Table 9

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Table 9. Repeated dose toxicity studies for PFCAs - PFOA

*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)	Stud comm

PFOA CAS No. not given 96%. Botelho et al. (2015)	C57BL/6, mice, Male, 4/dose.	0, 0.002, 0.005, 0.01 or 0.02% equivalent to 2.4, 6, 12 or 24**. Water, Diet, 10 days, Non-GL study, GLP not stated.	NR	Males (mean ± SE): ↑ relative liver weight (g): 5.04 ± 0.20 vs 7.84 ± 0.22. ↑ Hypertrophy of centrilobular hepatocytes: data only shown in figures. Recovery not assessed.	Males: NA / 2.4*	The p comp produ liver the re inflan media may lead t susce comp media (as ev increa AST a This s role o in live follow to PF

PFOA (ammonium salt) Cas No. 3825-26-1 95.2%. Butenhoff et al. (2002)	Cynomolgus monkeys Male 4-6/dose. Recovery group: 2/dose.	0, 3, 10 or 30 (highest dose suspended on day 12 and reduced to 20 from day 22). No vehicle, Gelatin capsules, 26 weeks (182 days) Non-GL study, GLP not stated. Recovery group: 0, 3, 10 or 30 90 days.	At 3 mg/kg bw/day at week 27 (mean ± SD (serum) or range (liver) Serum: 77 ± 39, Liver: 11.3-18.5. At 10 mg/kg bw/day at week 27, Serum: 86 ± 33, Liver: 6.29-21.9. At 10 mg/kg bw/day at end of recovery (week 40), Serum: Comparable to controls, Liver: 0.08-	Males (mean ± SD): ↑ absolute liver weight (g): 60.2 ± 6.9 vs 81.8 ± 2.8. ↑ total bilirubin (mg/dL): 0.1 ± 0.2 vs 0.3 ± 0.1 and 0.3 ± 0.1 at week 10 and 14 cf pretreatment values. ↓ G6P (µmol/min/g liver): 12.32 ± 3.11 vs 6.02 ± 0.33. Recovery: Absolute liver weight comparable to controls (g): 90.2 ± 2.5 vs 66.0 ± 5.2	Males: NA / 3	Hepa the a notab findir prese group statis signif the h there indica increa liver treatr This f appea most dose- obser study in live at lea to he hyper demo decre DNA which be ex mitoc prolif demo incre

	Males (mean ± SD): ↓ body weight gain (g): 357 ± 23 vs 268 ± 26. ↑ absolute liver weight (g): 8.08 ± 0.73 vs 15.54 ± 2.18. ↑ relative liver weight: 2.42 ± 0.17 vs 6.19 ± 0.39. ↑ ALT (IU): 55.8 ± 22.1 vs 66.5 ± 16.2. ↑ ALP (IU): 234 ± 51 vs 320 ± 67. ↑ Urea (mmol/L): 6.3 ± 1.5 vs 9.0 ± 1.5. ↓ TP (g/L): 60.3 ± 3.5 vs 56.2 ± 3.2. ↑ albumin (g/L): 31.3 ± 1.9 vs 33.1 ± 1.7. ↓ food consumption: data NR.	
At 30 mg/kg bw/day in males at end of treatment	↑ Hepatocellular hypertrophy: 0 vs 10 (1 minimal; 6	The g weigh hepat hyper respo in rat NH4+ comp treate NH4+

PFOA (ammonium salt) CAS No. not given 98%. Elcombe et al. (2010)	SD (CD) rats Male 30/dose.	0 or 300 ppm in diet equivalent to 27** . Powdered RMI feed. Diet, 7 days, Non-GL study, GLP not stated.	NR	Males (mean ± SD): ↓ body weight (g): 372 ± 22 vs 328 ± 30 on day 8. ↑ absolute liver weight (g): 15.3 ± 1.3 vs 19.2 ± 3.1 on day 8. ↑ relative liver weight (g/kg): 4.10 ± 0.26 vs 5.83 ± 0.55 on day 8. ↑ hepatic cell proliferation (%):1.42 ± 0.65 vs 5.94 ± 2.12 on day 8. ↓ liver DNA concentration (mg DNA/g liver): 2.07 ± 0.16 vs 1.61 ± 0.28 on day 8. ↓ cholesterol (mmol/L): 2.17 ± 0.25 vs 0.84 ± 0.37 on day 8. ↓ glucose (mmol/L): 19.41 ± 1.79 vs 12.12 ± 2.20 on day 8 ↓ TGs: 1.21 ± 0.45 vs 0.30 ± 0.16 on day 8.	NA / 27*	The c the w chara induc hepat male partic respe poter PPAR prolif possi apopt Clinic findin consi those with l activa decre total and t APFO increa of eit AST, with a histol ident hepat dama Histo demo APFO hepat glyco hyper hyper hyper chara increa

