

Table: Results from studies on PFSA's

Substance (%), EC/CAS, formula	study design, species, route of exposure, doses (guideline/similar to guideline/non-guideline), n animals	Observed effects and remarks	NO(A)EL (mg/kg bw/d)	LO(A)EL (mg/kg bw/d)	Key parameters / targets not add-ressed	Serum/tissue concentration of PFAS /metabolites (time of sampling)	Reference
PFBS							
PFBS (97.9% pure, K+-salt)	2-generation reproduction study according to OECD guideline 416	Increased liver weight (maternal)	100	300	Immune system, thyroid system?	Not determined	Lieder et al. 2009b
	Sprague Dawley rats Gavage. 0, 30, 100, 300, 1000 mg/kg bw per day.	Increased hepatocellular hypertrophy (P and F1 adult males)	100	300			
	Parental (F0) animals (males and females, n=29-30 per sex per group) dosed from 70 days prior to mating, females were continued through gestation and lactation. F1 offspring (n=29-30) was dosed from weaning (lactational day 22) onwards. F2 generation was exposed through placenta and lactation. Experiment was terminated at lactational day 22 of F2 generation animals	Increased incidence of mild microscopic findings in kidney (maternal).	100	300			
		Reproductive and developmental toxicity findings offspring not observed (highest dose LOAEL)		1000			
		Significant increase in diestrus cycling only at 100 mg/kg bw/day	30	100			

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	CrI:CD(SD)IGS BR VAF/PlusTM rats (m/f) Based on OECD 408 Gavage: 0, 60, 200, or 600 mg/kg bw per day Duration: 90 days No/sex/group: 10	Decreased abs &rel spleen weight(m) Decr red blood cells (m) Decreased hematocrit (m) Decr hemoglobin (m) Increased serum chloride (m) Decreased serum albumin and total protein (f)	200 60 60 200 200 200	60 600 200 200 600 600		Not determined	Lieder et al. 2009a
PFBS, potassium salt (98.2% purity)	Sprague Dawley rats (m/f) Gavage: 0, 100, 300, or 900 mg/kg bw per day. Duration: 28 days No/sex/group: 10	Decreased serum phosphorus and potassium (m) Incr rel and absolute liver weight (m)	100 300	300 900		Not determined	NICNA S, 2005

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PFBS (97% pure, K ⁺ -salt)	ICR mice Dosing: 0, 50, 200, and 500 mg/kg bw per day from GD 1 -20, orally. Only female offspring follow-up reported. 30 dams per dose group, randomly allocated to three experimental sub-groups per dose: <i>group 1</i> : perinatal survival and growth, pubertal onset, and ovarian and uterine development (10 dams, 50 female offspring per dose), <i>group 2</i> : hypothalamic–pituitary–gonadal hormone and hypothalamic–pituitary–thyroid hormone levels (10 dams, 30 PND 1 female offspring, 10 female PND 30 offspring, and 10 PND 60 female offspring), <i>group 3</i> : levels of serum PFBS (10 dams)	Decreased body weight from PND 1 to adulthood Delayed eye opening Delayed vaginal opening Impaired ovarian and uterine development Delayed estrus cyclicity and reduced E2/ increased LH Decreased T3/T4, increased TSH Decreased T3/T4, increased TSH at GD 20 (maternal)	50 50 50 50 50 50	200 200 200 200 200 200		Mean (10 dams) serum concentration (ng/mL) on GD 20, 12h after last dosing, at 0, 50, 200 and 500 mg/kg bw per day: 1.73, 74, 332, 721.	Feng et al., 2017
PFBS (>97% purity)	Sprague Dawley rats (m, f) Gavage: 0, 62.6, 125, 250, 500, or 1,000 mg/kg bw per day No/sex/group: 10 Duration: 28 days	Incr rel liver weight (m) Incr rel liver weight (f) Incr abs liver weight (m) Incr abs liver weight (f) Incr acyl-CoA-oxidase activity (m) Decr haematocrit (m,f) Decr RBC (m,f) Decr chol (m,f) Decr T3 (m,f) Decr total+free T4 (m,f) Incr albumin/globulin ratio (m,f)	 62.6 125 62.6	62.6 125 125 250 250 62.6 62.6 62.6 62.6 125		Plasma conc. (ug/ml) at 62.6mg/kg bw/day: 2.2 ± 4.8 (m) 0.2 ± 0.05 (f) Liver conc (ug/g) at 62.6mg/kg bw/day 1.3 ± 0.2 (m)	NTP, 2019b

