# Perfluorohexanoic Acid (CAS #307-24-4)
# GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

**Prepared by:**

**ToxServices LLC**

**June 3, 2016**


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# GreenScreen® Executive Summary for Perfluorohexanoic Acid (CAS #307-24-4)

Perfluorohexanoic acid is a six carbon (C6) perfluorinated carboxylic acid that functions as processing aid in fluorinated polymer production, and is used in aqueous firefighting foams, water/grease repellents, and other commercial products. Perfluoroalkylated and polyfluoroalkylated substances, including perfluorohexanoic acid, are used as components of and precursors for surfactants and surface protectors used in industrial applications and consumer products, including impregnating agents for clothing and textiles, coatings for paper and packaging, in waxes and cleaning agents, insecticides, fire-fighting foams and hydraulic fluids in airplanes. Perfluorohexanoic acid is also a breakdown product of fluorotelomer compounds used to produce stain- and grease-proof coatings on food packaging and household products. Perfluorohexanoic acid is a candidate chemical to replace perfluorooctanoic acid (PFOA), which has been largely phased out throughout the European Union and United States.

Perfluorohexanoic acid was assigned a **GreenScreen Benchmark™ Score of 1** ("Avoid – Chemical of High Concern"). This score is based on the following hazard score combinations:

- Benchmark 1c
    - Very High Persistence-P + Very High Group II Human Toxicity (skin irritation-IrS and eye irritation-IrE)

Data gaps (DG) exist for endocrine activity-E, single exposure neurotoxicity-Ns[1] and respiratory sensitization-SnR*. As outlined in GreenScreen® Guidance Section 11.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), perfluorohexanoic acid meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if perfluorohexanoic acid were assigned a High score for the data gaps E or SnR*, or a Very High score for Ns, it would still be categorized as a Benchmark 1 Chemical.

**GreenScreen® Benchmark Score for Relevant Route of Exposure:**
As a standard approach for GreenScreen® evaluations, all exposure routes (oral, dermal, and inhalation) were evaluated together, so the GreenScreen® Benchmark Score of 1 ("Avoid – Chemical of High Concern") is applicable for all routes of exposure.

**GreenScreen® Hazard Ratings for Perfluorohexanoic Acid**

| Group I Human | | | | | Group II and II* Human | | | | | | | | | Ecotox | | Fate | | Physical | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **C** | **M** | **R** | **D** | **E** | **AT** | **ST** | | **N** | | **SnS*** | **SnR*** | **IrS** | **IrE** | **AA** | **CA** | **P** | **B** | **Rx** | **F** |
| | | | | | | single | repeated* | single | repeated* | | | | | | | | | | |
| **L** | *L* | *L* | *M* | DG | **M** | **H** | *M* | DG | **L** | *L* | DG | *vH* | *vH* | **M** | **L** | **vH** | **L** | *M* | *M* |

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

[1] The lack of data for single exposure neurotoxicity is not counted as a data gap in the benchmarking process when there are data for repeated exposure neurotoxicity.

# GreenScreen® Assessment for Perfluorohexanoic acid (CAS #307-24-4)

**Method Version: GreenScreen® Version 1.3[2]**
**Assessment Type[3]: Certified**
**Assessor Type: Licensed GreenScreen® Profiler**

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Date: June 3, 2016

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Title: Toxicologist
Organization: ToxServices LLC
Date: June 3, 2016

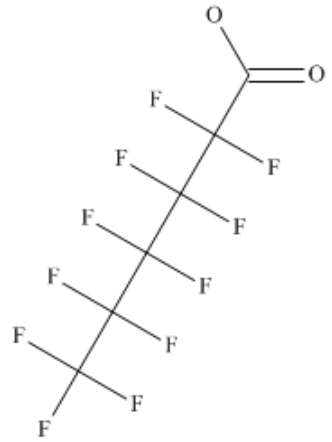
**Confirm application of the *Disclosure and Assessment Rules and Best Practice*[4]:** (List disclosure threshold and any deviations) No relevant information is available. The screen is performed on the theoretical pure substance.

**Notes related to production specific attributes[5]:**
No relevant information is available. The screen is performed on the theoretical pure substance.

**Chemical Name:** Perfluorohexanoic acid

**CAS Number:** 307-24-4

**Chemical Structure(s):**

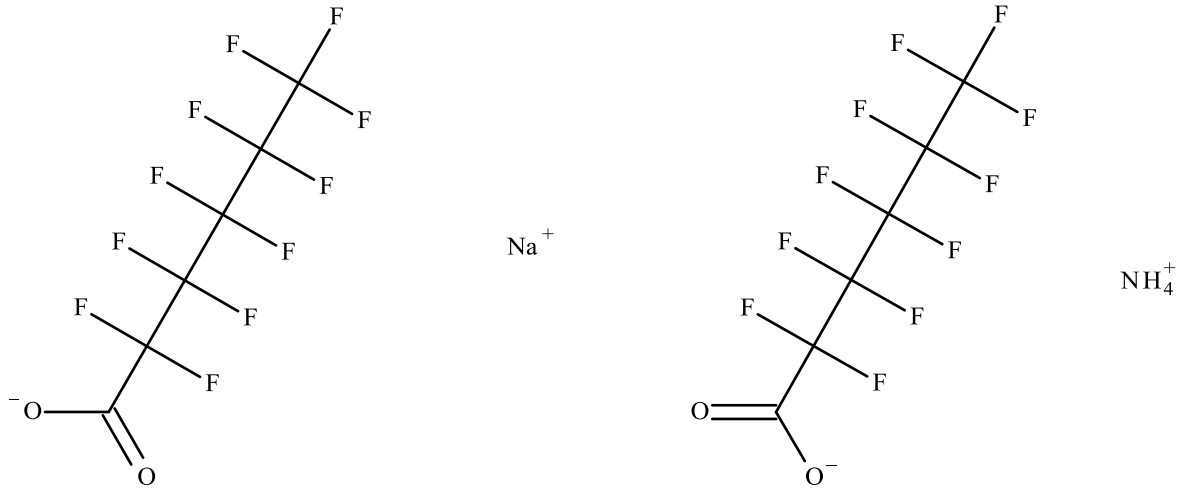


[2] Use GreenScreen® Hazard Assessment Guidance (Guidance) v1.3
[3] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen® Verification Program)
[4] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm

[5] Note any composition or hazard attributes of the chemical product relevant to how it is manufactured. For example, certain synthetic pathways or processes result in typical contaminants, by-products or transformation products. Explain any differences between the manufactured chemical product and the GreenScreen assessment of the generic chemical by CAS #.

**Also called:** C8, EINECS 206-196-6, NSC 5213, Perfluorohexanoic acid, Undecafluoro-1-hexanoic acid, UNII-ZP34Q2220R (ChemIDPlus 2016); PFHxA (NICNAS 2016)

**Suitable analogs or moieties of chemicals used in this assessment (CAS #'s):**
A limited toxicological dataset is available for perfluorohexanoic acid. Therefore, data on its sodium salt sodium perfluorohexanoate (CAS #2923-26-4) and ammonium salt (CAS # 21615-47-4) are used to fill the data gaps. Both the salt compounds and the acid form the perfluorohexanoate anion in water, and have been evaluated as a group (i.e. perfluorohexanoate) by various regulatory agencies (Swedish EPA 2012, Danish EPA 2015, NICNAS 2016). Perfluorohexanoic acid has a much lower water solubility (<<29 mg/L, reported in ENVIRON 2014) than sodium/ammonium perfluorohexanoate (29 mg/L, modeled, reported in ENVIRON 2014), although NICNAS (2016) expects it to be readily and completely dissociated in water, based on the measured water solubillity of PFOA and its ammonium salt (> 1,000 mg/L) and of a shorter-chain homologue trifluoroacetic acid (1,000,000 mg/L). The dissolution rate of perfluorohexanoic acid and its surrogate salt are not reported. In addition, perfluorohexanoic acid is highly volatile while the salt form is not (ENVIRON 2014). The differences in physical and chemical properties can potentially result in toxicokinetic differences between the target compound and the two salts. Therefore, ToxServices conservatively considers the sodium and ammonium salts weak surrogates for the acid for systemic toxicity endpoints. The acidic nature of target compound makes the non-acidic sodium/ammonium perfluorohexanoate inappropriate as surrogates for point-of-entry endpoints such as skin and eye irritation.



Sodium Perfluorohexanoate (CAS #2923-26-4) Ammonium Perfluorohexanoate (CAS # 21615-47-4)

**Identify Applications/Functional Uses:** (Swedish EPA 2012)
1. Breakdown product of 6:2 fluorotelomer compounds used to produce stain- and grease-proof coatings on food packaging and household products (NTP 2016, ENVIRON 2014)
2. Used in fluorinated polymer production (as a processing aid), aqueous firefighting foams, water/grease repellents, and other commercial products (ENVIRON 2014). Usage levels were not disclosed.
3. Perfluoroalkylated and polyfluoroalkylated substances, including perfluorohexanoic acid, are used as components of and precursors for surfactants and surface protectors used in industrial applications and consumer products, including impregnating agents for clothing and textiles, coatings for paper and packaging, in waxes and cleaning agents, insecticides, and fire-fighting foams and hydraulic fluids in airplanes. Usage levels were not disclosed.

2. An alternative to long chain per- and polyfluoroalkyl substances such as perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) for use as textile, carpet and paper additive, and tile surface treatment (U.S. EPA 2016a)

**GreenScreen® Summary Rating for Perfluorohexanoic Acid[6,7 8,9]:** Perfluorohexanoic acid was assigned a **GreenScreen Benchmark™ Score of 1** ("Avoid – Chemical of High Concern") (CPA 2016c). This score is based on the following hazard score combinations:

- Benchmark 1c
  - Very High Persistence-P + Very High Group II Human Toxicity (skin irritation-IrS and eye irritation-IrE)

Data gaps (DG) exist for endocrine activity-E, single exposure neurotoxicity-Ns[10] and respiratory sensitization-SnR*. As outlined in CPA (2016a) Section 11.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), perfluorohexanoic acid meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if perfluorohexanoic acid were assigned a High score for the data gaps E or SnR*, or a Very High score for Ns, it would still be categorized as a Benchmark 1 Chemical.

**Figure 1: GreenScreen® Hazard Ratings for Perfluorohexanoic Acid**

| Group I Human | | | | | Group II and II* Human | | | | | | | | Ecotox | | Fate | | Physical | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C | M | R | D | E | AT | ST | | N | | SnS* | SnR* | IrS | IrE | AA | CA | P | B | Rx | F |
| | | | | | | single | repeated* | single | repeated* | | | | | | | | | | |
| L | *L* | *L* | *M* | DG | M | H | *M* | DG | L | *L* | DG | *vH* | *vH* | M | L | vH | L | *M* | *M* |

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e. vH, H, M, and L) instead of three (i.e. H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

**Transformation Products and Ratings[11]:**
**Identify feasible and relevant fate and transformation products** (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[12]

[6] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
[7] See Appendix A for a glossary of hazard endpoint acronyms
[8] For inorganic chemicals only, see GreenScreen Guidance v1.3 Section 13. (Exceptions for Persistence)
[9] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen Guidance v1.3 Section 8.2.1.
[10] The lack of data for single exposure neurotoxicity is not counted as a data gap in the benchmarking process when there are data for repeated exposure neurotoxicity.
[11] See GreenScreen Guidance v1.3 Section 12.
[12] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

Perfluorinated carboxylic acids such as perfluorohexanoic acid are strong acids based on the measured acid dissociation constant (pKa) of 0.84 (NICNAS 2016). As a strong acid, perfluorohexanic acid dissociates at environmentally relevant pHs (ENVIRON 2014). The perfluorohexanoate anion has a modeled water solubility of 29.5 mg/L, and ENVIRON (2014) expected the solubility of the protonated acid to be much lower than that of the anion. The basis of this conclusion was not described. On the other hand, NICNAS (2016) expected perfluorohexanoic acid to be highly soluble in water based on the measured solubility of PFOA and its ammonium salt (> 1,000 mg/L) and of a shorter chain-length homologue trifluoroacetic acid (1,000,000 mg/L). The acid is highly volatile based on the experimentally determined vapor pressure of 264 Pa (NICNAS 2016) and therefore has a potential to partition to the air. No information is available on the extent and rate of perfluorohexanoic acid's partitioning into various environmental compartments.