PFOA (ammonium salt) CAS No. not given 98%. Elcombe et al. (2010)	SD (CD) rats Male 30/dose.	0 or 300 ppm in diet equivalent to 27**. Powdered RMI feed. Diet, 28 days, Non-GL study, GLP not stated.	No Data.	Males (mean ± SD): ↓ body weight (g): 462 ± 43 vs 358 ± 53. ↑ absolute liver weight (g): 18.3 ± 2.5 vs 20.8 ± 3.2. ↑ relative liver weight (g/kg): 3.96 ± 0.36 vs 5.83 ± 0.56. ↓ liver DNA concentration (mg DNA/g liver): 1.87 ± 0.16 vs 1.63 ± 0.15. ↑ AST (U/L): 138.35 ± 30.25 vs 112.15 ± 16.29. ↓ cholesterol (mmol/L): 2.04 ± 0.36 vs 1.24 ± 0.27. ↓ glucose (mmol/L): 16.98 ± 1.42 vs 10.56 ± 1.60. ↓ TGs: 1.89 ± 0.60 vs 0.51 ± 0.12. ↓ periportal hepatocellular glycogen: grade	NA / 27*	Same

PFOA (ammonium salt) CAS No. 3825-26-1 98%. Guo et al. (2019)	Balb/c mice Male 12/dose.	0, 0.4, 2 or 10. Milli-Q water, Gavage, 28 days, Non-GL study, GLP not stated.	Data only provided in figures.	Males (mean ± SE): ↑ relative liver weight (g): 1.03 ± 0.02 vs 1.68 ± 0.05. ↑ TP (g/L): 57.15 ± 0.68 vs 60.40 ± 0.89. ↑ albumin (g/L): 23.54 ± 0.32 vs 24.06 ± 0.36. ↑ globulin (g/L): 34.60 ± 0.47 vs 36.34 ± 0.63. ↑ hepatocellular hypertrophy: data only provided in figures. Recovery not assessed.	Males: NA / 0.4*	After expos and P simila mech leadi dysfu altho show sever same PFOA displa accur poter PFOA PFO2 PFO3 demo accur thus liver i

PFOA CAS No. 335-67-1 95%. Guruge et al. (2006)	Sprague-Dawley rats Male 6/dose.	0, 1, 3, 5, 10 or 15. 2% Tween® 80. Gavage. 21 days. Non-GL study. GLP not stated.	NR	Males: ↑ expression of genes involved in transport and metabolisms of fatty acids and lipids, cell communication, adhesion, growth, apoptosis, regulation of hormone, proteolysis and peptidolysis and signal transduction: data only provided in figures. ↓ expression of genes involved in apoptosis, regulation of hormone, metabolisms and G-protein	Males: NA / 1*	The e were depe expos PFOA causi in ex great gene Resul that a numb assoc lipid meta altere and s gene with fatty degra mitoc acid all co of PF rats. The P perox mitoc acid and t perox oxida creat stress prote reduc chole synth consi down the g

PFOA (ammonium salt) CAS No. 3825-26-1 99%. Kennedy Jr (1987)	Crl:CD-1 mice. Male and female, 5/sex/dose.	0, 30, 300 and 3000 ppm in diet equivalent to 2.7, 27 or 270**. Diet, 14 days, Non-GL study, GLP not stated.	NR	Males (mean): ↑ absolute liver weight (g): 1.76 vs 4.06. ↑ relative liver weight (g/100g): 5.1 vs 12.3. Females (mean): ↑ absolute liver weight (g): 1.31 vs 3.35. ↑ relative liver weight (g/100g): 5.0 vs 12.4. Recovery not assessed.	Males: NA / 30* Females: NA / 30*	Differ dispo amm perflu proba respo differ seen and f Rats chem urine where not. T sensi male the fe amm perflu is not mous reten chem blood time studi excre that t time longe rat. Mice amm perflu for 14 no in weigh liver- weigh Amm perflu led to

PFOA (ammonium salt) CAS No. 3825-26-1 99%. Kennedy Jr (1987)	Crl:CD-1 mice. Male and female, 5/sex/dose.	0, 0.01, 0.03, 0.1, 0.3, 1, 3, 10 or 30 ppm in diet equivalent to 0.0009, 0.0027.0.009, 0.027, 0.09, 0.27, 0.9 or 2.7 **. Diet, 21 days, Non-GL study, GLP not stated.	NR	Males (mean): ↑ absolute liver weight (g): 1.82 vs 2.45. ↑ relative liver weight (g/100g): 5.4 vs 7.1. Females (mean): ↑ absolute liver weight (g): 1.40 vs 1.85. ↑ relative liver weight (g/100g): 5.2 vs 6.7. Recovery not assessed.	Males 1 / 3*. Females: 1 / 3*.	See a

