# Updated EHS Summary of Perfluorohexanoic acid for the MA TURA Science Advisory Board Meeting – March 29, 2017

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| **CAS # 307-24-4**<br>  | **Perfluorohexanoic acid (PFHxA)**<br>Synonym[1]s: EINECS 206-196-6; NSC 5213; Perfluorohexanoic acid; Undecafluoro-1-hexanoic acid; UNII-ZP34Q2220R<br>**RTECS #[2]:** MO8445000<br>**EINECS #[3]:** 206-196-6<br>**Molecular Weight[4]**: 314.0499<br>**Molecular Formula[5]:** C6-H-F11-O2<br>**Common Salts:**<br>Sodium perfluorohexanoate, CAS # 2923-26-4<br>Ammonium perfluorohexanoate, CAS # 21615-47-4 |
| **PHYSICAL CHARACTERISTICS** | |
| *Primary Use* | Protective coatings for fabrics and carpet, paper coatings, insecticide formulations, surfactants /Perfluorochemicals/[6]<br>Long-chain perfluoroalkanecarboxylic acids and their salts are surface-active chemicals (surfactants), which greatly reduce the surface tension (surface energy) of water, aqueous solutions, and organic liquids even at low concentrations. These acids (C6-C12) and derivatives are used as wetting, dispersing, emulsifying, and foaming agents. /Long-chain perfluoroalkanecarboxylic acids/[7]<br>*"PFHxA is both a degradation product and potential impurity in fluorotelomer-based products and in perfluoroalkane sulfonyl-based electrochemical fluorination products. PFHxA is not generally manufactured and used itself for commercial purposes. PFCAs such as PFHxA were released directly into the environment during the historical manufacture and use (of) per- and poly-fluoroalkyl substances".*[8] |
| *Physical state, odor at room temperature & pressure* | Colorless liquid[9] |
| *Melting point; Boiling point* | Not found; BP = 157 deg C[10] |
| *Solubility* | In water, 15,700 mg/L at ambient temperature[11] |
| *Specific Gravity* | Not found |
| **SAFETY/PHYSICAL HAZARDS** | |
| *Vapor Pressure* | 1.98 mm Hg at 25 deg C (est)[12] 264 Pa (exp.)[13] |
| *Flammability* | Not found |
| *Flashpoint* | Not found |
| *Flammability Rating* | Not found |
| *Auto Ignition Point* | Not found |
| *Combustion products* | Special hazards arising from the substance or mixture: Carbon oxides, Hydrogen fluoride[14] |
| *Explosivity (UEL, LEL, shock sensitive)* | Not found |

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| *Oxidizer* | A molecular entity capable of donating a hydro[ge]n to an acceptor (Bronsted base).[15] Not an oxidizer, as is donating. |
| *Corrosivity* | Non-harmonized classifications: H290 Met. Corr. 1 (May be corrosive to metals); H314 – Skin Corr. 1B[16] |
| *pH* | Not found |
| *Reactivity* | Incompatible materials: Strong oxidizing agents[17] |
| *Viscosity* | Not found |
| *Odor Threshold* | Not found |
| *Particle size, shape, respirable fraction* | Not found |
| *Other physical hazards associated with process: Heat, gases under pressure, noise, vibration, ergonomic hazard* | Not found |
| **HEALTH HAZARDS** | |
| **Acute Toxicity** | |
| *Oral $LD_{50}$* | The acute toxicity of the sodium salt of perfluorohexanoic acid (PFHxA) is considered low with a rat oral $LD_{50}$ > 1,750 mg/kg bw.[18] |
| *Dermal $LD_{50}$* | Not found in RTECS |
| *Inhalation $LC_{50}$* | Not found in RTECS |
| *Intraperitoneal $LD_{50}$* | Not found in RTECS |
| *TDLo* | Values ranging from 4,500 mg/kg/90D-I to 18,000 mg/kg/90D-I[19] |
| **Chronic or Sub-chronic Toxicity** | |
| *IARC rating* | Not found in the IARC database |
| *Carcinogenicity* | Not found on Prop 65 list[20]; Not found in the CCRIS database |
| *Neurotoxicity* | Not found in HAZMAP<br>See wildlife toxicity below |
| *Developmental/Reproductive Toxicity* | Not found on Prop 65 list[21]<br><br>Details from developmental study re: NaPFHx and reproductive study re: $NH_4$PFHx available (Dewitt 2015)<br><br>The reproductive oral toxicity of the ammonium salt of PFHxA in pregnant female mice was investigated by Iwai and Hoberman (2014). PFHxA was administered once daily from gestation day 6 through 18 in doses up to 500 mg/kg b. w.[22] Adverse effects occurred only in the 175 mg/kg/d group (*from Phase 2*) and consisted of increased stillborn pups, pups dying on PPD I, and reduced pup weights on PPD I.[23] The maternal and reproductive no observable adverse effect level (NOAEL) of PFHxA ammonium salt was 100 mg/kg/d.[24]<br><br>See aquatic toxicity below |