No data are available on the abiotic degradation and hydrolysis of perfluorohexanoic acid. Limited experimental data indicate that polyfluorinated carboxylic acids may react with photo-chemically-generated hydroxyl radicals in the air. However, this process occurs at an extremely low rate. In a field study, the concentration of perfluorohexanoic acid decreased by only 0.8% after 106 days of solar irradiation (ENVIRON 2014). The atmospheric lifetime for perfluorocarboxylic acids is estimated to be 130 days (NICNAS 2016). Perfluorohexanoic acid was found to be non-biodegradable in a closed bottle test conducted in a manner similar to the OECD Guideline 301D (NICNAS 2016). Relevant data on 6:2 fluorotelomer alcohol (6:2 FTOH), of which perfluorohexanoic acid is a degradation product, suggest that perfluorohexanoic acid is not completely mineralized in soil and sediment, with half-lives exceeding 6 months (the exact half-life is not reported) (ENVIRON 2014). NICNAS concluded that short-chain perfluorocarboxylic acids and their direct precursors, including perfluorohexanoic acid, are highly resistant to biodegradation, hydrolysis or aqueous photolysis under environmental conditions (NICNAS 2016). Therefore, no feasible and relevant environmental transformation products are expected to form.

**Introduction**

Perfluorohexanoic acid is a synthetic perfluorinated carboxylic acid and fluorosurfactant that functions as a precursor and component of surfactants and surface protectors used in industrial settings and consumer products, such as impregnating agents for clothing and textiles, as paper and packaging coatings, in waxes and cleaning agents, in pesticides, and in hydraulic fluids in airplanes. The usage levels in these products are not reported. Perfluorohexanoic acid is a candidate chemical to replace perfluorooctanoic acid (PFOA), which has been largely phased out throughout the European Union (Swedish EPA 2012). Per- and polyfluoroalkyl substances, including long-chain perfluoroalkyl carboxylic acids with 8 carbons or more (e.g. PFOA) and perfluoroalkane sulfonates with 6 carbons or more, are persistent, bioaccumulative, and toxic (reproductive, developmental, and systemic toxicities). The U.S. EPA invited eight major leading companies in per- and polyfluoroalkyl substances to join the PFOA Stewardship Program to commit to stepwise reduction and ultimately elimination of the emission of PFOA, precursor chemicals that break down to PFOA and related higher homologue chemicals by 2015. U.S. EPA also proposed a Significant New Use Rule under TSCA to evaluate, limit or prohibit the new use of these chemicals (U.S. EPA 2016b). Perfluorohexanoic acid is currently not restricted by U.S. EPA. However, perfluorohexanoic acid is restricted and/or banned on restricted substances lists (RSLs) by many industries, such as Levi Strauss & Co (2015), Bluesign® system substances list (BSSL) (2015), and H&M (2016).

Perfluorohexanoic acid, along with the other perfluoroalkyl substances, is manufactured mainly by electrochemical fluorination (EFC) and telomerization (Danish EPA 2015).

ToxServices assessed perfluorohexanoic acid against GreenScreen® Version 1.3 (CPA 2016a) following procedures outlined in ToxServices' SOPs 1.37 and 1.69 (GreenScreen® Hazard Assessment) (ToxServices 2013a,b).

**U.S. EPA Safer Choice Program's Safer Chemical Ingredients List**

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2016c). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015).

Perfluorohexanoic acid is not listed on the SCIL.

**GreenScreen® List Translator Screening Results**

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2016a.b). Pharos (Pharos 2016) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b)[13] and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for perfluorohexanoic acid can be found in Appendix C and a summary of the results can be found below:

- TEDX – Potential Endocrine Disruptors – Potential Endocrine Disruptor
- EC – CEPA Toxic Substances (Sched 1) – CEPA Toxic

**Physicochemical Properties of Perfluorohexanoic Acid**

Perfluorohexanoic acid is a clear, colorless to very pale yellow liquid at room temperature and pressure. Its high vapor pressure (264 Pa, equivalent to 1.98 mmHg) indicates that it is volatile (vapor pressure $\geq 10^{-4}$ mmHg) and can form a vapor. NICNAS (2016) concluded that it is highly volatile. ENVIRON (2014) estimated that protonated perfluorohexanoic acid has a very low solubility (<<29 mg/L) (basis not reported), but NICNAS (2016) expected it to be highly soluble, based on the solubility of PFOA and trifluoroacetic acid (>1,000 mg/L). Perfluorohexanoic acid is considered a strong acid ($pK_a < 1$) (NICNAS 2016). While modeled partition coefficients (log $K_{ow}$) are between 3.12 and 3.26, perfluorohexanoic acid has surface active properties for which the octanol water partition coefficient may not be a reliable indicator of the partitioning behavior (NICNAS 2016). Surfactants can self-associate, stabilize emulsions, foam, and concentrate at the oil/water interface, and therefore partition coefficient (calculated by dividing the solubility in octanol by that in water) of surfactants are difficult to determine experimentally (Edler 2011).

**Table 1: Physical and Chemical Properties of Perfluorohexanoic Acid (CAS #307-24-4)**

| Property | Value | Reference |
|---|---|---|
| Molecular formula | C6-H-F11-O2 | ChemIDPlus 2016 |
| SMILES Notation | C(=O)(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)O | ChemIDPlus 2016 |
| Molecular weight | 314.0499 | ChemIDPlus 2016 |
| Physical state | Liquid | NICNAS 2016 |

[13] DOT lists are not required lists for GreenScreen List Translator v1.3. They are reference lists only.

| Table 1: Physical and Chemical Properties of Perfluorohexanoic Acid (CAS #307-24-4) | | |
|---|---|---|
| **Property** | **Value** | **Reference** |
| Appearance | Colorless to very pale yellow clear liquid | Oakwood Products 2015; TCI America 2014 |
| Melting point | Not available | NICNAS 2016 |
| Vapor pressure | 264 Pa (exp.) | NICNAS 2016 |
| Water solubility | Insoluble <<29 mg/L | TCI America 2014; ENVIRON 2014 |
| Dissociation constant | $pK_a$ = 0.84 at 25ºC (exp.) | NICNAS 2016 |
| Density/specific gravity | 1.762 g/mL at 20ºC | SynQuest Laboratories 2015 |
| Partition coefficient | 3.12-3.26 (est.) | ENVIRON 2014 |

**Toxicokinetics**

Perfluoroalkyl acids such as perfluorohexanoic acid are resistant to biotransformation (Anderson et al. 2008). Therefore, the relative toxicity of perfluoroalkyl acids has been suggested to be associated with bioaccumulation/elimination rate, which is related to the carbon chain length. Shorter chain lengths led to faster excretion in the urine and lower concentrations in serum and liver (Klaunig et al. 2015).

In an elimination/clearance study comparing the behavior of perfluorohexanoic acid (PFHxA, purity 98.5%) and nonafluorobutane-1-sulfonic acid (PFBS, purity 99.65%) in cynomolgus monkeys (*Macaca fascicularis*) and Sprague-Dawley rats, the test compounds were administered to monkeys (3/sex, same animals for both treatments 7 days apart) and rats (12/sex/group) by a single i.v. injection at 10 mg/kg, or to rats only (6/sex/group) by daily gavage at 50, 150 and 300 mg/kg/day for 26 days. Blood (monkeys and rats) and urine samples (rats only) were collected at various time points up to 24 hours after dosing. In the repeated dose study, samples were collected at various time points up to 24 hours after the 1$^{st}$ and 26$^{th}$ dosing. For monkeys, the half-life of PFHxA is 1.0h and 0.42h for males and females, respectively. In rats, half-lives are 2.1h (M) and 2.5h (F) after i.v. dose, 2.0h (M) and 1.9h (F) at oral dose of 50 mg/kg/day, 2.1h (M) and 2.2h (F) at 100 mg/kg/day, and 2.9h(F) and 3.0h (F) at 300 mg/kg/day. 84%(M) and 76.9% (F) of the administered dose were eliminated 24 hours after i.v. dosing, and approximately 90% (M) and 70-100% (F) were eliminated within 24 hours after dosing in the repeated dose study. Systemic exposure of PFHxA is lower than PFBS, and elimination of PFHxA is faster than PFBS. Repeated dosing led to lower systemic exposure (lower serum concentration) for PFHxA (Chenglis et al. 2009a). A review article reported the half-life of elimination for perfluorohexanoate to be 1 – 2 hours in males and females (Anderson et al. 2008)

Several toxicokinetic studies were identified for the ammonium perfluorohexanoate. In the first study, a single dose of 50 mg/kg radiolabeled test compound was orally administered to male and female rats and mice. The major route of elimination was urine (73.0% (M) and 90.2% (F) in rats and 80.3% (M) and 84.0% (F) in mice). Fecal elimination was 15.5% (M) and 7.3% (F) in rats and 10.5 (M) and 7.0% (F) in mice. Elimination via expired air was negligible at 0.05% in rat and 0.1% in mice. Total radioactivity was rapidly excreted, with 95.6 – 99.2% elimination in rats and 90.9-94.1% in mice within 24h after dosing, and 97.4 – 100.8% in rats and 95.4 – 97.3% in mice within 72h after dosing. At 72 hours, only 0.2% and 0.6 – 0.9% of the dose still remained in the gastrointestinal tract and carcass in rats and mice, respectively, indicating almost complete excretion (Charles River 2009a). In the second study, the excretion pattern and rate were examined following 13 daily oral doses of 50 mg/kg test compound (last dose was radiolabeled) in rats and mice. The major route of elimination was urine (80.7% (M) and 77.8% (F) in rats and 81.1% (M) and 83.4% (F) in mice). Fecal elimination was 12.9% (M) and 12.6% (F) in rats and 10.6% (M) and 9.6% (F) in mice. Excretion of the C6 ion was rapid with

93.7% (M) and 90.4% (F) (98.5% (M) and 96.5% (F) of the ultimately recovered material) recovered within 24 hours post exposure in rats, and 93.5% (M) and 92.2% (F) (96.4% (M) and 95.6% (F) of the ultimately recovered material) recovered within 24 hours post exposure in rats. Excretion was almost complete at 168 h post exposure, with total radioactivity recovery of 95.1% (M) and 93.7% (F) in rats and 97.0% (M) and 96.4% (F) in mice. Only 0.2% and 0.1% still remained in the gastrointestinal tract and carcass of rats and mice, respectively (Charles River 2009b). In the third study, a single dose of 35, 175 or 350 mg/kg test substance was administered to female mice (21/dose). Blood and liver samples were analyzed for the C6 ion. No mortality or adverse clinical signs occurred during the study. No test compound could be quantified after 6 hours at 35 mg/kg, and the mean concentration of the test compound was below the limit of quantification after 24 hours at 175 and 350 mg/kg. Only one individual mouse in the mid and high doses had quantifiable levels at 24 hours (Charles River 2010).