PFOA (ammonium salt) CAS 3825-26-1 >98%. Li et al. (2019)	C57BL/6 mice. Male 5/dose.	0 or 1. Distilled water, Gavage, 2 weeks, Non-GL study, GLP not stated.	NR	Males (mean ± SD): ↑ hepatocyte DNA synthesis: data only provided in figures. ↑ expression of genes related to fatty acid metabolism: cd36, Acox1, Srebf1, Srebf2, Cpt-1α, ApoB. ↑ expression of genes related to nuclear receptors: Cyp4a10, Car, Cyp2b10, Pxr, Cyp3a11. Recovery not assessed.	Males: NA / 1*	Pre-e alcoh disea chang accur effect the li Modu lipid r PFOA time- PFOA expre Srebf comp vehic after regar Howe effect at the point

PFOA (ammonium salt) CAS 3825-26-1 >98%. Li et al. (2019)	C57BL/6 mice Male 5/dose.	0 or 1. Distilled water, Gavage, 8 weeks, Non-GL study, GLP not stated.	NR	Males (mean ± SD): ↓ body weight: data only provided in figures. ↑ absolute liver weight: data only provided in figures. ↑ relative liver weight: data only provided in figures. ↑ hepatocyte DNA synthesis: data only provided in figures. ↑ expression of genes related to fatty acid metabolism; Cd36. ↑ expression of genes related to nuclear receptors: Ppar-α, Ppar-γ, Car, Cyp2b10, Pxr, Cyp3a11. Recovery not assessed.	Males: NA / 1*	Pre-e chang accur effect the li Modu lipid r PFOA time- PFOA expre Srebf comp vehic after regar Howe effect at the point

PFOA (ammonium salt) CAS 3825-26-1 >98%. Li et al. (2019)	C57BL/6 mice Male 5/dose.	0 or 1. Distilled water, Gavage, 16 weeks, Non-GL study, GLP not stated.	NR	Males (mean ± SD): ↑ relative liver weight after 8 weeks: data only provided in figures. ↑ hepatocyte DNA synthesis: data only provided in figures. ↑ expression of genes related to fatty acid metabolism; Cd36, Fasn. ↑ expression of genes related to nuclear receptors: Cyp4a10, Ppar-γ, Car, Cyp2b10, Pxr, Cyp3a11. Recovery not assessed.	Males: NA / 1*	Pre-e chang accur effect the li Modu lipid r PFOA time- PFOA expre Srebf comp vehic after regar Howe effect at the points

				Males (mean ± SD): ↑ absolute liver weight (g): 12.96 ± 0.41 vs 14.94 ± 0.32. ↑ relative liver weight (mg/g body weight): 37.34 ± 0.72 vs 43.41 ± 0.55. ↑ ALT (IU/L): 57 ± 3 vs 68 ± 3 ↑ ALP (IU/L): 207 ± 9 vs 233 ± 8. ↓ TP (g/dL): 6.6 ± 0.1 vs 6.0 ± 0.1. ↓ globulin (g/dL): 2.3 ± 0.1 vs 1.7 ± 0.1. ↑ albumin/globulin ratio: 1.9 ± 0.0 vs 2.5 ± 0.1. ↓ cholesterol (mg/dL): 114 ± 6 vs 72 ± 2. ↓ TG (mg/dL): 138 ± 12 vs 101 ± 8. ↑ hepatocytic cytoplasmic alterations: 0 vs 4 (minimal).		
PFOA CAS No. 335-67-1 >98%	Sprague-Dawley rats. Male and	0, 0.625, 1.25, 2.5, 5 or 10 (males) or 0, 6.25, 12.5, 25, 50 or 100 (females) 2% Tween® 80 in	At 0 mg/kg bw/day in males (mean ± SE) Plasma: 0.098 ± 0.006 Liver: <LOD. At 0.625 mg/kg bw/day in males: Plasma: 50.7 ± 2.2		Males: NA / 0.625.	A ma organ PFOA Cyp2 activa CAR-r activi Acox1 activa PPAR

