

Table 18

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This is a paper for discussion. This does not represent the views of the Committee and should not be cited.

Table 18 Repeated dose toxicity studies for PFSA's - PFHxS

*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)
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Males:

↓ 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.

↑ liver
weight: data
only reported
in figures.

↑ hepatic TG:
data only
reported in
figures.

↓ plasma TG:
data only
reported in
figures.

↓ bile acid
excretion:
data only
reported in
figures.

Males:
NA / 6*

PFHxS
(potassium
salt)
CAS no.
Not given
99.98%.
Bijland et
al. (2011)

APOE*3-
Leiden.CETP
mice.
Male,
6-8/dose.

0 or 0.006% in diet
equivalent to 6.
Diet (vehicle).
Diet,
4-6 weeks,
OECD 407,
GLP not stated.

At 6 mg/kg
bw/day at 4-6
weeks (mean
± SD)
Serum: 188.3-
217.6 ± 10.4-
31.5.

PFHxS			At 0.3 mg/kg bw/day in F0 males on day	
(potassium salt)	Crl:CD®(SD)	0, 0.3, 1, 3 or 10.	42 (mean ± SE).	Males (mean ± SE):
CAS no.	IGS BR	Gavage,	Serum: 44.22	↓ cholesterol
Not given	VAF/Plus®	Carboxymethylcellulose	± 12.66	(mg/dL): 57 Males:
99.98%.	rats.	42 days,	Liver: 43.80 ±	± 8 vs 41 ±
Butenhoff	Male	OECD 422,	8.07.	11.
et al.	15 /dose.	GLP not stated.		Recovery not assessed.
(2009)				

PFHxS		0, 0.3, 1, and 3			
(potassium salt)	Crl:CD1 mice.	Gavage.	At 0.3 mg/kg bw/day (mean \pm SD):	Males (mean \pm SD):	
CAS no.	Male	0.5% Tween20,	Liver: 25.9 \pm 3.5.	\uparrow centrilobular hypertrophy: 0 vs 8 [#] .	Males: NA / 0.3
Not given	30/dose.	OECD 422,		Recovery not assessed.	
98.9%.		GLP study.			
Chang et al. (2018)					

Wild type
males (mean
± SE):

↑ relative
liver weight:
data only
reported in
figures.

↑ absolute
liver weight:
data only
reported in
figures.

↑ liver cell
size: data
only reported
in figures. Males:
NA / 10

↓ DNA
content: data
only reported
in figures.

↑ lipid and
TGs in liver:
data only
reported in
figures.

Recovery not
assessed.

PFHxS		0 or 10.	
(potassium salt)	SV129 and PPAR alpha null mice.	Gavage, Vehicle not given,	
CAS no.	Male	7 days,	NR
Not given		Non-GL study,	
97%.	4/dose.	GLP not stated.	
Das et al. (2017)			

			Males (mean ± SE):	
			↑ body weight from week 7: data only reported in figures.	
			↑ ALT (U/L): 30.812 ± 3.503 vs 43.633 ± 3.568.	
PFHxS (potassium salt)	C57BL/6 mice (high fat diet).	0 or 450 µg/l in drinking water equivalent to 60-110. Drinking water,	↑ LDL-C (mml/L): 2.368 ± 0.089 vs 2.807 ± 0.067.	Males: NA / 60*
CAS no. Not given	Male	Water, 12 weeks,		
98%.	10/dose.	Non-GL study,		
He et al. (2022)		GLP not stated.	↑ TG: data only reported in figures.	
			↑ expression of genes relating to lipid metabolism, inflammation, and fibrosis.	
			Recovery not assessed.	

				Males (mean ± SE):	
				↑ absolute liver weight (g): 11.36 ± 0.32 vs 12.58 ± 0.25.	
				↑ relative liver weight (mg/g body weight): 33.77 ± 0.36 vs 36.81 ± 0.39.	
				↓ cholesterol (mg/dL): 109 ± 4 vs 96 ± 3.	
PFHxS potassium salt CAS no. 3871-99-6 >98%. NTP. (2022a)	Sprague- Dawley rats. Male and female. 10/sex/dose.	0, 0.625, 1.25, 2.5, 5 or 10 (males)	At 0.625 mg/kg bw/day in males (mean ± SE)	↑ gene expression of Cyp4a1: 1.08 ± 0.14 vs 2.29 ± 0.26.	
		0, 3.12, 6.25, 12.5, 25 or 50 (females).	Plasma: 66.76 ± 3.518.	↑ gene expression of Cyp2b1: 1.10 ± 0.15 vs 3.97 ± 1.08.	Males: 0.625 / 1.25
		Gavage, 2% Tween® 80, 28 days.	At 1.25 mg/kg bw/day in males. Plasma: 92.08 ± 3.348.	↑ gene expression of Cyp2b2: 1.28 ± 0.34 vs 4.22 ± 0.51.	Females: NA / 3.12
		NTP protocol.	At 3.12 mg/kg bw/day in females.		
		GLP study (FDA GLP Regs).	Plasma: 37.030 ± 1.651.		
				↑ relative liver weight (mg/g body weight):	