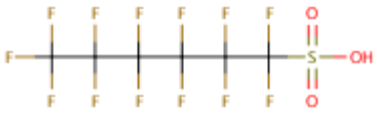
Updated EHS Summary of Perfluorohexane sulfonic acid for the MA TURA Science Advisory Board Meeting – April 11, 2018

CAS # 355-46-4 	**Perfluorohexane sulfonic acid (PFHxS)** Synonym[1]s: EINECS 206-587-1; 1,1,2,2,3,3,4,4,5,5,6,6,6-Tridecafluorohexane-1-sulfonic acid; Perfluorohexane sulfonic acid; UNII-ZU6Y1E592S **RTECS #[2]:** MO4247000 **EINECS #[3]:** 206-587-1 **Molecular Weight[4]**: 400.1109 **Molecular Formula[5]:** C6-H-F13-O3-S **Common Salts:** Tridecafluorohexane-1-sulfonic acid potassium salt, CAS # 3871-99-6[6] Tridecafluoro-1-hexanesulfonic acid, ammonium salt, CAS # 68259-08-5
PHYSICAL CHARACTERISTICS	
Primary Use	Used as surfactants, to make fluoropolymers and as water and stain protective coatings for carpets, paper and textiles[7]
Physical state, odor at room temperature & pressure	Crystalline, beige (for 3871-99-6)[8]
Melting point; Boiling point	MP = 190 deg C; BP = 452 deg C (estimated data from EPI Suite version 1.43)[9] BP = 238-239 deg C[10]
Solubility	Water solubility in mg/L @25C = 243.4 (estimated data from EPI Suite version 1.42)[11] In water, 6.2 mg/L at 25 deg C (est)[12]
Specific Gravity	Not found; density = 1.841 g/cm[3][13]
SAFETY/PHYSICAL HAZARDS	
Vapor Pressure	1.08×10^{-6} Pa @25C (estimated data from EPI Suite version 1.43)[14]
Flammability	Not found
Flashpoint	Not found
Flammability Rating	Not found
Auto Ignition Point	Not found
Combustion products	Not found
Explosivity (UEL, LEL, shock sensitive)	Not found
Oxidizer	Not found
Corrosivity	Not found
pH	Not found
Reactivity	Incompatible materials – strong oxidizing agents[15]
Viscosity	Not found
Odor Threshold	Not found
Particle size, shape, respirable fraction	Not found
Other physical hazards associated with process: Heat, gases under	Not found

pressure, noise, vibration, ergonomic hazard	
HEALTH HAZARDS	
Acute Toxicity	
Oral LD_{50}	No data in the short chain alternatives section in DeWitt; No Tox Data in ChemIDPlus
Dermal LD_{50}	Not found; No Tox Data in ChemIDPlus
Inhalation LC_{50}	Not found; No Tox Data in ChemIDPlus
Intraperitoneal LD_{50}	Not found; No Tox Data in ChemIDPlus
TDLo	Oral, mouse, 6.1 mg/kg[16]
Chronic or Sub-chronic Toxicity	
IARC rating	Not found
Carcinogenicity	Not found on Prop 65 list as of 2/15/17; Not found in CCRIS or GENETOX
Neurotoxicity	Not found in HAZMAP, NIOSH-PG or on the Scorecard list of Suspected Neurotoxicants Other studies have determined neurotoxicity in pups. Following treatment of 10 days (the peak of the brain growth spurt) old NMRI mouse pups with a single oral-oral gavage dose of the potassium salt of PFHxS (0, 0.61, 6.1 or 9.2 mg/kg b. w.), animals in the highest dose group exhibited dose–response related and long-lasting changes in both spontaneous and nicotine-induced behavior as adults (Viberg *et al.*, 2013). In a follow-up study by the authors it was shown that after 24 hours the neuroprotein levels were altered in the highly exposed mice, e.g. calcium/calmodulin-dependent kinase II (CaMKII), growth-associated protein-43 (GAP-43), synaptophysin and tau proteins, which are essential for normal brain development in mice. This was measured for both males and females, in hippocampus and cerebral cortex. There were also altered levels of neuroproteins in adult male mice explaining the results in the previous publication. These results suggest that PFHxS may act as a developmental neurotoxicant, and the effects are similar to that of PFOS and PFOA (Lee and Viberg 2013).[17] Data from the NHANES 1999-2004 and the C8-Health Project in the USA surveys found small positive association between PFHxS exposure and learning problems and attention deficit-hyperactivity disorder (ADHD) in children (Hoffman *et al.* 2010; Stein and Savitz 2011). The prevalence of ADHD plus medication increased with PFHxS levels, with an adjusted odds ratio of 1.59 (95% confidence interval, 1.21–2.08) comparing the highest quartile of exposure to the lowest.[18] Higher blood levels of PFOS, PFNA, PFDA, PFHxS and PFOSA (but not PFOA) were associated with significantly shorter "Impaired Response Inhibition" (IRT) during the "differential reinforcement of low rates of