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| *Genotoxicity/Mutagenicity* | Not found in the GENETOX database<br><br>• Micronucleus (G04048) Completed<br>  ○ Rats: Harlan Sprague-Dawley<br>  ○ Male Equivocal<br>  ○ Female Negative<br>• Salmonella (A97455) Completed<br>  ○ Negative[25]<br>PFHxA did not generate reactive oxygen species or cause DNA damage in human HepG2 cells (Eriksen et al. 2010), and was found not to be genotoxic based on negative results from both the bacterial reverse mutation assay and the in vitro chromosomal aberration assay (Loveless et al. 2009).[26]<br>Mulkiewicz *et al.* (2007) evaluated the acute cytotoxicity of among others PFHxA in several *in vitro* assays using eukaryotic cell lines, bacteria and enzymatic assays. The toxicity was in general low and increased with chain length, and the toxicity of PFHxA was about ten times lower than PFOA.[27]<br>In an *in vitro* assay with human colon carcinoma (HCT116) cells estimated values of $EC_{50}$ decreased with elongation of fluorocarbon chain from PFHxA > PFHpA > PFOA > PFNA etc. The cytotoxicity was rather low but intensified after longer exposure (72 h) (Kleszczynski *et al.* 2007). Again a study showing stronger effect by the substance with the shortest chain.[28] |
| *Endocrine Disruption/Thyroid Effects* | Found on TEDX List of Potential Endocrine Disruptors[29]<br>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. PFBA and FTOHs had no effect in that assay.[30]<br>See wildlife toxicity below |
| *Immunotoxicity* | |
| *Other organ toxicity* | PFHxA is hepatotoxic[31]<br>Not found in HAZMAP or NIOSH Pocket Guide |
| **Skin, Eye and Respiratory Effects** | |
| *Irritant – **S**kin, **E**ye, or **R**espiratory* | Non-harmonized classifications: H311 – Acute Tox. 3 (Toxic in contact with skin).[32] |
| *Corrosive – **S, E, or R*** | Non-harmonized classifications: H314 – Skin Corr. 1B; H318 – Eye Dam. 1[33] |