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PFHxS (3M, salt, purity not specified)	SV129 mice (m) Duration: 7 days Gavage: 0, 3 or 10 mg/kg bw per day No/sex/group: 4	Incr rel liver weight Incr abs liver weight	3	3 10		Not reported	Rosen et al., 2017
PFHxS (potassium salt, 97% purity)	SV129 mice (m) Duration: 7 days Gavage: 0 or 10 mg/kg bw per day No/sex/group: 4	Incr abs and rel liver weight Incr hepatic lipid and triglyceride content		10 10		Not reported	Das et al., 2017

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PFHxS (potassium salt; 98.9% purity)	CrI:CD1 (IRC) mice, OECD test guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test), modified (extended). Duration: 42 days. Gavage: 0, 0.3, 1, 3 mg/kg bw per day No/sex/group: 30 For F0 males treatment from 14 days prior to cohabitation for to at least 42 days total (one day post-last dosing). Treatment of F0 females started 14 days prior to cohabitation with continuation through mating, gestation, and lactation. F0 dams were sacrificed on lactation day 22 (one day after last dosing). F1 offspring, first exposure in utero and via lactation. After weaning (PND 22), F1 direct dosing for 14 days at maternal dose.	Incr abs & rel liver weight (F0 m,f) Centrilobular hypertrophy (F0 m) Incr ALP (F0 m) Decr Serum cholesterol (F0 m) Necrotic hepatocytes and lipid vesicles in hepatocytes (F0 m)	0.3 1 1 1	1 0.3 3 3 3		Liver conc. (µg/g): F0M at 0.3 mg/kg bw/day: 25.9 ± 3.5 F0M at 1 mg/kg bw/day: 98.5 ± 22.7 F0M at 3 mg/kg bw/day: 281.1 ± 45.4 Serum and liver in dams, and serum from pooled fetus on GD18: 0 mg/kg per day: <0.001 µg/mL, <0.005 µg/g and <0.001 µg/mL. 0.3 mg/kg per day: 16.8 µg/mL, 5.3 µg/g, and 20.8 µg/mL. 1 mg/kg per day: 51.5 µg/mL, 15.1 µg/g and 62.3 µg/mL. 3 mg/kg per day: 111.3 µg/mL, 88.4 µg/g and 137.7 µg/mL.	Chang et al., 2018

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	Toxicokinetic experiment: 12 animals per sex and dose. Subset 1 (5/sex/dose group) daily oral gavage for 14 days prior to sacrifice. Subset 2 (7/sex/dose group) dosing for 14 days prior to cohabitation. Serum and liver samples were collected at study day 14 for both sexes, at study day 28 for males and GD 18 (for females). On GD 18, pooled fetal blood and fetal liver samples were collected	Reduced litter size (without impact on born pup to implant ratio). F1: Increased relative liver weight (m, f) F1: Increased thyroid weight (m)	0.3 1 1	1 3 3			
PFHxS (potassium salt; >98% purity)	Sprague Dawley rats (m, f) Duration: 28 days Gavage: 0, 0.625, 1.25, 2.5, 5, or 10 mg/kg bw per day (males) 0, 3.12, 6.25, 12.5, 25, or 50 mg/kg bw per day (females) No/sex/group: 10	Incr rel and abs liver weight (m) Incr rel and abs liver weight (f) Decr T3 and cholesterol (m) Decr total T4 (m) Decr total T4 (f) Decr free T4 (m) Decr free T4 (f) Incr acyl-CoA- oxidase activity (m)	0.625 3.12 6.25 2.5	1.25 3.12 0.625 0.625 6.25 0.625 12.5 5		Plasma conc. (ug/ml) 0.625mg/kg bw/day: 66.8 + 3.5 (m) 3.12mg/kg bw/day: 37.0 + 1.7 (f) Liver conc (ug/g) 0.625mg/kg bw/day 39.9 + 1.3 (m)	NTP 2019b

