drinking water equivalent to 109. Drinking water. 28 days, OECD 407, GLP not stated.	At 109 mg/kg bw/day (mean ± SE) Liver: 10.73 ± 1.19.	Males: ↑ lipid droplets: data only reported in figures. ↑ inflammation and apoptosis: data only reported in figures. ↑ TG: data only reported in figures. ↑ CAT activities (data only reported in figures: 310 lipids changed. Changes in hepatic lipidome. Recovery not assessed.	Males: NA / 109*	PFOS is to accu in mou livers t substit PFBS, w could b most import contrib the diff in toxic strengt the sar exposu concen PFOS exposu induce toxicity through increas oxidati damag accumu of TG.

PFOS (potassium salt) CAS no. Not given	Sprague-Dawley rats. Male, 10/dose (total 40/dose, 10 sacrificed on days 1, 28,	0, 20 or 100 ppm in diet equivalent to 1.93 or 9.65. Diet, 7 days, Non-GL study GLP not stated.	At 1.93 mg/kg bw/day on day 1 (mean ± SD) Serum: 39.49 ± 7.76 Liver: 123.92 ± 23.95. At 1.93 mg/kg bw/day on day 28. Serum:15.49 ± 1.60 Liver: 44.17 ± 4.36. At 1.93 mg/kg	Males (mean ± SD): ↓ body weight (g): 412.2 ± 46.8 vs 384.8 ± 46.8 on day 21 and 428.2 ± 50.9 vs 397.0 ± 51.4 on day 28. Comparable to controls on day 84. ↑ relative liver weight (%): 4.53 ± 0.29 vs 5.06 ± 0.38 on day 1 and 3.63 ± 0.39 vs 4.09 ±0.51 on day 84. ↑ plasma cholesterol (nmol/L): 2.73 ± 0.44 vs 2.17 ± 0.37 on day 1 and 2.29 ± 0.24 vs 1.61 ± 0.33 on day 28. Comparable to controls on day 84. ↑ DNA in liver (mg DNA/whole liver): 39.10	Males: NA / 1.93*	Liver-re effects seen in rats du 84-day recove period followin day die exposu Exposu sufficie result i increas relative weight centrilo hepato hypertr Althoug many o hepatic respon observ the firs recove

PFOS (potassium salt) CAS no. Not given 98%. Han et al. (2018b)	Sprague-Dawley rats. Male, 6/dose.	0, 1 or 10 DMSO (0.4%) in corn oil. Gavage, 28 days, OECD 407, GLP not stated.	Data only reported in figures.	Males (mean ± SE): ↑ ALT (U/L): 38.83 ± 4.59 vs 49.86 ± 3.78. ↑ TBA (nmol/L): 10.57 ± 1.20 vs 16.23 ± 0.55. ↑ TNF-α (ng/mL): 3.87 ± 0.40 vs 5.809 ± 0.34. ↑ IL-6 (ng/mL): 2.72 ± 0.13 vs 3.85 ± 0.43. ↑ PCNA positive nuclei: data only reported in figures. ↑ gene expression (PCNA, c-Jun, c-MYC, CydD1): data only reported in figures Centrilobular hepatocyte hypertrophy: data only reported in figures. Recovery not	Males: NA / 1	The da sugges PFOS in Kupffer activat leading hepato prolifer by thro the NF- kB/TNF depend pathwa

PFOS (potassium salt) CAS no. Not given 98%. Han et al. (2018a)	Sprague-Dawley rats. Male, 6/dose.	0, 1 or 10 DMSO (0.4%) in corn oil. Gavage, 28 days, OECD 407, GLP not stated.	NR	Males: ↑ ALT: data only reported in figures. Recovery not assessed.	Males: NA / 1	The stu demon the mecha action PFOS-in hepatic throug genera