In summary, perfluorohexanoic acid is rapidly eliminated in monkeys, rats and mice with half-lives of 1 – 3 hours, and it is almost completely eliminated after 24 hours post dosing. The major routes of excretion are urine followed by feces. Perfluorohexanoic acid is resistant to biotransformation. Compared to longer chain perfluoroalkyl acids, perfluorohexanoic acid is expected to have a faster elimination rate and lower systemic exposure.

**Hazard Classification Summary Section:**

**Group I Human Health Effects (Group I Human)**

**Carcinogenicity (C) Score (H, M, or L): L**
Perfluorohexanoic acid was assigned a score of Low for carcinogenicity based on negative findings in a chronic study in rats. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and negative, there are no structural alerts, and they are not classified under GHS (CPA 2016b). The confidence in the score was high as it was based on a well-conducted study.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Klaunig et al. 2015
  - In a combined chronic toxicity/carcinogenicity study, male and female Sprague-Dawley rats (60 – 70/sex/dose) were exposed to perfluorohexanoic acid (98.1% purity) by daily gavage for up to 104 weeks. Sixty rats of each sex were assigned to treatment groups 1-3 while 70 of each were assigned to group 4. Treatment doses for male rats were 0, 2.5, 15, and 100 mg/kg/day for groups 1, 2, 3, and 4, respectively. For female rats, doses were 0, 5, 30, and 200 mg/kg/day for groups 1, 2, 3, and 4. The vehicle for this study was deionized water which was also the treatment for the control group. Parameters examined include body weight, food consumption, functional observation battery, ophthalmology, hematology, serum chemistry, urinalysis, hormone levels, organ weight, and histopathology. A significant dose-related decrease in survival rates was seen in female rats but not male rats. Female rat survival rates at week 80 were 76, 78, 85, and 69% in the control, low, mid, and high dose groups, respectively, and at week 104 were 36, 43, 33, and 22% in the control, low, mid, and high dose groups, respectively. No statistically significant increases in neoplasms or tumors were seen in any organ in either male or female rats. Study authors concluded that perfluorohexanoic acid was not carcinogenic in this bioassay.

**Mutagenicity/Genotoxicity (M) Score (H, M, or L):** *L*
Perfluorohexanoic acid was assigned a score of Low for mutagenicity/genotoxicity based on negative *in vitro* bacterial mutagenicity and mammalian cell chromosome aberration data on the surrogate sodium perfluorohexanoate. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative for both gene mutation and chromosomal aberration (CPA 2016b). The confidence in the score was reduced as it was based on well-conducted studies on a weak surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* In an Ames assay conducted according to OECD Guideline 471, *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 and *Escherichia coli* strain WP2*uvr*A were exposed to sodium perfluorohexanoate at dose levels of 333, 667, 1000, or 5,000 µg/plate in the presence and absence of rat liver S9 metabolic activation. No cytotoxicity or positive mutagenic responses were observed at any dose level in any strain in either the presence or absence of S9 activation. Study authors concluded that sodium perfluorohexanoate was not genotoxic in this assay.
  - *Sodium perfluorohexanoate:* In an *in-vitro* mammalian chromosome aberration study conducted according to OECD Guideline 473, human peripheral blood lymphocytes (HPBL) were exposed to sodium perfluorohexanoate in the presence and absence of rat liver S9 metabolic activation. Cells were treated for 4 or 22 hours in the non-activated test condition and for 4 hours in the S9-activated test condition. Dose levels were 2,000, 3,000, and 3,860 µg/mL for the 4-hour test without S9 activation and 250, 500, and 1,000 µg/mL for the 4-hour test with S9 activation and the 22-hour test without activation. Substantial cytotoxicity (reduction in the mitotic index of >50% in the treated cultures compared to the vehicle control) was observed in all testing conditions. None of the sodium perfluorohexanoate-treated groups, with or without metabolic activation, had significantly increased numbers of cells with structural or numerical aberrations compared to vehicle controls. Study authors concluded that sodium perfluorohexanoate was not genotoxic in this assay.

**Reproductive Toxicity (R) Score (H, M, or L):** *L*
Perfluorohexanoic acid was assigned a score of Low for reproductive toxicity based on lack of reproductive toxicity observed in a reproductive toxicity study in rats on the surrogate sodium perfluorohexanoate. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative, there are no structural alerts, and they are not classified under GHS (CPA 2016b). The confidence in the score was reduced as it was based on a well-conducted study performed on a weak surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* In a one-generation reproduction toxicity study conducted according to OECD Guideline 415, Crl:CD(SD) rats (20/sex/dose) were administered sodium perfluorohexanoate (NaPFHx) (100% purity) by gavage at doses of 20, 100, or 500 mg/kg/day. An additional control group received nanopure water vehicle. P1 females were dosed 70 days prior to cohabitation through gestation and lactation for a total of 126 days while P1 males were doses for approximately 110 days beginning 70 days prior to

cohabitation. F1 rats were not dosed. Clinical observations, body weight, and food consumption were determined weekly. Reproductive parameters including estrous cycle, sperm number/viability, survival, and reproductive performance were assessed. Litters were examined on day 4 and weekly during lactation. F1 offspring were given a gross pathological examination at weaning and a subset of F1 rats was maintained for 6 weeks post-weaning to assess developmental landmarks. This subset was then given a gross pathological examination and selected reproductive organs were weighed. No NaPFHx-related mortality was observed in either parental males or females at any dose. Clinical signs of toxicity included stained fur in both sexes at 500 mg/kg/day, reduced body weight parameters in males at 100 and 500 mg/kg/day (12% and 29%, respectively) and reduced maternal body weight gain at 500 mg/kg/day during the first week of gestation and at 500 mg/kg/day during lactation period. No NaPFHx-related effects were observed or measured on mating, fertility, gestation length, number of implantation sites, estrous cycling, sperm parameters, litter size, sex ratio, pup clinical observations, pup survival, or $F_1$ adult developmental landmarks at any dose. The only NaPFHx-related effect measured was decreased mean pup weights at 500 mg/kg/day. Study authors established a NOAEL of 20 mg/kg/day based on reduced body weight parameters seen in the parental generation at both 100 and 500 mg/kg/day. ToxServices identified a NOAEL of 500 mg/kg/day for reproductive toxicity based on a lack of effects at the highest dose tested.

**Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L):** *M*
Perfluorohexanoic acid was assigned a score of Moderate for developmental toxicity based on reduced body weight (gain) in a reproductive toxicity study and a developmental toxicity study in rats for the surrogate sodium perfluorohexanoate, and reduced pup body weight, increased stillborn pups and/or reduced post-natal survival observed in the absence of apparent maternal toxicity in mice for the surrogate ammonium perfluorohexanoate. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when there is limited or marginal evidence of developmental toxicity in animals (CPA 2016b). The confidence in the score was reduced as the studies were conducted on two weak surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* In the previously described one-generation reproductive toxicity study, conducted according to OECD Guideline 415, Crl:CD(SD) rats (20/sex/dose) were administered sodium perfluorohexanoate (NaPFHx) (100% purity) by gavage at doses of 20, 100, or 500 mg/kg/day. An additional control group received nanopure water vehicle. P1 females were dosed 70 days prior to cohabitation through gestation and lactation for a total of 126 days while P1 males were doses for approximately 110 days beginning 70 days prior to cohabitation. F1 rats were not dosed. No sodium perfluorohexanoate-related effects were observed or measured on litter size, sex ratio, pup clinical observations, pup survival, or $F_1$ adult developmental landmarks at any dose. Reduced mean pup weights were observed at the highest dose of 500 mg/kg/day (17 – 18% lower compared to control) throughout lactation in the presence of reduced maternal body weight gain, which was observed at 100 and 500 mg/kg/day. The overall post-weaning body weight gain was comparable across all doses. Authors identified a NOAEL and LOAEL of 100 and 500 mg/kg/day, respectively, based on reduced mean pup weight at the high dose.

  - *Sodium perfluorohexanoate:* In a developmental toxicity study performed according to OECD Guideline 414, Crl:CD(SD) rats (22 females/dose) were administered 20, 100, or 500 mg/kg/day sodium perfluorohexanoate (100% purity) daily by gavage on days 6-20 of gestation. An additional control group received nanopure water vehicle only. Rats were sacrificed on gestation day 21. All dams underwent a gross pathological examination and fetuses were removed from uteri to be weighed and examined for skeletal alterations. No treatment-related deaths or gross postmortem findings were observed in dams at any dose. Maternal toxicity occurred at the 500 mg/kg/day dose and consisted of reductions in body weight parameters (total weight gain and overall net weight gain). Developmental toxicity was limited to a 10% decrease in fetal weight at the 500 mg/kg/day dose. Study authors established maternal and developmental NOAELs of 100 mg/kg/day based on both maternal and developmental effects observed at the 500 mg/kg/day dose.
- Charles River 2011a
  - *Ammonium perfluorohexanoate:* In a GLP-compliant combined developmental and perinatal/postnatal toxicity study designed to evaluate ICH Harmonised Tripartite Guideline stages C through F, pregnant Crl:CD1(ICR) mice (20/group) received the test substance (purity 95%) via daily gavage at doses of 0 (water), 100, 350 or 500 mg/kg/day during gestational days (GDs) 6 and 18. Dams were sacrificed on day 20 post-partum or 23 post-partum (those that did not deliver a litter). F1 pups were sacrificed on day 20 or 41 post-partum. Parameters examined in dams include viability, clinical observations, body weight, maternal behavior, litter observations, natural delivery, pup body weights, dam and pup necropsy. F1 pups were examined for viability, clinical observations, body weights, body weight changes, eye opening, age of sexual maturity and necropsy. Maternal toxicity was found at the mid and high doses: single death at each dose, slight excess salivation and reduced body weight gain during lactation period. Significant reduction in pup body weight at birth was found in all treated groups. Average pup weights on post-partum day 20 were 89%, 80% and 88% of the control group at low, mid and high doses respectively. The authors attributed to the lack of dose-response to the differences in litter size. Postweaning body weight in males were comparable to controls in all groups, but remained reduced in females at mid and high doses, although body weight gains in females were comparable to controls during postweaning in females. Increased stillbirths, reduced viability indices, and delayed physical development were observed at mid and high doses. But none of the effects observed pre-weaning persisted into the postweaning period. The study authors identified a NOAEL of 100 mg/kg/day and LOAEL of 350 mg/kg/day for maternal toxicity based on mortality, excess salivation, and reduced body weight gain during lactation. The authors identified a LOAEL of 100 mg/kg/day for developmental toxicity presumably based on reduced pup body weight.
- Charles River 2012
  - *Ammonium perfluorohexanoate:* Charles River reanalyzed the reduced pup weight on postnatal day 0 at 100 mg/kg/day in the Charles River (2011a) study described above using an analysis of covariance with litter size as the covariant. This was because the average litter size at 100 mg/kg/day was the largest, and it is known that litter size and fetal/pup weight are closely related. The analysis revealed that the statistical significance associated with the reduced up weight at 100 mg/kg/day was clearly related to the larger litter size. Therefore, the NOAEL for developmental toxicity was changed to 100 mg/kg/day, and the LOAEL was 350 mg/kg/day.