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PFOS (91% K ⁺ -Salt) <i>"Our analysis indicated that approximately 71% of the chemical was straight-chain, and the remaining 29% was branched. Additional analysis indicated that the chemical obtained from Fluka appeared to be identical to that produced by 3M."</i>	Reproductive/developmental Sprague-Dawley rats Exposure: 0, 1, 2, 3, 5, 10 mg/kg per day per gavage GD2 – GD21	Decreased postnatal survival Decreased growth in surviving pups Delay in eye opening Decreased thyroxine (pups) No consistent change in liver weight or relative liver weight in surviving pups PND 0-35	1 1 1 1	2 2 2 2		Read from figures. Serum in pups at pnd 1: Control: 0; 1 mg/kg: 36 µg/mL; 2 mg/kg: 71 µg/mL; 3 mg/kg: 85 µg/mL; 5 mg/kg: 108 µg/mL; Slightly lower at pnd 5 Liver in pups at pnd 1: Control: 0; 1 mg/kg: 45 µg/g; 2 mg/kg: 68 µg/g; 3 mg/kg: 100 µg/g; 5 mg/kg: 160 µg/g	Lau et al. 2003
PFOS (86.9%, K ⁺ -Salt. Lesser homologs (C4–C7) at 8.4%; impurities (by quantitative ¹⁹ F Nuclear Magnetic Resonance) at 1.9%; metals (calcium, magnesium, sodium, nickel, and iron) at 1.5%; inorganic fluoride at 0.6%; perfluorooctanoic acid at 0.3%; nonfluoropentanoic acid at 0.3%; heptafluorobutyric acid at 0.1%.	2-generations reproductive/developmental Sprague Dawley rats, 20 dams per group. Exposure: 0, 0.1, 0.4, 1.6, and 3.2 mg/kg bw per day by gavage for 6 weeks prior to mating, during mating, and through gestation and lactation, across two generations for females (only 0, 0.1, 0.4 mg/kg bw per day continued to F2). Cross fostering (0 and 1.6 mg/kg bw per day) as follow up study	F0 males and females: reduced bw gain. In F0 shorter gestation, lower implantation sites, increase in stillborn pups or early neonatal death of litter.	0.4 1.6	1.6 3.2		Serum levels (µg/mL) from cross foster study at end of lactation available.	Luebke et al. 2005a

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		F1 reduced survival and bw gain. Delayed eye opening F1 Pre- and postnatal exposure was additive for pup toxicity	0.4 0.1	1.6 0.4			
PFOS (86.9%, K ⁺ -Salt. Impurities as in Luebker 2005a	Reproductive/developmental, Sprague Dawley rats, 35 dams per group. Exposure: 0, 0.4, 0.8, 1.0, 1.2, 1.6, 2.0 mg/kg bw per day by gavage from 6 weeks prior to mating to day four of lactation	Decrease in gestation length Decrease in postnatal survival day 5 Decreased mean pup weight at birth Increase in serum T4 on lactation day 5 (F0 and F1)	BMDL ₀₅ 0.31 BMDL ₀₅ 0.89 BMDL ₀₅ 0.39	 0.4	-	Measured in dams GD 1, 7, 15 and 21. Constant GD 1-15, drop at GD 21. Serum levels GD 1-15 (µg/mL): 0.1 mg/kg: 7.8-8.9 ; 0.4 mg/kg: 40.7- 41.4; 1.6 mg/kg: 154-160; 3.2 mg/kg: 275-318	Luebker et al 2005b