PFOA CAS No. not given 96%. Qazi et al. (2010a)	C57BL/6 mice. Male 4/dose.	0 or 0.002% equivalent to 4**. Water, Diet, 10 days, Non-GL study, GLP not stated.	At 0 mg/kg bw/day (mean ± SE) Serum: 0.070 ± 0.004. At 2.4 mg/kg bw/day Serum: 87.6 ± 2.1.	Males (mean ± SEM): ↑ liver mass: 6.95 ± 0.42 vs 11.64 ± 0.67. ↑ ALP (µkat/L): 2.42 ± 0.14 vs 3.54 ± 0.16. ↓ cholesterol (mmol/L): 2.34 ± 0.09 vs 1.80 ± 0.11. ↓ TGs (mmol/L): 1.80 ± 0.20 vs 1.15 ± 0.06. ↑ centrilobular hepatocellular hypertrophy, with elevated numbers of cytoplasmic acidophilic granules and occasional mitosis.: data only provided in figures. ↓ TNF-α (ng/mL): 0.43 ± 0.03 vs 0.29 ± 0.04. ↓ INF-γ (ng/mL): 0.65 ± 0.02 vs 0.41 ± 0.03. ↓ IL-4 (ng/mL): 0.13 ± 0.01 vs 0.09 ± 0.01.	Males: NA / 4*	PFOA histol altera liver centr hepat the m paren targe these fluorc These locate of the acinu prima respo detox toxic as we most up-re cytoc and p enzyr acid β In the exam sign c the li treate This a findir anima virtua in ser of AL comb mode in ser sugge doses

PFOA CAS No. not given Purity not given. Soltani et al. (2023)	C57BL/6J mice. Male 5/dose.	0, 1, 5, 10 or 20. 2% Tween® 80. Gavage, 28 days, Non-GL study, GLP not stated.	NR	Males (mean ± SD): ↑ liver weight: data only provided in figures. ↑ AST and ALT: data only provided in figures. ↑ cytokines IL-6, INF-γ and TNF-α: data only provided in figures. Moderate to severe steatosis and inflammation: data only provided in figures. Recovery not assessed.	Males: 1 / 5*	It has that P tissue the li dama centr of the the m fluorc Accor weigh liver d deger seen treate the cu inves norm funct comp seen patho (PFOA 20 m Analy tissue indica liver d follow expos oxida and i mark revea increa Hepa displa degre altera high- exhib great modif

PFOA (ammonium salt) CAS No. not given 98%. Son et al. (2008)	ICR mice. Male 10/dose.	0, 2, 10, 50 or 250 ppm in diet equivalent to 0.49, 2.64, 17.63, 47.21. Deionized water. Drinking water. 21 days. Non-GL study. GLP not stated.	NR	Males (mean ± SE): ↑ liver weight/body weight ratio (g/100g): 5.05 ± 0.10 vs 6.43 ± 0.18. Mild lymphocytic infiltration around the central vein. Recovery not assessed.	Males: NA / 0.49*	An in react after treatr expec Howe rema inflan react of PF mice Consi decre expre α alor increa hepat PFOA in ou PFOA hepat decre by m impe tissue Overa show induc hepat

PFOA CAS No. not given 98%. Wu et al. (2018)	Kunming mice. Male 8/dose.	0, 1 or 5. Peanut oil and DMSO, Gavage, 21 days, Non-GL study, GLP not stated.	NR	Males: ↑ liver mass and liver index: data only provided in figures. ↑ GPT and GOT: data only provided in figures. ↑ TG: data only provided in figures. ↓ FGF21 protein: data only provided in figures. ↑ visible vacuoles around liver portal area: data only provided in figures. ↑ CD36-positive cells: data only provided in figures. ↓ ApoB-labelled cells: data only provided in figures. Recovery not assessed.	Males: 1 / 5	Autho the cu sugge PFOA result poten body imply induc energ and u Liver PFOA were accor increa funct trans (GPT, serun curre obser sugge imme expos to pe liver adult affect horm expre

				Males (mean ± SD): ↑ AST, ALT, ALP, LDH and TBA: data only provided in figures. ↑ deranged liver architecture, marked oedema, vacuolar degeneration, hepatocellular necrosis, and inflammatory cell infiltration: data only provided in figures. ↑ MDA, H2O2 and 8-OHdG: data only provided in figures ↓ SOD, CAT, CRP, IL-6 and COX-2: data only provided in figures. ↓ nuclear DNA fragmentation: data only provided in figures. Recovery not assessed.		A sign increa serum AST, A and T obser admi PFOA MDA H2O2 and 8 forma signif increa expos in the More activi endog antiox and C signif decre
PFOA CAS No. not given >98%. Zou et al. (2015)	Kunming mice. Male 8/dose.	0 or 10. Vehicle, Gavage, 14 days, Non-GL study, GLP not stated.	NR		Males: NA / 10*	