- Charles River 2011b
    - *Ammonium perfluorohexanoate*: In a second GLP-compliant combined developmental and perinatal/postnatal toxicity study, lower doses were tested (0, 7, 35 and 175 mg/kg/day) using the same protocol as previously described in mice (Charles River 2011a). The study authors identified a NOAEL of 175 mg/kg/day for maternal toxicity, and a NOAEL and LOAEL of 35 and 175 mg/kg/day, respectively, for developmental toxicity based on increased number of stillborn pups and pups dying on post-partum day 1, reduced postnatal day 1 pup weights, and corneal opacity in two litters. The authors also noted that none of the effects observed in the pup preweaning persisted into the postweaning period.
- Based on the weight of evidence, a conservative score of Moderate was assigned. In the one-generation reproductive toxicity study on sodium perfluorohexanoate, reduced postnatal body weight gain in the F1 pups was observed at the highest dose in the presence of reduced body weight gain in maternal animals during lactation. While postweaning body weight gains were comparable among different dose groups, the final body weights were not reported, and F1 offspring were not dosed post-weaning. Therefore, it is not possible for ToxServices to determine if reduced body weight gain was carried over to adulthood in F1 offspring, or if continued exposure post-weaning would lead to persistent reduction in body weight gain at the highest dose in this study. In the developmental toxicity study on sodium perfluorohexanoate, reduced fetal body weight was also observed at 500 mg/kg/day in the presence of reduced maternal body weight gain. In the two combined developmental and perinatal/postnatal toxicity studies on ammonium perfluorohexanoate, reduced pup body weight, increased stillborn pups and/or reduced post-natal survival were observed in the absence of apparent maternal toxicity. Although reduced body weight in the offspring may be secondary to maternal toxicity, there are insufficient data to rule out the possibility of a direct developmental effect, and developmental toxicity was observed in the absence of maternal toxicities in both studies on ammonium perfluorohexanoate. It is not clear, however, if higher developmental toxicities observed with ammonium perfluorohexanoate is attributed to its higher developmental toxicity or to mice being more sensitive to the developmental toxicities of this class of compounds than rats. Therefore, ToxServices conservatively assigned a score of Moderate for this endpoint.

**Endocrine Activity (E) Score (H, M, or L):** DG

Perfluorohexanoic acid was assigned a score of Data Gap for endocrine activity based on lack of sufficient data. No effects on selected blood hormone levels were observed in a chronic toxicity study, while increased thyroid weight was reported in a subchronic toxicity study for the surrogate. Thyroid hormone levels were not monitored in either study.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* TEDX – Potential Endocrine Disruptors – Potential Endocrine Disruptor
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- Klaunig et al. 2015
    - In the previously described combined chronic toxicity/carcinogenicity study, male and female Sprague-Dawley rats (60 – 70/sex/dose) were administered perfluorohexanoic acid (98.1% purity) by daily gavage for up to 104 weeks. Sixty rats of each sex were assigned to treatment groups 1-3 while 70 of each were assigned to group 4. Treatment doses for male rats were 0, 2.5, 15, and 100 mg/kg/day for groups 1, 2, 3, and 4, respectively. For female rats, doses were 0, 5, 30, and 200 mg/kg/day for groups 1, 2, 3, and 4. The vehicle for this study was deionized water which was also the treatment for the control group. Hormone

levels (rat luteinizing hormone (rLH), testosterone, estradiol and cholecystokinin) in the blood were measured by immunoassay after 26 or 52-53 weeks of dosing. There were no statistically significant changes in any of these hormones. Testosterone and LH levels were slightly lower in all treated males after 26 weeks, but these changes were not dose-related, and returned to near control levels by 52 weeks.

- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* In a 90-day subchronic toxicity study conducted according to OECD Guideline 408, Crl:CD(SD) rats (10/sex/dose) were administered sodium perfluorohexanoate (NaPFHx) (100% purity) by gavage at doses of 20, 100, or 500 mg/kg/day. Thyroid weights were statistically significantly increased in female rats at 500 mg/kg/day. Study authors established a NOAEL and LOAEL of 20 mg/kg/day and 100 mg/kg/day (equivalent to 19 and 93 mg/kg/day perfluorohexanoic acid[14], respectively), based on a lack of NaPFHx-related effects at that dose.

**Group II and II* Human Health Effects (Group II and II* Human)**

***Note: Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.***

**Acute Mammalian Toxicity (AT) Group II Score (vH, H, M, or L): M**

Perfluorohexanoic acid was assigned a score of Moderate for acute toxicity based on an oral $LD_{50}$ of between 500 and 1,000 mg/kg in rats. GreenScreen® criteria classify chemicals as a Moderate hazard for acute toxicity when oral $LD_{50}$ values are between 300 and 2,000 mg/kg (CPA 2016b). The confidence in the score was high as it was based on a well-conducted study on the chemical of interest supported by data from a weak surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Riker Laboratories 1979
  - *Oral*: $LD_{50}$ between 500 and 1,000 mg/kg in male albino rats
- Loveless et al. 2009
  - *Oral: Sodium perfluorohexanoate:* Female Crl:CD(SD) rats were administered a single dose of NaPFHx (100% purity) by gavage at levels of 175, 550, 1750, or 5,000 mg/kg. All rats at doses 175 or 550 mg/kg survived. One rat dosed with 1,750 mg/kg died on the day of dosing, while all three rats dosed with 5,000 mg/kg were found dead on the day of dosing or the day afterwards.
    - While an $LD_{50}$ was not calculated by the study authors, based on the reported mortalities, the oral $LD_{50}$ is between 1,750 mg/kg and 5,000 mg/kg in rats.

**Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)**

***Group II Score (single dose)* (vH, H, M, or L): H**

Perfluorohexanoic acid was assigned a score of High for systemic toxicity (single dose) based on reduced body weight at a single oral dose of 500 mg/kg. GreenScreen® criteria classify chemicals as a High hazard for systemic toxicity (single dose) when oral LOAELs are between 300 and 2,000 mg/kg

[14] 20 mg NaPFHx/kg/day x MW (PFHxA)/MW (NaPFHx) = 20 mg/kg/day x 314/336 = 19 mg PFHxA/kg/day

(CPA 2016b). Confidence in the score was high as it was based on a well-conducted study on the chemical of interest.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Riker Laboratories 1979
  - In an acute oral toxicity study, male albino rats (5/group) received perfluorohexanoic acid (under the trade name of T-2712CoC) by gavage at 500, 1,000 or 5,000 mg/kg and were observed for 14 days afterwards. Mortalities were 1/5, 5/5 and 5/5 at the low, mid and high doses, respectively. Clinical signs included ataxia, dyspnea, emaciation, hypoactivity, salivation, prostration and unkempt appearance. These occurred from 1 – 30 min to 5 days after dosing, and subsided by day 5 in surviving animals. Decreased body weight was found in 3/4 surviving animals at 500 mg/kg. Findings from gross necropsy performed at the end of the observation period included hemorrhagic vas deferens and one incidence of testes atrophy. Necropsy of animals that died during the study found chemical burns of the stomach and intestine.
- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* Female Crl:CD(SD) rats were administered a single dose of NaPFHx (100% purity) by gavage at levels of 175, 550, 1750, or 5,000 mg/kg. Animals were then observed for up to 14 days post-dose for clinical signs of toxicity, body weight effects, and mortality. All rats at doses 175 or 550 mg/kg survived (number per group not reported). One of four rats dosed with 1,750 mg/kg died on the day of dosing, while all three rats dosed with 5,000 mg/kg were found dead on the day of dosing or the day afterwards. Clinical signs of systemic toxicity included abnormal gait, dehydration, high or low posture, clear oral or nasal discharge, wet or stained fur, salivation, ataxia, or lethargy.

***Group II* Score (repeated dose)*** **(H, M, or L):** *M*

Perfluorohexanoic acid was assigned a score of Moderate for systemic toxicity (repeated dose) based on the lowest LOAEL of 94 mg/kg/day in subchronic toxicity studies for the surrogate chemical and a NOAEL of 50 mg/kg/day for the target chemical in a subchronic toxicity study, classifying it to GHS Category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (repeated dose) when they are classified to GHS Category 2 (CPA 2016b). The confidence in the classification is reduced as the critical LOAEL of 94 mg/kg/day is assigned from studies on the weak surrogate, and due to dose spacing it is not possible to conclusively determine if effects seen in subchronic and chronic studies of the target chemical support GHS classification.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Chengelis et al. 2009b
  - In a 90-day subchronic toxicity study, perfluorohexanoic acid (PFHxA) (purity 98.5%) was administered orally (by gavage) 7 days/week to 3 groups of Crl:CD(SD) rats (20/sex for control and 200 mg/kg/day groups, 10/sex for 10 and 50 mg/kg/day groups) at doses of 10, 50, or 200 mg/kg/day. A control group received the deionized water vehicle. Authors recorded clinical observations daily and detailed physical examinations, body weights, and food consumption weekly. All rats were evaluated for clinical pathology parameters (hematology, serum chemistry, and urinalysis) at scheduled primary and recovery necropsies (study weeks 13 and 17, respectively). Ophthalmic examinations, a functional observational battery (FOB), and motor activity (MA) assessments were conducted prior to PFHxA

administration and during week 12. Necropsies were performed on 10 rats/sex/group after 90 days and the remaining 10 rats/sex in the control and high-dose groups were euthanized following a 28-day recovery period. Selected organs were weighed and tissues were examined microscopically. All animals survived to their scheduled necropsies and there were no clinical observations related to PFHxA administration. Mean body weights in 50 and 200 mg/kg/day males were statistically significantly lower than controls throughout the dosing period. The 200 mg/kg/day males retained 8% lower body weight compared to controls at the end of the recovery period. Similar trends were observed in 50 and 200 mg/kg/day females but these results were not statistically significant. The FOB and MA assessments provided no evidence of PFHxA-induced neurotoxicity. Hematology results included slightly lower mean red blood cell counts in 200 mg/kg/day males and higher mean reticulocytes in 200 mg/kg/day males compared to controls, though these effects were reversible following the recovery period. White blood cell counts were unaffected. Urinalysis parameters were unchanged and no ophthalmic lesions indicative of toxicity were observed. The gross necropsy did not indicate any toxicity and PFHxA-related effects on organ weights were limited to increased liver weight that correlated with centrilobular hepatocellular hypertrophy in males at 200 mg/kg/day. However, this effect was reversible following the recovery period. One high dose male had moderate random hepatocellular necrosis, which was attributed to treatment. Increased relative kidney weight was found in males at the high dose, but it was not associated with any histopathologic findings. Peroxisome beta oxidation activity was 1.37 times higher in 200 mg/kg/day males compared to the control group at week 13. This effect was statistically significant and considered PFHxA-related. Study authors determined a NOAEL for male rats of 50 mg/kg/day, based on liver weight increases and hepatocellular hypertrophy in high-dose males, and a NOAEL for female rats of 200 mg/kg/day, the highest dose tested.