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PFOS (98% K ⁺ -Salt)	Developmental study, ICR mice 15 dams/goup (5 each selected for specific endpoints Exposure: 0, 1, 10, 20 mg/kg per day , GD 1 – 17/18	Reduced weight gain (F0). Increased liver weight (F0). Liver hypertrophy (F0). Decreased neonatal survival. Developmental/teratological alterations. Sternal defects.	10 1 10 1 1	20 10 20 10 10 1		Not reported	Yahia et al., 2008
	Developmental study, B6C3F1 mice. Exposure: GD 1-17, 0, 0.1, 1.0, 5.0 mg/kg bw per day by gavage.	Decrease in NK cell activity at 8 weeks (F1 M). Decrease in NK cell activity at 8 weeks (F1 F). Decrease in IgM production assessed by PFC assay at 8 weeks (spleen) (F1 M). Decrease in IgM production assessed by PFC assay at 8 weeks (spleen) F1 F).	0.1 1 1 5	1 5 5		Not reported	Keil et al., 2008

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PFOS (purity 98%, K+-salt)	Developmental study ICR mice Exposure 0, 9, 13, 20, 30 mg/kg bw per day by gavage GD1-17 (3 dams/group). 20 mg/kg bw per day GD 1-17 and 50 mg/kg per day GD11 – 15. 5 – 8 dams per group 67 – 103 fetuses: (examined animals, total number higher). 20 mg/kg per day GD 1-15/18 for histology.	Sharp increase in cleft palate between 13 (7.3%) and 20 (78.35) mg/kg per day.	13	20 50 % effective dose expected 17.7 mg/kg per day		Serum level on GD17 (µg/mL) reported for dams at 30 mg/kg per day and other values estimated from figure: 9 mg/kg bw per day: 58 in dam, 62 in fetus. 13 mg/kg bw per day: 105 in dam and fetus. 20 mg/kg bw per day: 135 in dam and fetus. 30 mg/kg bw per day: 162.3 in dams and 130 in fetus. 30 mg/kg bw per day: 162.3 in dams and 130 in fetus. 50 % effective fetal serum concentration for cleft palate: 121 µg/mL	Era et al., 2009

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PFOS (purity 98%, salt not specified)	Developmental study CD1 mice Exposure: 0, 0.3, 3 mg/kg per day GD1 – PND21 by gavage. Then no dosing in offspring until sacrifice at PND 63. Dams: 6 per group (sacrifice after weaning (PND 21)) Offspring: animals per treatment equally distributed in a low and a high fat feeding group. Termination on PND 63	Increased abs. liver weight P0 Increased dam's liver weight F1 M Increased relative liver weight P0 and F1 Increased HOMA-IR (P0). Increased HOMA-IR (F1) Elevated fasting glucose (F1 PND 21) Elevated fasting glucose (F1 PND 63)	3 0.3 0.3 3 3 3	0.3		Liver levels in dams at 0, 0.3 and 3 mg/kg per day: 0.15, 49.1 and 338.9 µg/g. Serum levels in pups PND21 at 0.3 mg/kg per day: 12.7 µg/mL in males and 11.4 µg/mL in females. Serum levels at 3 mg/kg per day: 98.7 µg/mL in males and 87.2 µg/mL in females. Liver levels in pups PND21 at 0.3 mg/kg per day: 20.1 µg/g in males and 18.0 µg/g in females Liver levels at 3 mg/kg per day: 243 µg/g in males and 178 µg/g in females	Wan et al., 2014