	responding" (DRL) tasks measuring children's impulsivity (Gump *et al.* 2011). PFHxS was the second most abundant in the blood with a mean blood concentrations of about 6 ng/mL. The mean concentration of PFOS was higher and about 10 ng/mL, and the mean concentration of PFOA was about 3 ng/mL.[19] Lee and Yang *2014. NMDA receptor-mediated ERK 1/2 pathway is involved in PFHxS-induced apoptosis of PC12 cells -* **"Study demonstrated PFHxS induced apoptosis of neuronal cells via NMDA receptor-mediated ERK activation. The loss of neuronal cells by apoptosis is the common final step of most neurodegenerative diseases."[20]** Lee and Yang et al. 2016. *AMP-activated protein kinase is involved in perfluorohexanesulfonate-induced apoptosis of neuronal cells* **"AMPK and ERK play pro-apoptotic roles in neurons exposed to PFHxS, which are mediated by NMDA receptor and L-VGCC in a distinct manner. These findings provide some evidence for the underlying mechanisms responsible for PFHxS-induced neuronal damage, which may contribute to identifying target molecules for assessing PFC-related neurotoxicity."[21]** Zhang et al. 2016 *Effects of perfluorooctane sulfonate and its alternatives on long-term potentiation in the hippocampus CA1 region of adult rats in vivo.* **"The present study evaluated and compared the neurotoxic effects of PFOS, PFHxS, PFBS and Cl-PFAES in vivo on synaptic plasticity and elucidated the possible mechanism. To the best of our knowledge, this is the first study on LTP affected by perfluroalkyl compound (PFC) exposure in vivo. The findings added significant electrophysiological evidence that exposure to PFOS and its alternatives results in the impairment of synaptic plasticity. the present study provides some electrophysiological evidence and the potential mechanism of the neurotoxicity of PFOS and its alternatives. Exposure to PFOS and its alternatives repressed LTP, and PFHxS and Cl-PFAES even exhibited a comparable potency to PFOS. The higher potency of PFHxS and PFOS than PFBS to inhibit LTP points to the possibly higher neurotoxicity potential of the long carbon chain perfluoroalkyl compounds."[22]**

	Jeddy et al. 2017. *Prenatal concentrations of Perfluoroalkyl substances and early communication development in British girls* **"Maternal serum concentrations to select PFAS were both positively and negatively associated with early communication development among girls although associations were less apparent at 38 months of age compared to 15 months of age. The effect between maternal PFAS exposure and communication development varied by maternal age at delivery. There was an inconsistent pattern of association across all measured PFAS and endpoints."[23]** Oulhote et al. 2016 *Behavioral difficulties in 7-year old children in relation to developmental exposure to perfluorinated alkyl substances* **"In this prospective study from the Faroe Islands, we found a consistent association between postnatal, but not prenatal exposure to certain PFASs, (but not PFHxS, which was not significant for any behavioral outcome measures) as reflected by the serum concentrations at age 5 years in regard to behavioral problems assessed at age 7."[24]** Liew et al. 2015. *Attention Deficit/Hyperactivity Disorder and Childhood Autism in Association with Prenatal Exposure to Perfluoroalkyl Substances: A Nested Case–Control Study in the Danish National Birth Cohort* **"From Danish birth cohort randomly selected 220 cases each of ADHD and autism, and we also randomly selected 550 controls frequency matched by child's sex. Sixteen PFASs were measured in maternal plasma collected in early or mid-pregnancy. No consistent evidence to suggest that prenatal PFAS exposure increases the risk of ADHD or childhood autism in children.[25]** Wang et al. 2015 *Prenatal exposure to perfluroalkyl substances and children's IQ:The Taiwan maternal and infant cohort study* **"the present study provides first indications of possible associations of prenatal exposure to two long-chain PFASs (PFUnDA and PFNA) and with lower IQ scores in children. No significant associations were found for the other examined PFASs (including PFHxS)."[26]**
Developmental/Reproductive Toxicity	Not found on Prop 65 list as of 11/14/17 A study of a large cohort from Avon in the UK with prenatal blood