- Klaunig et al. 2015
    - In the previously described combined chronic toxicity/carcinogenicity study, male and female Sprague-Dawley rats (60 – 70/sex/dose) were exposed to perfluorohexanoic acid (98.1% purity) by daily gavage for up to 104 weeks. Sixty rats of each sex were assigned to treatment groups 1-3 while 70 of each were assigned to group 4. Treatment doses for male rats were 0, 2.5, 15, and 100 mg/kg/day for groups 1, 2, 3, and 4, respectively. For female rats, doses were 0, 5, 30, and 200 mg/kg/day for groups 1, 2, 3, and 4. The vehicle for this study was deionized water which was also the treatment for the control group. Parameters examined include body weight, food consumption (throughout study), functional observation battery (week 52), ophthalmology (weeks 51 and 103), hematology, serum chemistry, urinalysis, hormone levels (weeks 25-26 and 51-52), organ weight, and histopathology (week 104). A significant (at the high dose) dose-related decrease in survival rates was seen in female rats but not male rats. Female rat survival rates at week 80 were 76, 78, 85, and 69% in the control, low, mid, and high dose groups, respectively, and at week 104 were 36, 43, 33, and 22% in the control, low, mid, and high dose groups, respectively. Clinical signs of toxicity included rales and yellow material on the ventral trunk, anogenital, and/or urogenital areas, and slightly increased struggling during dosing at the highest doses in males and females, with females showing higher incidences than males. Decreased mean red blood cell and hemoglobin values and increased reticulocyte counts without correlating histological changes were found in high dose females, and were considered by the study authors to be secondary to renal effects or gastric ulceration. Statistically significant changes in triglycerides, free fatty acids, inorganic phosphorus, sodium, LDL, and/or VLDL at 2.5 – 200 mg/kg/day were sporadic in nature, of low magnitudes, lacked dose-response,

and/or not associated with histological changes, and were not considered toxicologically significant by the study authors. Higher mean urine volume and lower specific gravity was found at weeks 26 and 52 in females dosed with 200 mg/kg/day (statistically significant at week 26) and correlated with renal tubular degeneration and/or papillary necrosis. Lower pH values at weeks 26 and 52 were found at in males of the 100 mg/kg/day group, and were attributed to the acidity of perfluorohexanoic acid. At mid and high doses, acute pulmonary congestion and/or hemorrhage, increased alveolar macrophages, and erosion or ulceration of the glandular or nonglandular stomach were attributed to accidental aspiration of the irritating test substance. Hepatocellular necrosis and congestion throughout the liver and in the centrilobular region at mid and/or high doses were consistent with ischemia as the result of diminished hepatic blood flow. Most liver cell necrosis was found in animals that died or humanely killed prior to the scheduled sacrifice. On the basis of histological changes in the kidneys in females and lower pH values in males, the study authors identified the NOAELs of 15 and 30 mg/kg/day for males and females, respectively, and LOAELs of 100 and 200 mg/kg/day for males and females, respectively.

- These values are compared to the duration-adjusted GHS guidance values of 1.25 (Category 1) and 12.5 (Category 2) mg/kg/day[15] based on Haber's Rule.

- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* In a 90-day subchronic toxicity study conducted according to OECD Guideline 408, Crl:CD(SD) rats (10/sex/dose) were administered sodium perfluorohexanoate (NaPFHx) (100% purity) by gavage at doses of 20, 100, or 500 mg/kg/day. Rats were weighed at regular intervals and assessed prior to the study start and during the last week of dosing for ophthalmological and neurobehavioral effects (functional observation and motor activity). Clinical pathology evaluations were conducted halfway through the study, at the end of study, and at 1 month of recovery. Upon sacrifice, gross examinations and weighing/examinations of tissues were performed. β-Oxidation activity was also assessed in 5 rats from each group. No clinical signs of toxicity or mortality related to NaPFHx dosing were observed at any dose level during the study. Statistically significant decreases in mean body weight were observed in male rats at 500 mg/kg/day. No NaPFHx-related effects were observed related to food consumption, ophthalmology, functional observation battery, or motor activity, and no abnormal macroscopic observations were made at necropsy. β-Oxidation activity in was induced by NaPFHx male rats at 100 mg/kg/day and both males and females at 500 mg/kg/day and persisted through the 30-day recovery period. Liver and kidney weights were increased in both male and female rats at 500 mg/kg/day and thyroid weights were statistically significantly increased in female rats at 500 mg/kg/day. Study authors established a NOAEL and LOAEL of 20 mg/kg/day and 100 mg/kg/day (equivalent to 19 and 93 mg/kg/day perfluorohexanoic acid[16], respectively), based on a lack of NaPFHx-related effects at that dose.
  - *Sodium perfluorohexanoate:* In a one-generation reproduction toxicity study conducted according to OECD Guideline 415, Crl:CD(SD) rats (20/sex/dose) were administered sodium perfluorohexanoate (NaPFHx) (100% purity) by gavage at doses of 20, 100, or 500 mg/kg/day. An additional control group received nanopure water vehicle. P1 females were dosed 70 days prior to cohabitation through gestation and lactation for a total of 126 days while P1 males were doses for approximately 110 days. F1 rats were not dosed. Clinical observations, body weight, and food consumption were determined weekly. No NaPFHx-related mortality was observed in either parental males or females at any dose. Clinical

[15] 10 mg/kg/day x 13 weeks/104 weeks = 1.25 mg/kg/day
[16] 20 mg NaPFHx/kg/day x MW (PFHxA)/MW (NaPFHx) = 20 mg/kg/day x 314/336 = 19 mg PFHxA/kg/day

signs of toxicity included stained fur in both sexes at 500 mg/kg/day, reduced body weight parameters in males at 100 and 500 mg/kg/day (12% and 29%, respectively) and reduced maternal body weight gain at 500 mg/kg/day during the first week of gestation and at 500 mg/kg/day during lactation period. Study authors established a NOAEL of 20 mg/kg/day and LOAEL of 100 mg/kg/day (equivalent to 19 and 93 mg/kg/day perfluorohexanoic acid[17], respectively) based on reduced body weight parameters seen in the parental generation at both 100 and 500 mg/kg/day.

- Based on the weight of evidence, a score of Moderate was assigned. The lowest LOAELs were 100 mg/kg/day for male rats based on effects on urine pH (at weeks 26 and 52) and 200 mg/kg/day for female rats based on effects on survival, urinalysis (at weeks 26 and 52), and kidney pathology in the chronic toxicity study for the target chemical. These values are higher than the duration-adjusted GHS guidance values for 26, 52, and 104 weeks of treatment (GHS Category 2 corresponds to 10-100 mg/kg/day for 13-week study, 5-50 mg/kg/day for 26 week study, 2.5-25 mg/kg/day for 52 week study[18]). Based on dose spacing, it is not possible to determine if effects observed at 26 and 52 weeks in males or 26 weeks in females would have been observed below the adjusted guidance values. As no interim sacrifices were conducted, it is also uncertain whether the histopathological effects at 100 mg/kg/day in females would have been observed after only 90 days, which would warrant GHS classification. The subchronic study of the target chemical identified a NOAEL of 50 mg/kg/day and LOAEL of 200 mg/kg/day; therefore, it is not possible to conclusively determine if effects would have been observed below the guidance value of 100 mg/kg/day. However, a LOAEL of 100 mg/kg/day was identified in a subchronic toxicity study and a one-generation reproductive toxicity study for the surrogate chemical, which is equivalent to 94 mg/kg/day target compound. These values warrant classification to GHS Category 2. The NOAEL of 50 mg/kg/day identified in the subchronic toxicity study for the target compound and the NOAELs of 20 mg/kg/day for the surrogate (equivalent to 19 mg/kg/day target compound) indicates that classification to GHS Category 1 is not warranted (i.e., LOAEL < 10 mg/kg/day).

**Neurotoxicity (N)**

***Group II Score (single dose)* (vH, H, M, or L):** DG

Perfluorohexanoic acid was assigned a score of Data Gap for neurotoxicity (single dose) based on lack of sufficient data. While clinical signs of ataxia, emaciation, hypoactivity, and/or abnormal gait were reported in acute oral toxicity studies, they are likely secondary to the administration of a high dose of chemical by gavage rather than specific neurotoxicity symptoms.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- Riker Laboratories 1979
  - In an acute oral toxicity study, male albino rats (5/group) received perfluorohexanoic acid (under the trade name of T-2712CoC) by gavage at 500, 1,000 or 5,000 mg/kg and were observed for 14 days afterwards. Mortalities were 1/5, 5/5 and 5/5 at the low, mid and high doses, respectively. Clinical signs included ataxia, dyspnea, emaciation, hypoactivity, salivation, prostration, and unkempt appearance. These occurred from 1 – 30 min to 5 days after dosing, and subsided by day 5 in surviving animals. Decreased body weight was found in ¾ surviving animals at 500 mg/kg. Findings from gross necropsy performed at the end of the observation period included hemorrhagic vas deferens and one incidence of testes

[17] 20 mg NaPFHx/kg/day x MW (PFHxA)/MW (NaPFHx) = 20 mg/kg/day x 314/336 = 19 mg PFHxA/kg/day
[18] Using Haber's Rule, 100 mg/kg/day x 13 weeks/26 weeks = 50 mg/kg/day

atrophy. Necropsy of animals that died during the study found chemical burns of the stomach and intestine.

- Loveless 2009
    - *Sodium perfluorohexanoate:* Female Crl:CD(SD) rats were administered a single dose of NaPFHx (100% purity) by gavage at levels of 175, 550, 1750, or 5,000 mg/kg. Animals were then observed for up to 14 days post-dose for clinical signs of toxicity, body weight effects, and mortality. All rats at doses 175 or 550 mg/kg survived (number per group not reported). One of four rats dosed with 1,750 mg/kg died on the day of dosing, while all three rats dosed with 5,000 mg/kg were found dead on the day of dosing or the day afterwards. Clinical signs of systemic toxicity included abnormal gait, dehydration, high or low posture, clear oral or nasal discharge, wet or stained fur, salivation, ataxia, or lethargy.

***Group II* Score (repeated dose)*** **(H, M, or L): L**

Perfluorohexanoic acid was assigned a score of Low for neurotoxicity (repeated dose) based on lack of neurotoxicity observed in subchronic and chronic studies on the target chemical and the surrogate at oral doses up to 500 mg/kg/day. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when adequate data are available and negative, there are no structural alerts, and they are not classified under GHS based on a lack of effects up to the guidance value of 100 mg/kg/day (CPA 2016b). The confidence in the score was high as it was based on well-conducted studies on the target compound supported by surrogate data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- Chengelis et al. 2009b
    - In a previously described 90-day subchronic toxicity study, perfluorohexanoic acid (PFHxA) (purity 98.5%) was administered orally (by gavage) 7 days/week to 3 groups of Crl:CD(SD) rats (20/sex for control and 200 mg/kg/day groups, 10/sex for 10 and 50 mg/kg/day groups) at doses of 10, 50, or 200 mg/kg/day. A control group received the deionized water vehicle. Authors recorded clinical observations daily and detailed physical examinations, body weights, and food consumption weekly. A functional observational battery (FOB) (home cage observations, handling observations, open field observations, sensory observations, neuromuscular observations, and physiological observations), and motor activity (MA) assessments were conducted prior to PFHxA administration and during week 12 in 10 animals/sex/dose. No adverse effects were observed. ToxServices observed a NOAEL of 200 mg/kg/day for this study based on the lack of effects on neurotoxicity.
- Klaunig et al. 2015
    - In the previously described combined chronic toxicity/carcinogenicity study, male and female Sprague-Dawley rats (60 – 70/sex/dose) were exposed to perfluorohexanoic acid (98.1% purity) by daily gavage for up to 104 weeks. 60 rats of each sex were assigned to treatment groups 1-3 while 70 of each were assigned to group 4. Treatment doses for male rats were 0, 2.5, 15, and 100 mg/kg/day for groups 1, 2, 3, and 4, respectively. For female rats, doses were 0, 5, 30, and 200 mg/kg/day for groups 1, 2, 3, and 4. The vehicle for this study was deionized water which was also the treatment for the control group. FOB and locomotor assessments were performed in 12 animals/sex/dose during the 52$^{nd}$ week as described above by Chengelis et al. (2009b). No treatment-related statistically significant changes were observed regarding locomotor activity patterns or habituation pattern. Increased number of male rats asleep or lying on their side was observed at 100 mg/kg/day.