PFOS (potassium salt) CAS no. Not given Purity not given. Huck et al. (2018)	C47BL6/J mice, Male, 5/dose.	0 or 0.089, Diet, 6 weeks, Non-GL study, GLP not stated.	NR	Males: ↑ relative liver weight: data only reported in figures. ↑ TG in liver: data only reported in figures. ↓ gene expression of APOA1, APOA2, PEPCK, G6PC: data only reported in figures. ↑ gene expression of SREBF1: data only reported in figures. ↑ expression of CD36 and PPARγ: data only reported in figures.	Males: NA / 0.089	PFOS treatm signific affecte expres lipid traffick genes f favour steatos CD36, f major hepato lipid im and PP were in by PFO

PFOS (potassium salt) CAS No. 2795-39-3 >98%. Kim et al. (2011)	Sprague-Dawley rats, Male and female, 12/sex/group.	0, 1.25, 5 or 10 0.1% DMSO in saline. Gavage, 28 days, OECD 407, GLP not stated.	NR	Males (mean ± SD or SE (not specified)): ↑ relative liver weight: data only reported in figures. ↑ AST (IU/L): 56.8 ± 16.4 vs 89.4 ± 7.7. ↓ TGs (mg/dL): 58.7 ± 34.8 vs 12.9 ± 3.4. ↑ apoptosis: data only reported in figures. ↑ mRNA and protein levels of Cyp4A1: data only reported in figures. Females: ↓ body weight in females: data only reported in figures ↑ relative liver weight: data only reported in figures	Males: 5 / 10*. Females: 5 / 10*.	PFOS r a signif hepato in Spra Dawley the dos levels c 10 mg/ bw/day Howev respon showed appare gender differen PFOS primari affecte by indu apopto signals CYP4A1 expres which r be a po cause c hypolip

				Males (mean ± SE): ↑ relative liver weight (mg/g body weight): 34.92 ± 0.22 vs 38.66 ±0.47. ↑ absolute liver weight (g): 11.79 ± 0.29 vs 13.14 ± 0.28. ↓ cholesterol in serum (mg/dL): 115 ± 2 vs 97 ± 3. ↑ gene expression of Cyp4a1: 1.04 ± 0.1 vs 2.09 ± 0.18. ↑ gene expression of Cyp2b1: 1.17 ± 0.21 vs 5.87 ± 1.05.		A majo organ f PFOS w liver. PFOS f showed increas weight Cyp2b1 expres and hepato hypertr in the presen minima increas Cyp4a1 expres
PFOS (potassium salt) CAS No. 1763-23-1 >96%. NTP. (2022a)	Sprague-Dawley rats, Male and female, 10/sex/dose.	0, 0.312, 0.625, 1.25, 2.5 or 5. 2% Tween® 80 in deionized water. Gavage, 28 days,	At 3.12 mg/kg bw/day in males (mean ± SE) Plasma: 23.7 ± 1.1 Liver: 87.2 ± 3.04. At 3.12 mg/kg bw/day in	↑ gene expression of Cyp2b2: 1.22 ± 0.23 vs 6.60 ± 1.01. Females (mean ± SE): ↑ relative liver weight	Males: NA / 0.312* Females: NA / 0.312*	Hepato hypertr observ PFOS is due to peroxis

Males (mean ± SD):

↓ body weight gain (%): 14 ± 11% vs -8 ± 8% on day 182.

↑ mortality (0 vs 2)

↓ total cholesterol from day 91 (mg/dL): 152 ± 28 vs 48 ± 19.

↑ HDL from day 153 (mg/dL): 63 ± 11 vs 13 ± 5.

↑ TG (mg/dL): 45 ± 9 vs 30 ± 12.

↓ total bilirubin from day 91 (mg/dL): 0.6 ± 0.2 vs 0.2 ±0.1

↑ SBA from day 153 (mg/dL): 6 ± 0.8 vs 18 ± 9.

↓ SDH from day 37 (IU/L): 6 ± 4 vs 3 ±1.