	concentration (medians) of 19.2 ng/mL PFOS, 3.7 ng/mL PFOA and 1.6 ng/mL PFHxS showed that the most exposed mothers from the upper tertile gave birth to girls weighing 140 gram less than for the less exposed but at 20 months the girls with high PFOS exposure weighed 580 gram more (Maisonet *et al.* 2012). In a study from Canada there was no significant effect of PFAS on birth weight. The blood levels were, however, somewhat lower with medians of 7.8, 1.5 and 0.97 ng/mL for PFOS, PFOA and PFHxS, respectively (Hamm *et al.* 2010). That may not be a problem of the mother alone, because another Danish study found that high levels of perfluorinated acids (PFAAs) (medians: 24.5 ng PFOS/mL, 4.9 ng PFOA/mL and 6.6 ng PFHxS/mL) in blood serum were associated with fewer normal sperm cells in normal young men included in the study (Joensen *et al.* 2009). After adjusting for age, race/ethnicity, education, ever smoking, and parity, women with higher levels of PFAS had still earlier menopause than did women with the lowest PFAS levels (Taylor *et al.* 2014. Specifically, a monotonic association with PFHxS was observed: The hazard ratio (HR) was 1.42 (95% CI: 1.08, 1.87) for serum concentrations in tertile 2 versus tertile 1, and 1.70 (95% CI: 1.36, 2.12) for tertile 3 versus tertile 1).[27] The potential reproductive and developmental toxicity of PFHxS was studied in a study with rats dosed by gavage at 0.3, 1, 3, and 10 mg/kg/d 14 days prior to co-habitation, during cohabitation, and until the day before sacrifice (21 days of lactation or presumed gestation day 25 (if not pregnant) for females and minimum of 42 days of treatment for males). Offspring were not dosed by gavage but were exposed by placental transfer in utero and potentially exposed via milk. At all doses reductions in serum total cholesterol and other biochemical changes in the blood but no reproductive or developmental effects were observed, and there were no treatment-related effects in dams or offspring (Butenhoff *et al.* 2009). Thus, in this rodent study the metabolism of lipids was affected at a daily exposure for 0.3 mg/kg b. w., and liver damage was observed after exposure to 3 mg/kg b. w. per day (NOAEL = 1 mg/kg per day). A NOAEL of 10 mg/kg b. w. per day (highest concentration tested) for effects on the reproduction was determined for PFHxS.[28] Plasma concentrations of … perfluorohexane sulfonic acid (PFHxS)… were inversely associated with endometriosis-related infertility, but the associations were attenuated in the sensitivity analyses. Our preliminary evidence suggests that exposure to PFBS may increase the risk of female infertility due to endometriosis. Future prospective

	studies are necessary to confirm these findings (Wang et al 2017).[29] Our results add to the evidence that exposure to PFOA and PFHxS, even at lower levels than previously reported, may reduce fecundability (Velez et al 2015).[30] Adjusted total testosterone concentrations were also higher in daughters with prenatal concentrations of PFOA (β = 0.24; 95% CI: 0.05, 0.43) and PFHxS (β = 0.18; 95% CI: 0.00, 0.35) in the upper tertile compared with daughters with concentrations in the lower tertile (Maisonet et al 2015).[31]
Genotoxicity/Mutagenicity	Not found in CCRIS or GENE-TOX
Endocrine Disruption/Thyroid Effects	Found on TEDX List of Potential Endocrine Disruptors[32] Data from National Health and Nutrition Examination Survey (NHANES) for the years 2007–2008 were used to evaluate the effect of PFOS, PFOA, PFNA, PFDA, PFHxS, and 2-(*N*-methyl-perfluorooctane sulfonamide) acetic acid on the levels of six thyroid function variables (Jain 2013). Levels of triiodothyronine were found to increase with the levels of PFOA (p=0.01), and total thyroxine levels were found to increase with increase in PFHxS levels (p<0.01).[33] In many PFAS toxicology studies decreased thyroid hormone levels are observed. The mechanism is a competitive binding to the thyroid hormone plasma transport protein transthyretin (TTR) that will alter/decrease the free thyroxine (T4) in blood. This competitive binding capacity of some poly- and perfluorinated compounds was studied by Weiss *et al.* (2009) with a radio-ligand-binding assay. The binding potency of the fluorinated chemicals was 12-300 times lower than for thyroxine itself and decreased in the order: PFHxS > PFOS/PFOA > PFHxA > PFBS.[34] PFHxS (and PFOS and PFOA) acts as a 17β-Estradiol (E2) agonist *in vitro* and enhanced significantly the E2-induced estrogen receptor (ER) response in human MVLN breast cancer cells (Kjeldsen *et al.* 2013).[35] "EC_{50} values of the three ER active test compounds were estimated to be in the range of $2.9X10^{-5}$ to $6.5X10^{-5}$M, indicating similar potencies of PFHxS, PFOS, and PFOA. However, the relative potencies of the three PFAAs were approximately 10^6-fold lower than the positive control 17β-Estradiol (E2, Table 2). Thus, the observed estrogenic effects of PFHxS, PFOS, and PFOA were relatively weak compared to the natural estrogen ligand."(Kjeldsen et al. 2013)[36]

