Table 8

In this guide

Table 8. Repeated dose toxicity studies for PFCAs – PFHxA

*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 auth comments

PFHxA CAS No. not given 98.5%. Chengelis et al. (2009)	Sprague-Dawley rats Male and female 10/sex/dose.	0, 10, 50 or 200, Deionized water, Gavage, 90 days, Non-GL study, GLP not stated. Recovery group: 0 and 200, 28 days.	NR	Males (mean ± SD): ↓ body weight: data only provided in figures. ↓ cholesterol (mg/dL): 57 ± 12.5 vs 42 ± 9.4. Females: No adverse effects reported (NOAEL is highest dose tested). Recovery: Data not presented as animals only treated with	Males: 10 / 50. Females: 200 / NA*.	Effects seen typically suggest an impact on th liver, but the only histolog change in th liver was hepatocellul hypertrophy This histolog change is considered a adaptive change and not associat with the seru chemistry changes identified. In the absence any correlat target organ changes, the slight clinica chemistry changes, wh possibly rela to PFHxA treatment, a

PFHxA (sodium salt) CAS No. 2923-26-4 100%. Loveless et al. (2009)	Crl:CD Sprague-Dawley rats. Male and female. 10/sex/dose.	0, 20, 100 or 500, NANOpure® water. Gavage. 92 days. OECD 408. GLP not stated. Recovery group: 0 and 200. 10/sex/dose. 30 and 90 days.	NR	Males (mean ± SD): ↑ ALT (U/L): 27 ± 5 vs 63 ± 64. Females: No adverse effects reported (NOAEL is highest dose tested). Recovery: Data not presented as animals only treated with 200 mg/kg bw/day and not 20 mg/kg bw/day (LOAEL).	Males: NA / 20*. Females: 500 / NA*.	Statistically significant differences from control were observ for a numbe parameters (e.g., AST, A bilirubin, TP) particularly males dosed with 500mg/ but these changes wer considered non-adverse a variety of reasons. Son of these reasons included low incidence, n occurring in dose–respon fashion, direction of change not associated w adversity, or the changes reflected adaptive responses following effects on th liver.

PFHxA Cas No. 307-24-4 >99%. NTP. (2022b)	Sprague-Dawley rats Male and female 10/sex/dose.	0, 62.6, 125, 250, 500 or 1000 (half doses administered twice daily). Tween® 80 in deionized water, Gavage, 28 days, NTP protocol, GLP study (FDA GLP, Regs).	At 0 mg/kg bw/day in males (mean ± SE) Plasma: <LOD Liver: <LOD. At 62.6 mg/kg bw/day in males. Plasma: 0.378 ± 0.178 Liver: <LOD. At 0 mg/kg bw/day in females. Plasma: <LOD. Liver: not measured. At 62.6 mg/kg bw/day in females. Plasma: 0.129 ± 0.016. Liver: not	Males (mean ± SE): ↓ cholesterol (mg/dL): 126 ± 4 vs 101 ± 4. ↑ gene expression of Acox1: ↑ gene expression of Cyp4a1: 1.03 ± 0.09 vs 2.81 ± 0.33. ↑ gene expression of Cyp2b1: 1.29 ± 0.35 vs 2.65 ± 0.32. ↑ gene expression of Cyp2b2: 1.16 ± 0.20 vs 2.22 ± 0.25. Females: ↑ gene expression of Cyp2b1: 1.83 ± 0.62 vs 4.66 ±	Males: NA / 62.6*. Females: NA / 62.6*.	A major targ organ of toxicity for PFHxA was t liver. Cyp2b1/Cyp activation indicates CA mediated activity, and Acox1/Cyp4 activation suggests PP α activity. PFHxA is the least potent Cypinduction This pattern potency was also reflecti of the chang in liver weig and the occurrences hepatocellul hypertrophy PFAS administrati increased th levels of ser biomarkers