Females at 5 mg/kg/day had lower mean grip strength. Due to the lack of dose-dependence and correlation with other FOB parameters, these effects were not considered adverse by the study authors, who concluded that no adverse effects on neurobehavior was caused by the test substance. ToxServices identified a NOAEL of 100 mg/kg/day (males) and 200 mg/kg/day (females) based on the lack of neurotoxicity in the study.

- Loveless et al. 2009
  - *Sodium perfluorohexanoate:* In the previously described 90-day subchronic toxicity study conducted according to OECD Guideline 408, Crl:CD(SD) rats (10/sex/dose) were administered sodium perfluorohexanoate (NaPFHx) (100% purity) by gavage at doses of 20, 100, or 500 mg/kg/day. An FOB (grip strength and sensory motor function) and motor activity assessment were performed prior to study initiation and during the last week of dosing. There were no effects on any of the parameters examined. ToxServices identified a NOAEL of 500 mg/kg/day based on the lack of neurotoxicity in the study.

**Skin Sensitization (SnS) Group II* Score (H, M, or L):** *L*
Perfluorohexanoic acid was assigned a score of Low for skin sensitization based on modeled data. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative, there are no structural alerts, and they are not classified under GHS (CPA 2016b). The confidence in the score was reduced as no experimental data were available on the chemical of interest.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Payne and Walsh 1994
  - Perfluorohexanoic acid does not possess any known structural alerts for skin sensitization as identified by Payne and Walsh (1994). See Appendix D for a complete list of structural alerts.
- OECD 2015
  - Perfluorohexanoic acid was predicted to be a non-sensitizer using the OECD Toolbox read-across methodology (Appendix E).
- Toxtree 2015
  - Perfluorohexanoic acid does not contain any skin sensitization reactivity domains alerts (Appendix F).
- VEGA 2015
  - Perfluorohexanoic acid was predicted to be a skin sensitizer using the CAESAR model. However, the results may not be reliable as only moderately similar compounds with known experimental data were found in the training set, the accuracy of the prediction for similar molecules in the training set is not accurate, and the compound contains fragments not represented in the training set (Appendix G).
- Based on the weight of evidence, a score of Low was assigned. Three of the four QSAR/SAR methods above predicted perfluorohexanoic acid to be a non-sensitizer. The other model, VEGA, predicted it to be a sensitizer, but this result is not reliable as the compound was out of the applicability domain of the model.

**Respiratory Sensitization (SnR) Group II* Score (H, M, or L):** DG
Perfluorohexanoic acid was assigned a score of Data Gap for respiratory sensitization based on lack of data identified.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- No data were identified.

**Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L):** *vH*
Perfluorohexanoic acid was assigned a score of Very High for skin irritation/corrosivity based on being a strong acid and association with non-harmonized hazard statement H314. GreenScreen® criteria classify chemicals as a Very High hazard for skin irritation/corrosivity when they are classified to GHS Category 1 and associated with H314 (CPA 2016b). Confidence in the score was reduced as no experimental data or measured pH values were identified.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- ECHA 2016
    - Perfluorohexanoic acid is self-classified to GHS Category 1B skin irritant with the hazard statement H314 by 29/29 REACH notifiers.
- NICNAS 2016, ENVIRON 2014
    - Perfluorinated carboxylic acids are strong acids ($pK_a$ <1) in water under environmental conditions.

**Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L):** *vH*
Perfluorohexanoic acid was assigned a score of Very High for eye irritation/corrosivity based its low pH and association with the non-harmonized hazard statement H314 for skin corrision, which indicates that it is also expected to be corrosive to the eyes. GreenScreen® criteria classify chemicals as a Very High hazard for eye irritation/corrosivity when they are corrosive to the skin (CPA 2016b). The confidence in the score was reduced as no experimental data were available, and the H314 classification is not harmonized.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- NICNAS 2016, ENVIRON 2014
    - Perfluorinated carboxylic acids are strong acids ($pK_a$ <1) in water under environmental conditions.

**Ecotoxicity (Ecotox)**

**Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): M**
Perfluorohexanoic acid was assigned a score of Moderate for acute aquatic toxicity based on the lowest acute $EC_{50}$ of 86 mg/L in algae. GreenScreen® criteria classify chemicals as a Moderate hazard for acute aquatic toxicity when acute aquatic $L/EC_{50}$ values are between 10 and 100 mg/L (CPA 2016b). The confidence in the score was high as it was based on reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- NICNAS 2016
    - *Fish* 96 h $LC_{50}$ > 100 mg/L (species not reported)
    - *Invertebrate* 48 h $EC_{50}$ = 1,048 mg/L (*Daphnia magna*, OECD 202)

  - *Algae* 72 h $EC_{50}$ = 86 mg/L (*Scenedesmus subspicatus*)
- ENVIRON 2014 (data for both perfluorohexanoic acid and its salts were included, and the compounds tested in each study was not specified; may contain the same studies as described in NICNAS 2016)
  - 72h $EC_{50}$ = 4,032 mg/L (nominal) in green algae (*Chlorella vulgaris*)
  - 72h $EC_{50}$ = 998.7 mg/L (nominal) in blue-green algae (*Geitlerinema amphibium*)
  - 72h $EC_{50}$ = 86 mg/L (nominal) in green algae (*Scenedesmus subspicatus*)
  - 72h $EC_{50}$ = 1,482 mg/L (nominal) in diatom (*Skeletonema marinoi*)

**Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): L**
Perfluorohexanoic acid was assigned a score of Low for chronic aquatic toxicity based on chronic NOECs of at least 10.1 mg/L in fish, daphnia and algae. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic toxicity values are greater than 10 mg/L (CPA 2016b). The confidence in the score was high as it was based on reliable studies on three tropic levels.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- NICNAS 2016
  - *Fish* 56 d NOEC ≥ 10.1 mg/L (*Oncorhynchus mykiss,* rainbow trout, egg hatching success, post-hatch survival, length and weight)
  - *Algae* 72 h NOEC = 50 mg/L (*Scenedesmus subspicatus*, growth rate)
  - *Invertebrate* 21 d $EC_{50}$ = 776 mg/L (*Daphnia magna,* OECD 211)
- ENVIRON 2014 (data for both perfluorohexanoic acid and its salts, and the compounds tested in each study was not specified)
  - 72h NOEC ≥628 mg/L (nominal) in green algae (*Scenedesmus obliquus*)

**<u>Environmental Fate (Fate)</u>**

**Persistence (P) Score (vH, H, M, L, or vL): vH**
Perfluorohexanoic acid was assigned a score of Very High for persistence based on data demonstrating it is recalcitrant in air, soil, and sediment, and modeling predicting that it is highly persistent in water. GreenScreen® criteria classify chemicals as a Very High hazard for persistence when they are recalcitrant (CPA 2016b). The confidence in the score was high as it was based on data from degradation studies and environmental monitoring studies for the predicted dominant compartment of soil.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- NICNAS 2016
  - Categorized as persistent based on non-degradability of perfluorinated carboxylic acids
- ENVIRON 2014
  - Perfluorohexanoic acid is not likely to be degradable under normal environmental conditions.
  - Polyfluorinated carboxylic acids may react with photochemically-generated hydroxyl radicals in the air. Perfluorohexanoic acid concentrations decreased by 0.8% after 106 days of solar irradiation, suggesting extremely slow atmospheric oxidation rate.

  - Perfluorohexanoic acid is a degradation product of 6:2 fluorotelomer alcohol (6:2 FTOH). Biodegradation studies on 6:2 FTOH in soil and sediment indicates that perfluorohexanoic acid is not completely mineralized and the half-life is greater than 6 months.
  - Perfluorohexanoic acid has been detected in urban and remote environments – indicative of long range transport. Snow core analysis indicates that it was deposited on the Tibetan Plateau as early as 1985 – 1986, with increasing concentrations with time up till 1999. It is also detected at relatively low concentrations in surface snow in Greenland. Perfluorohexanoic acid was detected in the sediment of Faroe Island, but not in marine sediment of Gufunes Bay, Iceland. It is also detected in seawater from the Arctic and Subarctic in the Canadian archipelago. It was hypothesized that perfluorohexanoic acid is transported through volatile precursors such as 6:2 FTOH in the air to remote areas, or directly through seawater.
- U.S. EPA 2012
  - The BIOWIN modeling Ready Biodegradable Predictor indicates that perfluorohexanoic acid is not expected to be readily biodegradable (see Appendix H). Fugacity modeling predicts 78.2% will partition to soil with a half-life of 360 days, 11.7% will partition to water with a half-life of 180 days, and 8.77% will partition to air with a half-life of 21 days.

**Bioaccumulation (B) Score (vH, H, M, L, or vL): L**
Perfluorohexanoic acid was assigned a score of Low for bioaccumulation based on bioaccumulation factors of up to <520 in aquatic and marine species and expert judgment. GreenScreen® criteria classify chemicals as a Low hazard for bioaccumulation when BCF values are between 100 and 500 (CPA 2016b). The confidence in the score was high as it was based on experimental data consistent with NICNAS' conclusions.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- NICNAS 2016
  - Categorized as not bioaccumulative.
  - Some perfluorinated chemicals are known to be bioaccumulative due to binding to protein in plasma and liver, rather than partitioning to lipid fractions. However, two bioconcentration studies in fish did not detect accumulation of perfluorohexanoic acid in any tissues. Bioaccumulation potential decreases with perfluorinated chain length.
- ENVIRON 2014
  - BAF = 0.02 L/kg, BCF = 0.07 L/kg in rainbow trout
  - BCF < 1 L/kg in rainbow trout (modeled)
  - BCF < 9 L/kg in rainbow trout as determined in a laboratory experiment
  - BAF < 270 L/kg in sea mullet and < 520 L/kg in oyster as determined in a field study.

**Physical Hazards (Physical)**

**Reactivity (Rx) Score (vH, H, M, or L):** *M*
Perfluorohexanoic acid was assigned a score of Moderate for reactivity based on GHS Category 1 classification as being corrosive to metal on an MSDS. GreenScreen® criteria classify chemicals as a Moderate hazard for reactivity when they are classified as substances corrosive to metal Category 1 (CPA 2016b). Confidence in the score is reduced due to the lack of experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists

  - *Screening:* Not present on any screening lists
- UN 2013
  - Based on examination of the structure, ToxServices determined that perfluorohexanoic acid is not an organic peroxide, does not contain reactive groups associated with self-reactive substances, and is not an organometallic substance that may produce flammable gases on contact with water.
- UN 2010
  - Based on examination of the structure, ToxServices determined that perfluorohexanoic acid does not have any alerts for explosivity (Appendix I).
- TCI America 2014
  - Perfluorohexanoic acid has an NFPA instability score of 0 ("Normally stable, even under fire exposure conditions, and is not reactive with water") (NFPA 2016) and HMIS physical hazard score of 0 ("Materials that are normally stable, even under fire conditions, and will not react with water, polymerize, decompose, condense, or self-react. Non-explosives") (ILPI 2015).
  - Perfluorohexanoic acid is classified to GHS Category 1 as corrosive to metals.