	Maternal serum concentrations of HCB, PFOS and PFOA were associated with increased BMI z-scores and/or overweight risk (i.e. BMI z-score≥85th WHO percentile). No clear association was found for maternal serum-PCBs, p,p'-DDE, PFHxS, PFNA and PFDA. (Karlsen et al., 2017).[37] Levels of certain PFASs (… perfluorohexane sulfonate [PFHxS]) showed a moderate to weak correlation with relevant antibodies. … Based on these negative correlation results between relevant antibodies and PFASs in this study, it may suggest that the exposure of PFASs can cause an altered metabolism resulting from the disease, including hypothyroidism. … some PFASs that were higher in infants with CH (Congenital Hypothyroidism) correlated with antibodies, specifically TSI (Thyroid Stimulating Immunoglobulin), which is indicative of metabolic disease (Kim and Oh, 2014)(Kim et al 2016).[38] "A significant increase was observed for $\sum_8$PFASs, PFOS, and PFHxS concentrations with age ($p<0.01$). Gender-related differences were found; PFOS, PFHxS, PFBS, and PFOA levels were higher in males ($p<0.05$), and the mean concentration of $\sum_8$PFASs was 1.5 times greater in males (6.02 ng/mL) than in females (4.15 ng/mL). PFOS and $\sum_8$PFASs were significantly negatively correlated with FT3 and FT4 and positively correlated with TSH while PFPeA and PFHxA were significantly positively correlated with TGAb and TMAb in all the samples. The opposite associations between FT3, TSH, and PFOS, PFOA and PFHxS levels in hypothyroidism and hyperthyroidism group indicate that the PFOS, PFOA and PFHxS enhance the negative feedback mechanisms of the thyroid gland." PFHxS was detected in 98.0% of the serum of samples. (Li et al 2017c)[39] Transcriptional effects of PFHxS on thyroid related genes, *Pax 8* and *Hex* were studied (Naile et al 2012).[40]
Immunotoxicity	An investigation of children aged 5 and 7 years from Faroe Island in the Atlantic showed that commonly prevalent exposures to PFOS, PFOA, PFHxS, PFNA and PFDA measured in blood serum were associated with lower anti-body responses to childhood immunizations (vaccinations) and an increased risk of antibody concentrations below the level needed to provide long-term protection against diphtheria and tetanus (Grandjean *et al.* 2012).[41]
Other organ toxicity	Many PFAS are highly potent peroxisome proliferators in rodent livers

	and affect mitochondrial, microsomal, and cytosolic enzymes and proteins involved in lipid metabolism (Ikeda *et al.* 1985; Van den Heuvel 1996; Upham et. al. 1998; Kudo *et al.* 2000). The liver fatty acid–binding protein (L-FABP) is a transport protein known to bind PFAS (Luebker *et al.*, 2002). The liver toxicity and peroxisome proliferation potency in rats depends on the carbon chain length. PFCA activated both mouse and human PPARα in a concentration dependent fashion, and activation of PPARα by PFCA was positively correlated with carbon chain length, up to C9. PPARα activity was higher in response to carboxylates compared to sulfonates. Activation of mouse PPARα was generally higher compared to that of human PPARα (Wolf *et al.* 2008). The relative activity increased from PFBS < PFOS < PFHxS < PFBA < PFHxA < PFOA. [42] At all doses reductions in serum total cholesterol and other biochemical changes in the blood … (Butenhoff *et al.* 2009).[43] "All PFCAs led to increased PPARα and PPARγ activity from exposure concentrations of 30 uM or 100uM, except for PFBA, which did not cause any change in PPARγ activity" (Rosenmai 2016).[44] Increases in liver weight and cell size, and decreases in DNA content per mg of liver, were observed for all compounds in WT mice, and were also seen in PPARα-null mice for …PFHxS, … (Das et al 2017).[45] These results indicate that most of the PFAAs increase liver TG load and promote steatosis in mice (Das et al 2017).[46] ITC measurement revealed that PFOA/PFNA displayed a moderate affinity for hL-FABP at a 1:1 molar ratio, a weak binding affinity for PFHxS and no binding for PFHxA (Sheng et al 2016).[47] The strongest overall effect was a nearly 10-fold induction of Scd1 by PFHxS. The sulfonated PFAAs produced numerous, strong changes in gene expression similar to the effects after treatment with the PPARγ agonist rosiglitazone. … In summary, all perfluorinated compounds increased cell number, decreased cell size, increased total triglyceride, and altered expression of genes associated with adipocyte differentiation and lipid metabolism (Watkins et al, 2015).[48] "All PFASs induced PPARα activity statistically significantly, as compared to the vehicle control, except PFUnDA, PFOS and FOSA (Figure 2B). The lowest observed effect concentrations (LOECs), expressed as nominal concentrations, causing statistically significant