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| *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<br>One human study examined the association between PFHxA exposure and childhood asthma. The study reported no difference in serum levels (median = 0.2 ng/mL) in children aged 10-15 years with (n = 231) or without (n = 225) asthma, and no dose-response trend (Dong *et al.*, 2013).[34] |
| *Skin Absorption, Kp* | Not found |
| *LOAEL* | As initially described in section 4.2.1, COS-1 cells were transfected with mouse or human PPARα plasmids to investigate the effects of different PFASs on PPARα activation. PFHxA (5-100 µM) caused a significant dose -dependent activation of mouse and human PPARα compared with controls lowest observed adverse effect level (LOAEL, 20 and 10 µM, respectively). Greater PPARα activity was induced by PFASs with longer chain lengths and sulphonates were more potent than carboxylates. PFNA (mouse, 5 µM; human, 11 µM) and PFOA (6 µM; 16 µM) were most potent at activating PPARα, followed by PFDA (20 µM; human not active), PFHxA (38 µM; 47 µM), PFBA (51 µM; 75 µM), PFHxS (76 µM; 81 µM), PFOS (94 µM; 262 µM) and PFBS (317 µM; 206 µM) (Wolf et al., 2008a).[35] |
| *NOAEL* | In a 90-day gavage study in rats a NOAEL value for PFHxA of 20 mg/kg bw/day was identified based on effects on the liver and blood parameters (Loveless et al., 2009). In another study, in which PFHxA was administered in drinking water, a NOAEL of 50 mg/kg bw/day males and 200 mg/kg bw in females was determined (Chengelis et al., 2009). This is higher than the NOAEL for PFOA.[36] The Chengelis et al., 2009 study NOAELs were based on liver histopathology and liver weight changes.[37]<br>The reproductive arm of a 90-day toxicological evaluation in which Sprague Dawley rats were administered PFHxA (0, 20, 100 or 500 mg/kg b.w. per day NaPFHx) by oral gavage (see Section 5.2.3) indicated NOAELs of 20 mg/kg b.w. per day (P1 adult males) and 100 mg/kg b.w. per day (F1 pups), based on reduced body-weight parameters. A parallel developmental toxicity study (same doses, GD 6-20) indicated a maternal and developmental NOAEL of 100 mg/kg b.w. per day, based on maternal and fetal reduced body weight (Loveless et al., 2009).[38] |
| *Benchmark Dose Response (BMD)* | Russell *et al.* (2013) calculated the benchmark dose (BMD10 = 95% lower confidence limit of a dose resulting in a 10% increase in risk) to 13 mg PFHxA/kg b. w. per day.[39] |
| *Metabolites* | PFHxA was not metabolized in rat or mouse hepatocytes, nor were any |

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| | metabolites observed after oral dosing in either rodent species (Gannon *et al.* 2011).[40] |
| *Synergistic or Antagonistic Effects* | It was also observed that exposure of JEG-3 cells to a *mixture* of the eight PFASs (0.6 µM each) altered/increased cellular lipid pattern (up to 3.4-fold) at concentrations well below those that generate toxicity.[41] |
| *Interactions* | ... **PFHxA** and PFOA were used as model perfluorinated carboxylic acids (PFCAs) to characterize the major site of PFCA interaction in human sera. Using novel heteronuclear saturation transfer difference nuclear magnetic resonance spectroscopy experiments, human serum albumin (HSA) was identified as the major site of interaction for both PFHxA and PFOA in human sera. Heteronuclear single quantum coherence nuclear magnetic resonance experiments were then performed to interrogate site-specific interactions of PFHxA and PFOA with isolated HSA. **PFHxA** was found to bind specifically to Sudlow's drug-binding site II, whereas PFOA interacted preferentially with Sudlow's drug-binding site I at the lower concentration, with additional interactions developing at the higher concentration. These experiments highlight the utility of nuclear magnetic resonance spectrometry as a tool to observe the in situ interactions of chemical contaminants with biological systems. Both PFCAs displaced the endogenous HSA ligand oleic acid at concentrations lower than observed for the drugs ibuprofen and phenylbutazone, which are established HSA ligands. Interactions between PFCAs and HSA may affect the pharmacokinetics and distribution of fatty acids and certain drugs in the human body and warrant further investigation.[42] |
| *GHS Codes* | Non-harmonized classifications: H314 – Skin Corr. 1B; H290 – Met. Corr. 1; H318 – Eye Dam. 1; H301 and H311 – Acute Tox. 3; H330 – Acute Tox. 2[43] |
| **Environmental and Human Health Exposure and Risk Values** | |
| *RfC/RfD* | Not found in EPA IRIS database |
| *ATSDR-MRL* | Not found on the March 2016 ATSDR Minimal Risk Levels List |
| *Adverse Effect Levels: DNEL, PNEC, PNEL* | |
| **Health Based Exposure Limits** | |
| *NIOSH-REL/IDLH/Ceiling Limits* | Not found in NIOSH Pocket Guide |
| *OSHA-PEL* | Not found on OSHA website |
| *ACGIH TLV-TWA* | None |
| *TLV-STEL* | Not found in NIOSH Pocket Guide |
| *Biomonitoring Action Limits* | |
| *Drinking Water Standards* | Concentrations found in Drinking Water indicated HSDB; There are no set threshold values for the content of PFAS in groundwater / drinking water in Denmark.[44] |