**Flammability (F) Score (vH, H, M, or L):** *M*
Perfluorohexanoic acid was assigned a score of Moderate for flammability based on the flash point of 40.3ºC that classified it to GHS Category 3 (flash point between 23 and 60ºC) as a flammable liquid. GreenScreen® criteria classify chemicals as a Moderate hazard for flammability when they are classified to GHS Category 3 or 4 as flammable liquids (CPA 2016b). Confidence in the score was reduced as it is unclear how the report flash point was determined.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- TCI America 2014
  - A safety data sheet for perfluorohexanoic acid states that it has an NFPA and HMIS flammability rating of 0. An NFPA and HMIS flammability rating of 0 corresponds to "Materials that will not burn" (NFPA 2016, ILPI 2015).
- ChemNet Undated
  - A flash point of 40.3ºC was identified for perfluorohexanoic acid.

## References

Anderson, M.E., J.L. Butenhoff, S-C. Chang, D.G. Farrar, G.L. Kennedy, Jr., C. Lau, G.W. Olsen, J. Seed, and K.B. Wallace. 2008. Perfluoroalkyl acids and related chemistries – toxicokinetics and modes of action. Toxicological Science3s 102(1): 3-14.

Bluesign®. 2015. Bluesign® system substances list (BSSL) consumer safety limits. Version 5.1. Available: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=6&cad=rja&uact=8&ved=0ahUKEwj0j4LV5onNAhUJKB4KHbB9AVoQFgg-MAU&url=http%3A%2F%2Fwww.bluesign.com%2Findustry%2Finfocenter%2Fdownloads%2FdownloadFile%2F2%2Find-bssl%2Fbssl-v5-1-pdf&usg=AFQjCNGKd5iKGAXMSaG0wLSWbk-_hcYe_w&sig2=av1NGe5yf-lUYpjJt5w5ug&bvm=bv.123325700,d.dmo

Charles River. 2009a. The excretion of [$^{14}$C]-ammonium perfluorohexanoate in the mouse and the rat following a single oral administration at 50 mg/kg. Test facility study no. 198541, Report No. 30417. Available: https://www.daikin.com/chm/csr/

Charles River. 2009b. The excretion and tissue distribution of [$^{14}$C]-ammonium perfluorohexanoate in the mouse and the rat following multiple oral administration of 50 mg/kg. Test facility study no. 190300, Report No. 30572. Available: https://www.daikin.com/chm/csr/

Charles River. 2010. Oral (gavage) acute pharmacokinetic study of PFH ammonium salt (ammonium salt of perfluorinated hexanoic acid) in mice. Testing facility study no. UZS00009. Available: https://www.daikin.com/chm/csr/

Charles River. 2011a. Oral (gavage) combined developmental and perinatal/postnatal reproduction toxicity study of PFH ammonium salt (ammonium salt of perfluorinated hexanoic acid) in mice. Charles River Laboratories preclinical Services Protocol Number 20005045. Available: https://www.daikin.com/chm/csr/pdf/PFHxA/13)_PFHxA_E.pdf

Charles River. 2011b. Oral (gavage) combined developmental and perinatal/postnatal reproduction toxicity study of PFH ammonium salt (ammonium salt of perfluorinated hexanoic acid) in mice. Charles River Laboratories preclinical Services Protocol Number UZS00010. Available: https://www.daikin.com/chm/csr/pdf/PFHxA/14)_PFHxA_E.pdf

Charles River. 2012. Oral (gavage) combined developmental and perinatal/postnatal reproduction toxicity study of PFH ammonium salt (ammonium salt of perfluorinated hexanoic acid) in mice. Final report amendment. Charles River Laboratories preclinical Services Protocol Number 20005045. Available: https://www.daikin.com/chm/csr/pdf/PFHxA/15)_PFHxA_E.pdf

ChemIDplus. 2016. Entry for Perfluorohexanoic Acid (CAS #307-24-4). United States National Library of Medicine. Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp.

ChemNet. Undated. Information for perfluorohexanoic acid. CAS #307-24-4. Available: http://www.chemnet.com/cas/en/307-24-4/Perfluorohexanoic-acid.html

Chengelis, C.P., J.B. Kirkpatrick, N.R. Myers, M. Shinohara, P.L. Stetson, and D.W. Sved. 2009a. Comparison of the toxicokinetic behavior of perfluorohexanoic acid (PFHxA) and nonafluorobutane-1-sulfonic acid (PFBS) in cynomolgus monkeys and rats. Reproductive Toxicology 27: 400-406.

Chengelis, C. P., J. B. Kirkpatrick, A. Radovsky, M. Shinohara. 2009b. A 90-day repeated dose oral (gavage) toxicity study of perfluorohexanoic acid (PFHxA) in rats (with functional observational battery and motor activity determinations). Reproductive Toxicology 27: 342-351

Clean Production Action (CPA). 2016a. The GreenScreen® for Safer Chemicals Chemical Hazard Assessment Guidance. Version 1.3 Guidance. Dated March, 2016. Available at: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2016b. GreenScreen Version 1.3 Hazard Criteria. Dated: March 2016. Available at: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2016c. The GreenScreen® for Safer Chemicals Version 1.3 GreenScreen Benchmarks™. Dated March 2016. Available at: http://www.greenscreenchemicals.org/.

Danish Environmental Protection Agency (Danish EPA). 2015. Perfluoroalkylated substances : PFOA, PFOS and PFOSA. Available : http://www2.mst.dk/Udgiv/publications/2015/04/978-87-93283-01-5.pdf

Edler, J. 2011. Relative solubility number RSN- an alternative measurement to logPow for determining the bioaccmulation potential. Master of Science Thesis. Department of Chemical and Biological Engineering. Chalmers University of Technology. Available: http://publications.lib.chalmers.se/records/fulltext/148789.pdf

ENVIRON. 2014. Assessment of POP criteria for specific short-chain perfluorinated alkyl substances. FluoroCouncil. Available : https://fluorocouncil.com/PDFs/Assessment-of-POP-Criteria-for-Specific-Short-Chain-Perfluorinated-Alkyl-Substances.pdf

European Chemicals Agency (ECHA). 2016. C&L Inventory. Entry for perfluorohexanoic acid. Available: http://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/125329

Grandjean, P., and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

Grandjean, P., and P.J. Landrigan. 2014. Neurobehavioral effects of developmental toxicity. The Lancet 13: 330-338.

H&M. 2016. H&M chemical restrictions. Manufacturing restricted substance list (MRSL). Available: http://sustainability.hm.com/content/dam/hm/about/documents/masterlanguage/CSR/Policies/HM%20Chemical%20Restrictions%202016_Manufacturing%20Restricted%20Substances%20List.pdf

ILPI. 2015. The MSDS Hyper Glossary. HMIS® - Hazardous Materials Identification System. Available at: http://www.ilpi.com/msds/ref/hmis.html

Klaunig, J.E., M. Shinohara, H. Iwai, C.P. Chengelis, J.B. Kirkpatrick, Z. Wang, R.H. Bruner. 2015. Evaluation of the Chronic Toxicity and Carcinogenicity of Perfluorohexanoic Acid (PFHxA) in

Sprague-Dawley Rats. Tox Path, 43: 209-220. Available at: http://tpx.sagepub.com/content/43/2/209.full.pdf+html

Levi Strauss & Co. 2015. Restricted Substances List. Available: http://levistrauss.com/wp-content/uploads/2015/11/RSL-2015.pdf

Loveless, S.E., B. Slezak, T. Serex, J. Lewis, P. Mukerji, J.C. O'Connor, E. M. Donner, S. R. Frame, S. H. Korzeniowski, R. C. Buck. 2009. Toxicological evaluation of sodium perfluorohexanoate. Toxicology 264: 32-44.

National Fire Protection Association (NFPA). 2016. NFPA Hazard Rating System. Available: https://www.fm.colostate.edu/files/forms/safety/CH-23.NFPA.ratings.pdf

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2016. Environment Tier II Assessment for Short-Chain Perfluorocarboxylic Acids and their Direct Precursors. Australian Government Department of Health. Available at: https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessments/tier-ii-environment-assessments/short-chain-perfluorocarboxylic-acids-and-their-direct-precursors

National Toxicology Program (NTP). 2016. Information page on perfluorohexanoic acid (PFHXA) – M040048. Available: https://ntp.niehs.nih.gov/testing/status/agents/ts-m040048.html#Known-Uses

Oakwood Product, Inc. 2015. Safety data sheet for perfluorohexanoic acid. Version 1.2. Available: http://www.oakwoodchemical.com/ShowMSDS.aspx?Number=008504

Organisation for Economic Co-operation and Development (OECD). 2015. OECD QSAR Toolbox for Grouping Chemicals into Categories Version 3.3.5. Available at: http://toolbox.oasis-lmc.org/?section=download&version=latest.

Payne, M.P., and P.T. Walsh. 1994. Structure-activity relationships for skin sensitization potential: development of structural alerts for use in knowledge-based toxicity prediction systems. J Chem Inf Comput Sci. 34:154-161.

Pharos. 2016. Pharos Chemical and Material Library Entry for Perfluorohexanoic acid (CAS #307-24-4). Available at: http://www.pharosproject.net/material/.

Riker Laboratories, Inc. 1979. Acute oral toxicity screen with T-2712CoC in Albino rats. Experiment No. 0479AR0680. Available: https://yosemite.epa.gov/oppts/epatscat8.nsf/ALLIDS/9BD75F9597CED4C9852577DF006B5CBB/$FILE/88040000247.pdf?OpenElement

Swedish Environmental Protection Agency (Swedish EPA). 2012. Environmental and Health Risk Assessment of Perfluoroalkylated and Polyfluoroalkylated Substances (PFASs) in Sweden. Available at: http://www.naturvardsverket.se/Documents/publikationer6400/978-91-620-6513-3.pdf?pid=3822

SynQuest Laboratories, Inc. 2015. Safety data sheet of perfluorohexanoic acid. Product code 2121-3-39. Available: http://www.synquestlabs.com/msds/2121-3-39.pdf

TCI America. 2014. Safety data sheet for perfoluorohexanoic acid. Revision number 2. Available: https://www.spectrumchemical.com/MSDS/TCI-U0067.pdf

ToxServices. 2013a. SOP 1.37: GreenScreen® Hazard Assessments. Dated: April 24, 2013.

ToxServices. 2013b. SOP 1.69: GreenScreen® Hazard Assessments. Dated: August 17, 2013.

Toxtree. 2015. Estimation of Toxic Hazard- A Decision Tree Approach v2.6.13. Available at: http://toxtree.sourceforge.net.

United Nations (UN). 2010. UN Manual of Tests and Criteria. Manual of Tests and Criteria. Revised Fifth Edition. Available: http://www.unece.org/trans/danger/publi/manual/rev5/manrev5-files_e.html.

United Nations (UN). 2013. UN Recommendations on the Transport of Dangerous Goods - Model Regulations Eighteenth revised edition. Available: http://www.unece.org/trans/danger/publi/unrec/rev18/18files_e.html.

United States Department of Transportation (U.S. DOT). 2008a. Chemicals Listed with Classification. 49 CFR § 172.101. Available at: http://www.gpo.gov/fdsys/pkg/CFR-2008-title49-vol2/pdf/CFR-2008-title49-vol2-sec172-101.pdf.

United States Department of Transportation (U.S. DOT). 2008b. Classification Criteria. 49 CFR § 173. Available at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title49/49cfr173_main_02.tpl

United States Environmental Protection Agency (U.S. EPA). 2012. Estimation Programs Interface (EPI) Suite™ Web, v4.11, Washington, DC, USA. Available at: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

United States Environmental Protection Agency (U.S. EPA). 2015. Safer Choice Standard. Available at: http://www2.epa.gov/saferchoice/safer-choice-standard.