	PPARα activation were 30 or 100 µM, except PFTeDA for which an effect was observed from 10 µM. For all treatment concentrations, there was an apparent increase in PPARα activity with PFCA perfluorocarbon chain length, which peaked with PFOA. Short-chain (PFBA and PFPeA) and long-chain (PFDoDA and PFTeDA) PFCAs induced PPARα activity up to twofold. Similar fold-induction was observed for PFBS and PFHxS. The highest induction of PPARα activity, 2.5–3.7-fold, was observed after treatment of cells with PFHxA, PFHpA, PFOA, PFNA and PFDA." (Rosenmai 2017) [49]
Skin, Eye and Respiratory Effects	
*Irritant – **S**kin, **E**ye, or **R**espiratory*	Skin irritation (Category 2), H315 (for 3871-99-6); Eye irritation (Category 2A), H319 (for 3871-99-6); Specific target organ toxicity – single exposure (Category 3), Respiratory system, H335 (for 3871-99-6)[50]
*Corrosive – **S**, **E**, or **R***	Skin corrosion 1B causes severe skin burns and eye damage[51]
*Permanent Damage – **S**, **E**, or **R***	Not found
*Sensitizer– **S** & **R***	Not found in AOEC database
Asthmagen – Initiator or Exacerbator	Not found in AOEC database In a study from Taiwan PFAS serum levels including of PFHxS were reported to be significantly higher in children with asthma compared to children without asthma (Dong *et al.* 2013).[52]
Skin Absorption, Kp	It is known from animal studies that the studied short chain polyfluoroalkylated substances (PFAS) are almost completely absorbed orally and by inhalation but that skin absorption may be negligible.[53]
LOAEL	Not found
NOAEL	Thus, in this rodent study the metabolism of lipids was affected at a daily exposure for 0.3 mg/kg b. w., and liver damage was observed after exposure to 3 mg/kg b. w. per day (NOAEL = 1 mg/kg per day). A NOAEL of 10 mg/kg b. w. per day (highest concentration tested) for effects on the reproduction was determined for PFHxS.[54]
Benchmark Dose Response (BMD)	Not found
Toxicokinetics	In retired workers from the fluorochemical producing industry serum half-lives for PFHxS (perfluorohexane sulfonate) were 7.3-8.5 years or about twice the half-lives for PFOS and PFOA (Olsen *et al.* 2007). Thus, the half-life for PFHxS in rats is, like for other PFAS, much shorter than in humans. However, the half-life of PFHxS is shorter in rats than the half-life (40 days) of PFOS in rats. The toxicokinetics of the potassium salt of PFHxS after a single intravenous exposure (10 mg/kg b. w.) was compared in rats, mice and monkeys (Sundström *et al.* 2012). Urine was the major route of excretion in male and female rats, and mean daily fecal excretion was <0.5% of administered dose at all times. Within 96 hours females