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| *Other* | In autopsy tissues PFHxA partitioned mostly to the liver and brain (median: 68.3 and 141 ng/g, respectively).[45]<br>Analysis of Spanish human autopsy tissues revealed that the highest concentrations of most PFAS, including PFHxA, were found in lung tissues but the highest PFAS in the brain was PFHxA. PFOS concentration in the brain was less than a third of that (Perez *et al.* 2013). Thus the body half-life of PFHxA seems to be much longer in humans than in experimental animals.[46]<br>PFCAs mimic fatty acids, and specifically PFHxA is attached to a different binding site on serum albumin compared to PFOA; however, PFOA is more strongly bound, and 5-6 PFOA molecules can interact with each albumin molecule (D'eon and Mabury 2010).[47] |
| **ENVIRONMENTAL & ECO-SYSTEM HAZARDS (Bulk of information cited UNEP 2015a and UNEP 2015b)** | |
| **PBT** | As with PFOA, PFHxA is very persistent and is not transformed or degraded by abiotic mechanisms (e.g. hydrolysis and photolysis) or biotic mechanisms in water or soil. Precursors such as fluorotelomers or PFAS with other functional groups attached will undergo primary degradation to PFHxA.[48]<br><br>On ECHA Public Activities Coordination Tool (PACT) list for PBT; Risk Management Option Analysis is under development[49]<br><br>Categorized by the Australian government as P, but not B or T.[50]<br><br>Data on the degradation half-life of PFHxA in soil, sediment, and water are not available. However, based on a read-across from degradation studies of PFOA, PFHxA is likely to be environmentally persistent.[51]<br>Although, the biodegradation of PFHxA has not been directly studied, PFHxA is a metabolite of 6:2 FTOH degradation (Butt et al. 2014). Studies of 6:2 FTOH degradation in soil and sediment do not indicate that PFHxA completely mineralizes with a half-life less than the six month criterion listed in Annex D 1 (b) (i).[52]<br><br>Limited experimental data suggest that PFCAs may react with photochemically-generated hydroxyl radicals in the atmosphere. Taniyasu et al. (2013a) conducted a field study on the photolysis of perfluoroalkyl substances at Mt. Mauna Kea, Hawaii (4200 m). PFHxA concentrations decreased by 0.8% after 106 days of solar irradiation. This suggests that the atmospheric oxidation of PFHxA occurs extremely slowly and is not expected to impact the half-life of PFHxA in the atmosphere.[53]<br>Therefore, it would meet the POP criteria for persistence. |

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| *Bioaccumulation* | As for PFOA, PFHxA is both hydrophobic and lipophobic, and so does not follow typical pattern of partitioning to fatty tissues and accumulating there. Instead it tends to bind to proteins, so protein-rich tissues such as liver; kidney and blood are their main repositories. Precursors such as fluorotelomers may be partially responsible for the observed bioaccumulation of the acids. [54]<br>There are two mechanistic theories for observed bioaccumulation of perfluoroalkyl acid substances: 1) partitioning to membrane phospholipid (PL) which have higher affinity for charged species than neutral storage lipids; and 2) protein binding (PB) model assumes interactions with proteins, including serum albumin, liver fatty acid binding proteins (L-FABP) and organic anion transporters determine distribution, accumulation and half-lives. Likely that both mechanisms are at work, where the protein component would account for the accumulation in the blood and elimination and reabsorption as mediated by transporter proteins, and phospholipid describing the distribution into tissues where little or no binding occurs (e.g., liver). Increasing bioaccumulation tendency with increasing C chain length could be explained in the PL model by increasing hydrophobicity which decreases elimination rates, For PB model, bioaccumulation is determined based on balance of affinities for albumin, L-FABP and renal transporter proteins.[55]<br>Serum Elimination Half-lives[56]:<br>**Rat:** Male – 1.6 hours; Female – 0.6 hours (concentrated in tissues: bladder, plasma, kidney, liver and skin[57])<br>**Mouse:** 1 hour[58] (concentrated in tissues: plasma, bladder, liver, kidney, lung, heart[59])<br>**Monkey:** 14-47 hours[60]<br>**Human:** 32 days**<br>** The toxicokinetics of perfluorohexanoic acid (PFHxA) has recently been evaluated in human ski waxers (Russell *et al.* 2013). The decline in blood levels after the ski season was used to determine the apparent human blood elimination half-life to 14-49 days with a geomean of 32 days. These calculations assume that PFHxA is eliminated from the body, when it leaves the blood, however, instead PFHxA may be distributed to various organs as it was measured in liver, kidney, bone and brain from some autopsy samples from Spain (Perez *et al.* 2013).[61]<br>The log BCFs of the C4-C7 carboxylic acids were found to be below 1 thus indicating little bioaccumulation potential of these substances in fish. Short chain PFCAs are not considered bioaccumulative according to the regulatory criteria of 1000–5000 L/kg.[62] |