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PFOS (purity not specified, K ⁺ -salt)	Developmental study CD1 mice Exposure: Gavage, 0, 0.5, 2, 8 mg/kg per day, GD11 – GD16 10 dams per group	Body weight decrease (P0) Dose dependent decrease of placental weight and capacity. Dose dependent increase of number of resorptions and dead fetuses. Decrease in the numbers of glycogen trophoblast cells in the junctional zone and the number of sinusoidal trophoblast giant cells in the labyrinth zone. Decrease of mPL-II, mPLP-C α and mPLP-K expression levels and serum concentrations	2	8 0.5 0.5 0.5 0.5		Not reported	Lee et al., 2015

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PFOS (>96% purity)	28 days toxicity study SD rats (m, f) Gavage: 0, 0.312, 0.625, 1.25, 2.5, 5 mg/kg bw per day No/sex/group: 10	Incr rel and abs liver weight (m/f). Incr acyl-CoA-oxidase activity (m). Decr blood cholesterol (m) Decr total and free T4 (m, f) No change sin reproductive parameters (m) Increased probability of transitioning to extended diestrous in F (all exposure groups, Markov analysis).	1.25	0.312 2.5 0.312 0.312		Plasma conc. (ug/ml) at 0.312mg/kg bw per day: 23.7 ± 1.1 (m), 30.5 ± 0.9 (f). Information available for all doses. Liver conc (ug/g) at 0.312 mg/kg bw per day: 87.2 ± 3.04 (m) information available for all doses (m only)	NTP, 2019b
PFOS, 98%	Repeated dose, immunotox. C57BL/6 mice (4–8 males per group), administered via diet for 10 days, at 0.001 or 0.02% (2 or 40 mg/kg bw per day) (0.02% equals a total of 6 mg/animal over 10 days)	Several immune parameters up or down, but also reduced body weight gain		0.02% (40 mg/kg bw per day)		340 µg/mL	Qazi et al. (2009a, b)
PFOS, 98%	Repeated dose study, immunotox. C57BL/6 mice (4 males), restricted food diet, 10 days, 0.001, 0.002, 0.02 (1.6, 3.1 or 23.5 mg/kg bw per day)	Reduced B-cell numbers	0.001% (1.6 mg/kg bw per day)	0.02% (23.5 mg/kg bw per day)		50.8 µg/mL at 0.001%, 340 µg/mL at 0.02%	Qazi et al. (2012)
PFOS, 98%	Repeated dose study, immunotoxicity, Balb/c mice (8 per group, males and females), gavage, 5, 20 mg/kg bw per day, 14 days	Thymus and spleen histopathology, but in addition to liver effects and PPARα changes	5	20		4.89 µg/mL at 5 mg/kg bw per day, 25.2 µg/mL at 20 mg/kg bw per day	Wang et al. (2011a)