	excreted 28% of a dose in urine. Males excreted only about 6–7% of a dose in urine and had very much higher levels of PFHxS in blood and liver. The excretion increased with the dose. The mean serum elimination half-lives in male and female rats were calculated to 6.83 days and 1.83±0.26 days, respectively. These values are not likely to be reliable due to the short duration (24 hours). A comparison between intravenous- and oral exposures showed a PFHxS bioavailability of about 50%. After 10 weeks the mean serum elimination half-lives in male rats was calculated to about 29 days. In females the levels of PFHxS in the blood after 10 weeks were too low to quantify. In mice given oral doses of 20 mg PFHxS-K/kg body weight the mean serum elimination half-lives in males and females were 30.5 and 24.8 days, respectively, and not so different as for rats. Elimination in urine dominated also in mice but it was less than for rats. After 24 hours <3% of a dose was recovered in urine. In monkeys, PFHxS was much more long-lived in the blood with mean serum elimination half-lives for females and males of 87±27 days versus 141±30 days, respectively; however, this difference was not statistically significant. Less than 0.1 % of a dose was determined in the urine, thus renal elimination was very slow in monkeys.[55]
Synergistic or Antagonistic Effects	Not found
Environmental and Human Health Exposure and Risk Values	
RfC/RfD	Not found in IRIS database "VTi = 0.004 mg/kg/day; Critical impact/effect: Hepatic effects, Butenhoff et al. 2012, NOAEL 1 mg/kg/day"[56]
ATSDR-MRL	Not found on ATSDR-MRL June 2017 list (Note PFOA and PFOS are on the list)
Adverse Effect Levels: DNEL, PNEC, PNEL	Not found
Health Based Exposure Limits	
NIOSH-REL/IDLH/Ceiling Limits	Not found in NIOSH-PG
OSHA-PEL	Not found in Z tables
ACGIH TLV-TWA	Not found in Z tables or in RTECS
TLV-STEL	Not found in Z tables
Biomonitoring Action Limits	Not found
Drinking Water Standards	CT DPH Action level = 70 ppt for Σ(PFOS, PFOA, PFHxS, PFNA, PFHpA) - same as EPA advisory level for Σ(PFOS and PFOA)
Other	Not found
ENVIRONMENTAL & ECO-SYSTEM HAZARDS	
Persistence	PFHxS is considered as persistent and stable in the environment and is regarded as degradation product of other perfluorinated compounds.[57] Photolysis: AOPWIN v1.92 predicted the atmospheric half life = 76.4

	days (12.hr day; 1.5E6 OH/cm3); Photolysis in water: Taniyasu and co-workers (2013) No significant photolysis observed for PFHxS.[58] The stability of organic fluorine compounds has been described in detail by Siegemund et al. (2000). When all valences of a carbon chain are satisfied by fluorine, the zig-zag shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to envelope the carbon skeleton completely and shield it from chemical attack.[59]
Bioaccumulation	Presence in humans: In blood from some office workers in Boston exposed to FTOHs. PFHxA was not detectable but PFHxS reached 0.2-13 ng/mL with a geomean of 1.5 ng/mL (Fraser *et al.* 2012).[60] The long residence time of PFHxS in human blood (half-life 7-8 years) may explain the relatively low organ concentrations of this chemical compared to other PFASs measured in Spanish autopsy tissues. The highest concentration of PFHxS was found in the kidneys but 20 times lower compared to PFBA (Perez *et al.* 2013).[61] Significantly higher concentrations of PFBS and PFHxS were found among women who lived in districts modeled to have received contaminated drinking water compared to unaffected districts both in 1996-1999 and 2008-2011, indicating that the contamination was already present in the late 1990s. Isomer-specific analysis of PFHxS in serum showed that women in districts with contaminated drinking water also had an increased percentage of branched isomers (Gyllenhammar et al, 2015).[62] In the serum of 755 Spanish adults aged 18–65: The geometric mean concentrations (and P95 values) for … PFHxS was 0.91 (2.84), µg/L,… (Bartolome et al 2017).[63] Men presented higher levels than women, and results confirmed that lactation contributes to a reduced body burden for PFAS in women. PFOS was the predominant PFC detected in almost all Asian breastmilk samples, followed by perfluorohexanesulfonate (PFHxS) and PFOA. PFHxS was found in more than 70% of the samples analyzed from Japan, Malaysia, Phillipines, and Vietnam, at mean concentrations ranging from 6.45 (Malaysia) to 15.8 (Phillipines) pg/mL.[64]