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| | The bioaccumulation of PFOS and other PFAS is higher in the marine environment than in soil.[63] These findings are believed to be valid also for the short-chain perfluorinated carboxylic and sulfonic acids and their salts. According to a number of reports (e.g. Ellis et al. (2004), Butt et al. (2010), Martin et al. (2013)), the acids are not very bioaccumulative in themselves but precursors such as fluorotelomer alcohols and acrylates accumulate and are subsequently transformed in the organs of animals to the corresponding acids, which are retained in the body.[64]<br>Presence in environment and biota:<br>Study of Spanish Jucar river basin, water and biota samples –water conc. 1.44-18.7 ng/L, detected in 40% of samples, non-detect in sediment; non-detect in biota sampled (limits of quantification 0.02-2.26 µg/kg.)[65]<br>Human: study of 20 individuals at autopsy Catalonia, Spain. Mean concentrations: 180 ng/g ww brain, 115 ng/g liver, 50 ng/g lung, 36 ng/g bone, 6 ng/g kidney. [66] Concentration in brain of PFHxA significantly higher than all other PFAS tested.<br>Plant bioaccumulation: hydroponic (water only) uptake rate constant $k_1$ (per day) NA (no good slope fit) in roots, 0.6±0.2 in shoots; elimination half life 0.21 days; (this rapid elimination was similar for all PFAS studied except PFBA, which had 1.83 day half life).[67]<br>Cape Cod groundwater: detected in 50% of 20 private wells sampled, max concentration 2 ng/L. Sampling from other studies and locations, groundwater and surface water, varied from 14 – 110 ng/L.[68]<br>An additional study on the uptake of PFHxA by marine ogliochetes in sediment also determined a BSAF (The Biota-Sediment (or Biota-Soil) Accumulation Factor) of 2.2 to 3.5 g, dw/g, ww, indicating some uptake of PFHxA into sediment dwelling invertebrates (Lasier et al. 2011). ... There are currently no regulatory screening criteria for bioaccumulation based on BSAFs in sediment, however typically BSAFs > 1 are associated with a potential for bioaccumulation.[69]<br>Controlled laboratory bioaccumulation experiments with terrestrial worms indicate that BSAF values for PFHxA are greater than 1 g, dw/g, ww (Table 6.5). Although there are no formal criteria for interpreting BSAF values, BSAF values greater than one indicate that PFHxA may accumulate from soil or sediment to invertebrates.<br>BSAFs for a number of terrestrial plants were available in the literature, ranging from 0.3 to 7.7 g, dw/g, ww for plants (Table 6.5).[70] |
| *BAF* | |
| *BCF* | **PFHxA** was not found to bioaccumulate in laboratory experiments using rainbow trout (*Onchorynchus mykiss*) with a reported BCF of |