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PFOS, 85%	Repeated dose study, immunotoxicity,, Balb/c mice (5 females per group), gavage, 20 mg/kg bw per day, 7 days	Values various immune parameters reduced, but in addition to body weights		20		Not reported	Vetvicka and Vetvickova (2013)
PFOS, 98%	Repeated dose study, immunotoxicity,, C57BL/6 mice (12 males per group), gavage, 1, 5, 10 mg/kg bw per day, 7 days	Inconsistent; some ex vivo apoptotic parameters in splenocytes and thymocytes up and others go down	1	5		24.37 µg/mL at 1 mg/kg bw per day, 87.56 µg/mL at 5 mg/kg bw per day	Zhang et al. (2013d)
PFOS, 98%	Repeated dose study, immunotoxicity, C57BL/6 mice (12 males per group), gavage, 5, 20, 40 mg/kg bw per day, for 7 days	Reduced NK activity, antibody response, lymphocyte proliferation		5		97.25 µg/mL	Zheng et al. (2009, 2011)
PFOS, 85%	Repeated dose study, immunotoxicity, BALB/c mice (5 females per group), gavage, 20 mg/kg bw per day, 21 days	Reduced antibody response and NK activity, but accompanied by body weight effects		30		Not reported	Vetvicka and Vetvickova (2013)
PFOS	Repeated dose study, immunotoxicity, B6C3F1 mice (5 males per group), food, 0.25 mg/kg bw per day for 28 days	Effects on body weight and liver , no immune effects	0.25			11.6 µg/mL	Qazi et al. (2010)
PFOS, 98%	Repeated dose study, immunotoxicity, B6C3F1 mice (5 females per group), gavage, 0.0331, 0.0993, 9.3 mg/kg bw per day, 28 days	TNFα and IL-6 up and down, but no dose-response		0.0331		Not reported	Mollenhauer et al. (2011)
PFOS, 98%	Repeated dose study, B6C3F1 mice (5–10 females), gavage, 3.31, 16.6, 33.1, 166 µg/kg bw per day, 28 days	Increased ex vivo IL-6		0.00331		<1 ng/mL (LOQ)	Fair et al. (2011)
PFOS, 98%	Repeated dose study, Sprague-Dawley rats (15 males or female per group), diet, 0.14, 1.33, 3.21, 6.31 mg/kg bw per day, 28 days	Reduced total IgG1 levels in serum	0.14	1.33		0.95 µg/mL at 0.14 mg/kg bw per day, 13.45 µg/mL at 1.33 mg/kg bw per day	Lefebvre et al. (2008)
PFOS, 98%	Repeated dose study, B6C3F1 mice (5 males or females per group), gavage, 0.166, 1.66, 3.31, 16.6, 33.1, 166 µg/kg per day, 28 days	Reduced specific antibody Response (PFCs)	0.000166	0.00166		17.8n/ ng/mL at 0.000166 mg/kg bw per day, 91.5 ng/mL at 0.00166 mg/kg bw per day	Peden-Adams et al. (2008)

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PFOS	Repeated dose study, B6C3F1 mice (30 females per group), gavage, 5, 25 µg/kg per day, 21 days	Reduced survival after challenge with influenza virus	0.005	0.025		189 ng/mL at 0.005 mg/kg bw per day, 670 ng/mL at 0.025 mg/kg bw per day	Guruge et al. (2009)
PFOS, 98%	Repeated dose study, C57BL/6 mice (10–12 males per group), gavage, 8.3, 16.7, 83.33, 416.7, 833.3 µg/kg bw per day for 60 days	Antibody responses down.	0.0083	0.0833		0.84 µg/mL at 0.0083 mg/kg bw per day, 8.21 µg/mL at 0.0833 mg/kg bw per day	Dong et al. (2009)
PFOS, 98%	Repeated dose study, C57BL/6 mice (6 males per group), gavage, 8.3, 16.7, 83.33, 416.7, 833.3 µg/kg bw per day for 60 days	IL-4 and IL-10, TNF-α, IL-1β, values up and down. IgM decrease IgG, IgE increase	0.0167	0.0833		10.75 µg/mL at 0.0833 mg/kg per day, 2.36 µg/mL at 0.0167 mg/kg per day	Dong et al., 2011
PFOS, 98%	Repeated dose study, C57BL/6 mice (12 males per group), gavage, 8.3, 16.7, 83.33, 416.7, 833.3 µg/kg bw per day for 60 days	Apoptotic lymphocytes,	0.0167	0.0833		0.84 µg/mL at 0.0833 mg/kg per day, not reported at 0.0167 mg/kg per day	Dong et al., 2012
PFOS, 98%	Repeated dose study, C57BL/6 mice (4 per group), 6-8 weeks old, exposed to 2 mg PFOS/kg bw per day for 7 days	IL 12 production after Citrobacter rodentium infection		2		Not reported	Suo et al., 2017
PFOS (purity NR)	Repeated dose study, ICR mice (number, sex NR), sensitized to ovalbumin on day 0, and orally exposed to 50-150 mg PFOS/kg bw on days 9, 11, and 13	Aggravated allergic inflammation in an ovalbumin model		50 mg/kg, three times		Not reported	Lee et al., 2018
PFDS							
TFMS							