	Presence in environment and biota: - Study of Spanish Jucar river basin, water and biota samples – water conc. 12.07-36.7 ng/L, detected in 13% of samples, non-detect in sediment; detected in biota 0.63 µg/kg in one fish sample (limits of quantification 0.02-2.26 µg/kg.)[65] - Harbor seals 33 µg whole body burden (compared with 2,500 µg PFOS). Concentration in tissues: thymus 10.5 ng/g wet wt, lung 8 ng/g, liver, kidney, heart, thyroid btwn 4-7 ng/g.[66] - Female herring gull eggs: 0.8 ng/g ww yolk, albumen ND - Herring gull tissue: plasma 8 ng/g ww, liver 0.8 ng/g, brain ND – 1.5 ng/g, muscle ND – 2.1 ng/g, adipose ND-0.2 ng/g[67] - Arctic food web frequency of detection: 30% capelin, 67% cod (up to 3.5 ng/g ww), 0% sediments, macroalgae, and duck liver; 50% beluga whale fetus (up to 4 ng/g), 11-14% blood and liver (up to 3.7 ng/g)[68] - Rainbow trout PFHxS half-life: carcass 11 days, blood 10 days, liver 12 days. Tissue concentrations ~0.05 – 0.1 µg/g kidney, liver, gall bladder, blood plasma, gill, gonads. <0.01 in muscle, but given that muscle is ~67% of trout by wt, could contain ~60% of total body burden of PFHxS.[69] - Human: mean concentration kidney 20.8 ng/g ww, lung 8.1 ng/g, brain 3.2 ng/g, bone 1.8 ng/g, liver 4.6 ng/g[70] Plant bioaccumulation: hydroponic (water only) uptake rate constant k_1 (per day) 2±1 in roots, 0.04±0.04 in shoots; elimination half life 0.17 days; (this rapid elimination was similar for all PFAS studied except PFBA, which had 1.83 day half life)(Muller 2016).[71] Cape Cod groundwater: detected in 55% of 20 private wells sampled, max concentration 41 ng/L. Sampling from other studies and locations, groundwater and surface water, varied from 9.3 – 32 ng/L (Schaider 2016).[72]
BAF	Measured in field [biota]/[water]; ww log BAF in fish, not growth correct or normalized to lipid content. May be influenced by both absorption from surrounding water and diet. European Chub in Orge River, France (Labadie and Chevreuil, 2011): Plasma 3.3 ±0.2 Liver 2.1 ±0.3 Gills 1.5 ±0.2 Gonads 2.4 ±0.4 Muscle 0.9 ±0.3 South Korea (Naile et al, 2013): Fish: Whole body 2.58 ±0.55 Liver 3.08

	Crab: whole body 2.58 ±0.55 Gastropod: whole body 3.28 ±0.22 Bivalve: whole body 2.61 ±0.41[73]
BCF	Rainbow trout 10-12 days; calculated steady state BCF 100 (liver), 76 (blood), 12 day accumulation ratio = 54-59[74] In one study, the Log BCFs of the C4-C7 sulfonic acids were all found to be below 1 in fish thus indicating little bioaccumulation potential of these substances in this organism group in contrast to long-chain (C11-C13) PFSAs.[75] Note: Use caution in applying typical BCF criteria given different behavior of these surfactants.
BMF	(Predator-prey magnification via diet – for field studies this incl water) *All BMF>1 indicate biomagnification potential – there are significant uncertainties and assumptions included in the following calculated BMFs, but as a whole they indicate a potential for biomagnification.* Rainbow trout, multiple PFAS: whole body BMF = 0.18 (Goeritz et al 2013) Dolphin/striped mullet: whole body BMF = 4.0 (Houde 2006) Dolphin/red drum: whole body BMF = 14 (Houde 2006) Dolphin/spotfish: whole body BMF = 6.0 (Houde 2006) Dolphin/seatrout: whole body BMF = 3.3 (Houde 2006) Dolphin/pigfish: whole body BMF = 2.0 (Houde 2006) Dolphin/pinfish: whole body BMF = 1.8 (Houde 2006) Pigfish/zooplankton: whole body BMF = 9.1 (Houde 2006) Pinfish/zooplankton: whole body BMF = 10 (Houde 2006) Black guillemot/polar cod (liver) BMF = 6.0 (Haukas 2007) Glaucous gull/Polar cod (liver) BMF = 7.2 (Haukas 2007) Glaucous gull/black guillemot (liver) BMF = 8.5 (Haukas 2007) Polar bear/ringed seal (liver) BMF = 251, 373, 163, 285 (depending on location), Canadian Arctic mean=199 (Butt 2008) Polar bear/ringed seal (liver) BMF =20.1 (Riget et al 2013)[76] **TMF**: Houde et al 2006 also attempted to calculate Trophic Magnification Factors (TMF) for dolphin. *Note very high uncertainty*: Dolphin (plasma) TMF = 0.2 ±0.9 Dolphin (whole body) TMF = 0.1 ±0.4[77]
Ecological Toxicity	[Eco-]Toxicity data on PFHxS have not been available. Considering the conclusions on chain length and presence of functional groups of PFAS, it can be expected that PFHxS shows increased toxicity compared to PFBS, as well as increased toxicity compared to PFHxA.[78]
Aquatic Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	Not found