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| | 0.59(1). According to a classification scheme(2), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC).[71]<br>Modelled BCF ~ 0.1 in fish assuming Log BCF:C chain length linear relationship, based on experimentally determined BCF for long chain carboxylic acids in rainbow trout (carcass, liver and blood)[72]<br>Study in muscle tissue of two fish species in Chinese lake determined Log BCF of C4-C7 carboxylic and sulfonic acids all below 1 (little bioaccumulation potential of these substances in fish)[73] |
| *BMF* | |
| *Ecological Toxicity* | $EC_{50}$; Species: *Geitlerinema amphibium* (Blue-green Algae) Exponential Growth Phase BA-13; Conditions: saltwater, static, 20 deg C, pH 7.6-7.8; Concentration: **3.18 mM for 72 hr;** Effect: decreased population growth rate /formulation/[74] 2 other higher values available from this paper in HSDB, species = *Chlorella vulgaris* (Green Algae) and *Skeletonema marinoi* (Diatom)<br><br>Toxicity tests with rainbow trout, *Daphnia magna*, and the alga (*P. subcapitata*) showed corresponding 50 % effect concentrations of >100 mg/L. Other algae (*S. marinoi* and *G. amphibium*) as well as a marine bacterium were less susceptible to PFHxA with effect concentrations ranging from 998.7 – 1482 mg/L.[75] |
| *Aquatic Toxicity: $LC_{50}$, $EC_{50}$, $ErC_{50}$, NOAEC/NOEC* | Rainbow trout 96 hr $LC_{50}$ >99.2 mg/L[76]<br>Rainbow trout 56 d. NOEC reprod. =10.1 mg/L [77]<br>Algae (*P. subcapitata*) 72 hr $ECb_{50}$ and $EcR_{50}$ >100 mg/L; (Hoke 2012)[78]<br>Algae (*G. amphibium*) 72 h. $IC_{50}$ optical density 999 mg/L (Ding 2013)[79]<br>Algae (*S. Subspicatus*) 72 h. $ErC_{50}$ = 86 mg/L; NOEC=50 mg/L (ENVIRON 2014)[80]<br>*Daphnia magna*: 48 hr $LC_{50}$ = >96.5 mg/L[81]<br>*d. magna*: 48 hr $EC_{50}$ 1,048 mg/L; $EC_5$ 596 mg/L<br>*d. magna:* 21 d. chronic $EC_{50}$ 1,273 mg/L (survival) 776 mg/L per capita no. offspring.[82]<br>General: The acute toxicity decreased with decreasing carbon chain length, but the polymer did not show a dose related effect. In a chronic toxicity test performed with PFHxA, mortality was observed at similar concentrations as in the acute toxicity test, indicating that toxicity did not increase with increasing exposure time. Effects on mortality, reproduction and population growth rate occurred at similar concentrations, indicating no specific effect of PFHxA on sublethal endpoints. C4-C6 chemistry is thus less hazardous to daphnids than C7-C8 chemistry. Yet, these compounds are persistent, hard to remove from the environment and production volumes are increasing.[83] |
| *Mammalian Toxicity: $LC_{50}$, $EC_{50}$,* | |

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| *$ErC_{50}$, NOAEC/NOEC* | |
| *Wildlife Toxicity: $LC_{50}$, $EC_{50}$, $ErC_{50}$, NOAEC/NOEC* | There is some evidence to suggest that perfluoroalkyl acids (PFAA's) can impact essential endocrine pathways and neurodevelopment in birds and other animals. In a study by Vongphachan *et al.* (2011), PFHxA altered the messenger RNA (mRNA) expression of thyroid hormone (TH)–responsive transcripts in chicken embryonic neuronal (CEN) cells.<br>In a later study, the same research group determined *in ovo* effects of PFHxA exposure (maximum dose 5 9700 ng/g egg) on embryonic death, developmental endpoints, tissue accumulation, mRNA expression in liver and cerebral cortex, and plasma TH levels. PFHxA accumulated in the three tissue compartments analyzed as follows: yolk sac > liver > cerebral cortex (Cassone *et al.* 2012).[84] |
| *Breakdown/degradation /combustion products* | Results of studies in soil and sediment for 6:2 FTOH demonstrated primary biodegradation with half-lives of less than 2 days. Transformation products such as PFHxA did not degrade appreciably within half a year.[85] |
| *Anaerobic degradation* | They are neither biodegradable under aerobic or anaerobic environmental conditions in water or soil.[86] |
| *Aerobic degradation* | They are neither biodegradable under aerobic or anaerobic environmental conditions in water or soil.[87] |
| *Other observable ecological effects (e.g. BOD)* | In the present study, we assessed the developmental toxicity and teratogenicity of PFCs with different numbers of carbon atoms on Xenopus embryogenesis. An initial frog embryo teratogenicity assay-Xenopus (FETAX) assay was performed that identified perfluorohexanoic (PFHxA) and perfluoroheptanoic (PFHpA) acids as potential teratogens and developmental toxicants. The mechanism underlying this teratogenicity was also investigated by measuring the expression of tissue-specific biomarkers such as phosphotyrosine-binding protein, xPTB (liver); NKX2.5 (heart); and Cyl18 (intestine). Whole-mount in situ hybridization, reverse transcriptase-polymerase chain reaction (RT-PCR), and histologic analyses detected severe defects in the liver and heart following exposure to PFHxA or PFHpA. In addition, immunoblotting revealed that PFHpA significantly increased the phosphorylation of extracellular signal-regulated kinase (ERK) and c-Jun N-terminal kinase (JNK), while PFHxA slightly increased these, as compared with the control. These results suggest that PFHxA and PFHpA are developmental toxicants and teratogens, with PFHpA producing more severe effects on liver and heart development through the induction of ERK and JNK phosphorylation.[88] |

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| *Fate and Transport: Aquatic* | The shorter chain length acids tend to be more soluble in water and have a lower potential for sorption to particles than the long-chain analogues. Thereby, they have a higher potential for aqueous long-transport.[89]<br>Based on a classification scheme (1), log Koc values of 1.63-2.35(2), indicate that **PFHxA** is expected to adsorb to suspended solids and sediment (SRC). A pKa of -0.16(3) indicates **PFHxA** will exist entirely in the anion form at pH values of 5 to 9 and, therefore, volatilization from water surfaces is not expected to be an important fate process(SRC). **PFHxA** is not expected to undergo hydrolysis in the environment due to the lack of functional groups that hydrolyze under environmental conditions (4). According to a classification scheme (5), a reported BCF of 0.59 in rainbow trout (6), suggests bioconcentration in aquatic organisms is low (SRC). Biodegradation data in water were not available (SRC, 2016).[90]<br>Fate data on PFHxA are sparse. PFCAs are degradation products of other PFASs and are not trans-formed/degraded by hydrolysis or photolysis in water to any appreciable extent.[91] |
| *Fate and Transport: Terrestrial* | Based on a classification scheme (1), log Koc values of 1.63-2.35(2), indicate that **PFHxA** is expected to have very high to moderate mobility in soil (SRC). The pKa of **PFHxA** is -0.16(3), indicating that this compound will exist entirely in anion form in the environment and, therefore, volatilization from moist soil surfaces is not expected to be an important fate process(SRC). **PFHxA** is expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 2.0 mm Hg at 25 deg C(SRC), determined from a fragment constant method(4). Biodegradation data in soil were not available (SRC, 2016).[92] |
| *Fate and Transport: Atmospheric* | According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere (1), **PFHxA**, which has an estimated vapor pressure of 2.0 mm Hg at 25 deg C (SRC), determined from a fragment constant method (2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **PFHxA** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be 31 days(SRC), calculated from its rate constant of 5.2X10-13 cu cm/molecule-sec at 25 deg C(SRC) that was derived using a structure estimation method(2). **PFHxA** does not contain chromophores that absorb at wavelengths >290 nm (3) and, therefore, is not expected to be susceptible to direct photolysis by sunlight (SRC).[93]<br>Fluorotelomers (FTOHs) are volatile and will be transported over long distances via the atmosphere[94] |

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| *Transport Issues* | |
| *Factors affecting bioavailability* | **See "Interactions" endpoint** |
| **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<br>**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<br>**Survey of PFOS, PFOA and other perfluoroalkyl and polyfluoroalkyl substances** – Part of the LOUS-review, Environmental project No. 1475, 2013 http://www2.mst.dk/Udgiv/publications/2013/04/978-87-93026-03-2.pdf |

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

[1] www.expub.com; Chemical Identity Page for Perfluorohexanoic acid.
[2] www.expub.com; RTECS for Perfluorohexanoic acid.
[3] www.expub.com; Chemical Identity Page for Perfluorohexanoic acid.
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