Mammalian Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	Not found
Wildlife Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	Not found
Breakdown/degradation /combustion products	The compound is not expected to undergo hydrolysis or photolysis, and no biodegradation is expected.[79] Biodegradation in water: modeled using BIOWIN v4.10 (not all PFHxS molecular fragments are incl in training sets of model, but along w/ results for PFOS, it adds to weight of evidence of persistence): BIOWIN 2 = 0.0000 (<0.5 = persistent) BIOWIN 3 = 0.9340 (<2.2 to 2.75 = persistent) BIOWIN 6 = 0.0000 (<0.5 = persistent) PFHxS can, based on the above BIOWIN predictions, be said to fulfil the SVHC P-screening criteria. All other justification is read across using structural analog PFOS[80]
Anaerobic degradation	Not found
Aerobic degradation	Not found
Other observable ecological effects (e.g. BOD)	**MEASURED LEVELS IN WILDLIFE:** The measured concentrations of PFHxS in: • Wildlife are summarised in Fig 1. The values presented are mean values sampled per species/year/location/author(s). For measurements below the limit of detection (LOD), half LOD is used. Fig 2 includes the same values as in Fig 1, apart from the values on invertebrates, fish and birds from Zhou et al. (2014), which are sampled in a region heavily polluted by perfluorinated compounds. • Invertebrates, fish and birds are by far highest in the study by Zhou et al. (2014), with reported concentrations of PFHxS ranging from 4.1-18 µg/kg ww in invertebrates, 0.2-74 µg/kg ww in fish and 1.5- 27 µg/kg ww in birds. Zhou and coworkers (2014) sampled invertebrates, fish and birds from lake Tangxun, China, which is situated in a region which is heavily polluted by perfluorinated compounds due to a lot of several small-scale fluorochemical manufacturers. • In Zhou (2014) (invertebrates, fish and birds) PFOS is always detected at the highest concentrations (up to more than a factor of ten higher compared to the other PFAS analysed), with PFHxS most often being the PFAS detected at the second highest levels. • With the exception of Zhou (2014), the levels of PFHxS detected

	in invertebrates are roughly about the same as those of PFOS, sometimes higher, sometimes lower. In fish, birds and mammals the levels of PFOS, with only a few rare exceptions, are always higher to substantially higher than those of PFHxS. • The levels of PFHxS in invertebrates, fish, birds and mammals are sometimes higher and sometimes lower than those measured of PFOA. An observation that can be made is that the concentrations of PFHxS generally are lower than those of PFOA in seals from arctic regions, but the concentrations of PFHxS in polar bears from the same regions are generally higher, which may be an indication of biomagnification. See ECHA SVHC document pg. 40, or TURI PFHxS SVHC Mar 2017 PBT Notes for Figures 1 & 2.[81]
Fate and Transport: Aquatic	The Danish Report noted that fate data on PFHxS are very sparse.[82] Based on the read-across approach, conclusions applying to the fate of PFBS can be anticipated to be valid for PFHxS as well. Thus, the compound is not expected to undergo hydrolysis or photolysis, and no biodegradation is expected. The substance was, like other PFAS, found to be poorly removed in WWTPs.[83]
Fate and Transport: Terrestrial	Not found
Fate and Transport: Atmospheric	Not found
Transport Issues	Not found
Factors affecting bioavailability	Not found
Global Environmental Impacts	
Ozone Depletion Potential (ODP)	Not found
Global Climate Change	Not found
Greenhouse Gas Production	Not found
Acid Rain Formation	Not relevant
Special Reports	
EU	**Short-chain Polyfluoroalkyl Substances (PFAS)** – A literature review of information on human health effects and environmental fate and effect aspects of short-chain PFAS, Environmental project No. 1707, 2015 http://www2.mst.dk/Udgiv/publications/2015/05/978-87-93352-15-5.pdf **Polyfluoroalkyl substances (PFASs) in textiles for children** – Survey of chemical substances in consumer products No. 136, 2015 http://www2.mst.dk/Udgiv/publications/2015/04/978-87-93352-12-4.pdf **Survey of PFOS, PFOA and other perfluoroalkyl and polyfluoroalkyl substances** – Part of the LOUS-review, Environmental project No. 1475,

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Notes on chemical research: Not found in NIOSH Pocket Guide; HSDB; HAZMAP

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