United States Environmental Protection Agency (U.S. EPA). 2016a. New chemicals program review of alternatives for PFOA and related chemicals. Assessing and managing chemicals under TSCA. Available: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/new-chemicals-program-review-alternatives-pfoa-and

United States Environmental Protection Agency (U.S. EPA). 2016b. Per- and polyfluoroalkyl substances (PFASs) under TSCA. Available: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/and-polyfluoroalkyl-substances-pfass-under-tsca#tab-3

United States Environmental Protection Agency (U.S. EPA). 2016c. Safer Chemical Ingredients List (SCIL). Available at: http://www2.epa.gov/saferchoice/safer-ingredients.

Virtual Models for Evaluating the Properties of Chemicals within a Global Architecture (VEGA). 2015. Predictive Model Platform version 1.1.1. Available at: http://www.vega-qsar.eu/index.php.

## APPENDIX A: Hazard Benchmark Acronyms
**(in alphabetical order)**

**(AA) Acute Aquatic Toxicity**

**(AT) Acute Mammalian Toxicity**

**(B) Bioaccumulation**

**(C) Carcinogenicity**

**(CA) Chronic Aquatic Toxicity**

**(D) Developmental Toxicity**

**(E) Endocrine Activity**

**(F) Flammability**

**(IrE) Eye Irritation/Corrosivity**

**(IrS) Skin Irritation/Corrosivity**

**(M) Mutagenicity and Genotoxicity**

**(N) Neurotoxicity**

**(P) Persistence**

**(R) Reproductive Toxicity**

**(Rx) Reactivity**

**(SnS) Sensitization- Skin**

**(SnR) Sensitization- Respiratory**

**(ST) Systemic/Organ Toxicity**

# APPENDIX B: Results of Automated GreenScreen® Score Calculation for Perfluorohexanoic Acid (CAS #307-24-4)

**GreenScreen® Score Inspector**

**Table 1: Hazard Table**

| | | | Group I Human | | | | | Group II and II* Human | | | | | | | | | Ecotox | | Fate | | Physical | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Carcinogenicity | Mutagenicity/Genotoxicity | Reproductive Toxicity | Developmental Toxicity | Endocrine Activity | Acute Toxicity | Systemic Toxicity | | Neurotoxicity | | Skin Sensitization* | Respiratory Sensitization* | Skin Irritation | Eye Irritation | Acute Aquatic Toxicity | Chronic Aquatic Toxicity | Persistence | Bioaccumulation | Reactivity | Flammability |
| **Table 2: Chemical Details** | | | | | | | | | S | R * | S | R * | * | * | | | | | | | | |
| **Inorganic Chemical?** | **Chemical Name** | **CAS#** | **C** | **M** | **R** | **D** | **E** | **AT** | **STs** | **STr** | **Ns** | **Nr** | **SNS*** | **SNR*** | **IrS** | **IrE** | **AA** | **CA** | **P** | **B** | **Rx** | **F** |
| No | PFHxA | 307-24-4 | L | *L* | *L* | *M* | DG | M | H | *M* | DG | L | *L* | DG | *vH* | *vH* | M | L | vH | L | *M* | *M* |

**Table 3: Hazard Summary Table**

| Benchmark | a | b | c | d | e | f | g |
|---|---|---|---|---|---|---|---|
| 1 | No | No | Yes | No | No | | |
| 2 | STOP | | | | | | |
| 3 | STOP | | | | | | |
| 4 | STOP | | | | | | |

**Table 4**

| Chemical Name | Preliminary GreenScreen® Benchmark Score |
|---|---|
| PFHxA | 1 |

**Note:** Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

**Table 6**

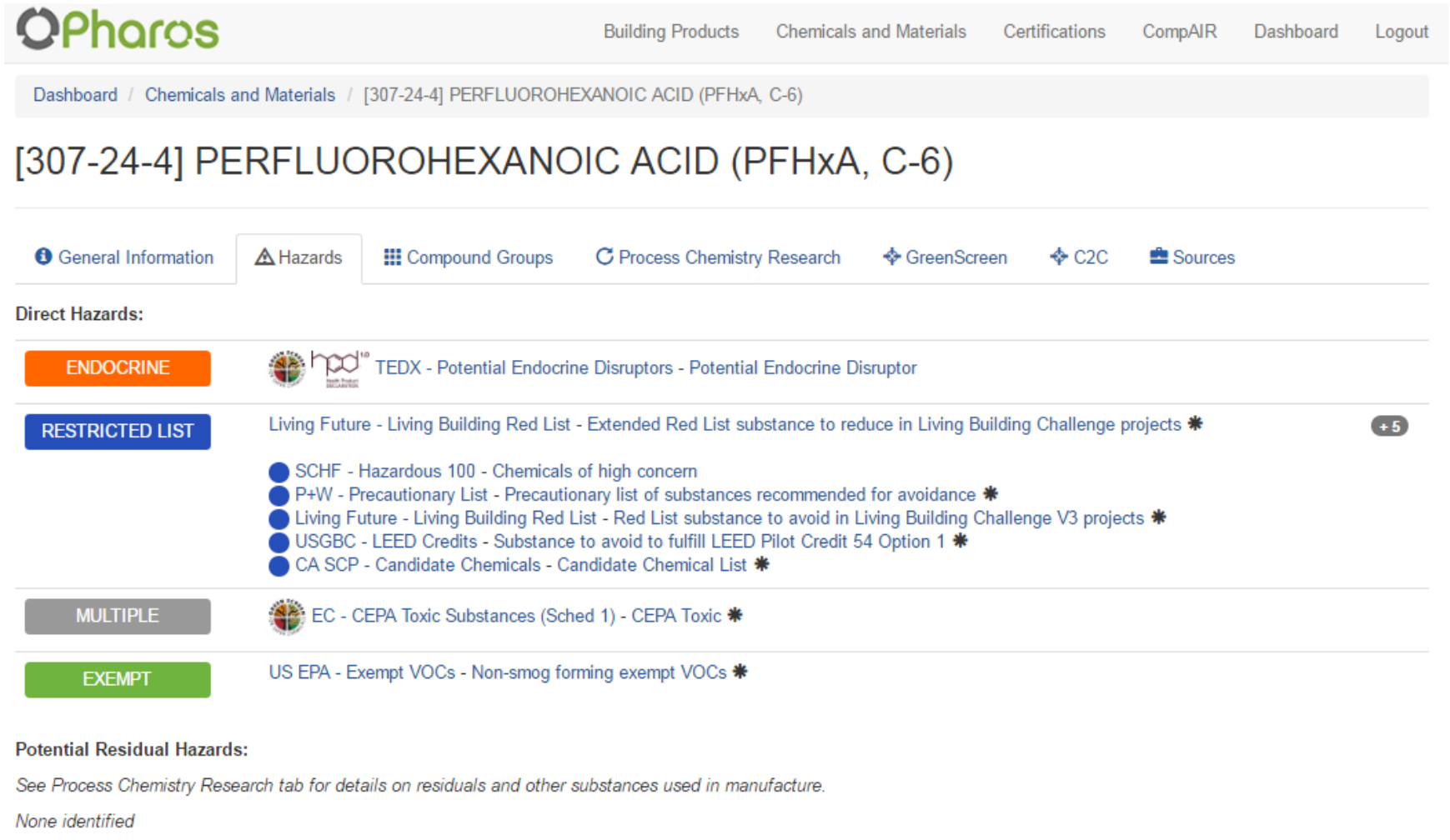
| Chemical Name | Final GreenScreen® Benchmark Score |
|---|---|
| PFHxA | 1 |

After Data gap Assessment
**Note:** No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

**Table 5: Data Gap Assessment Table**

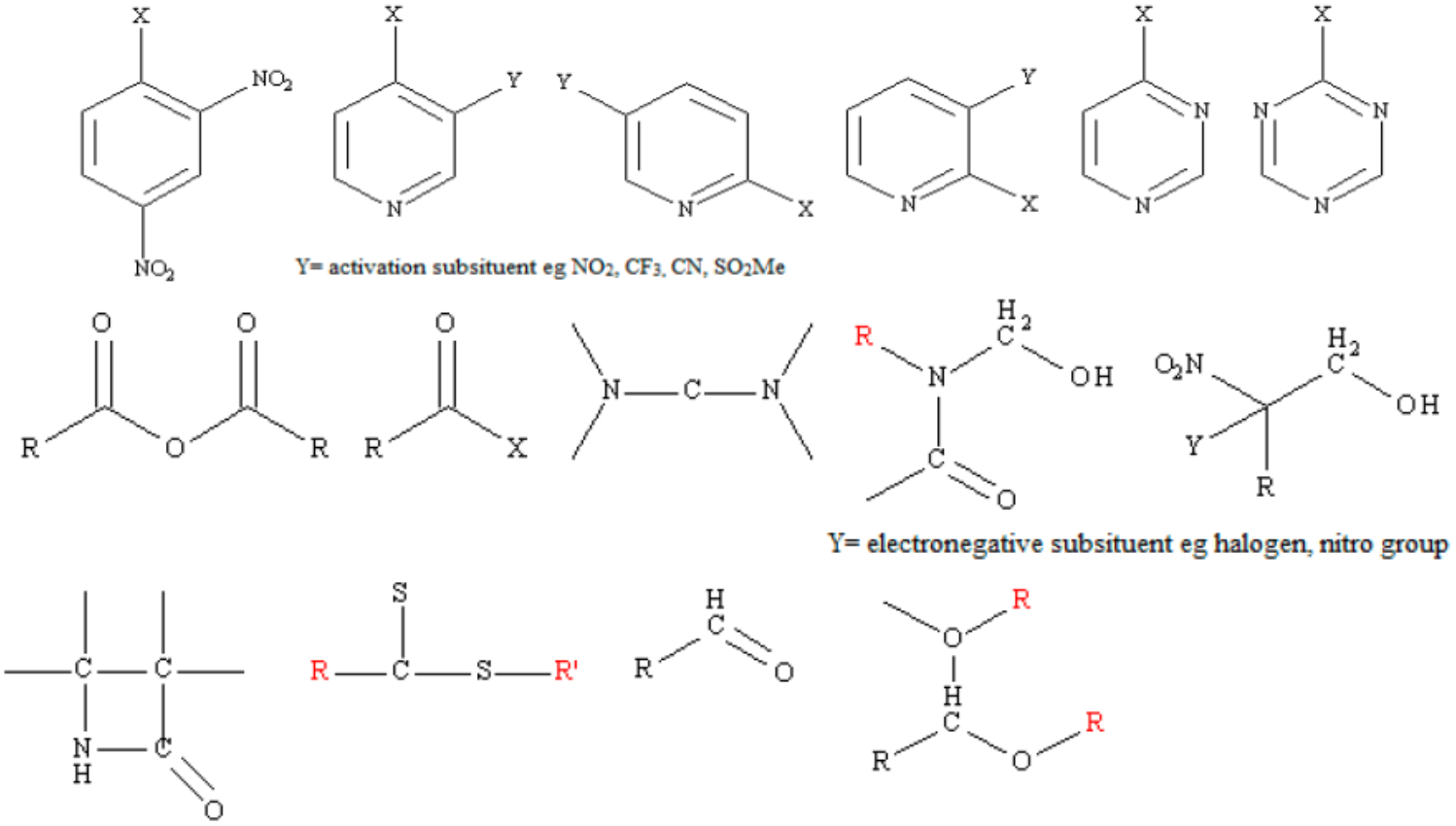
| Datagap Criteria | a | b | c | d | e | f | g | h | i | j | bm4 | End Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | | | | | | | | | | | 1 |
| 2 | | | | | | | | | | | | |
| 3 | | | | | | | | | | | | |
| 4 | | | | | | | | | | | | |

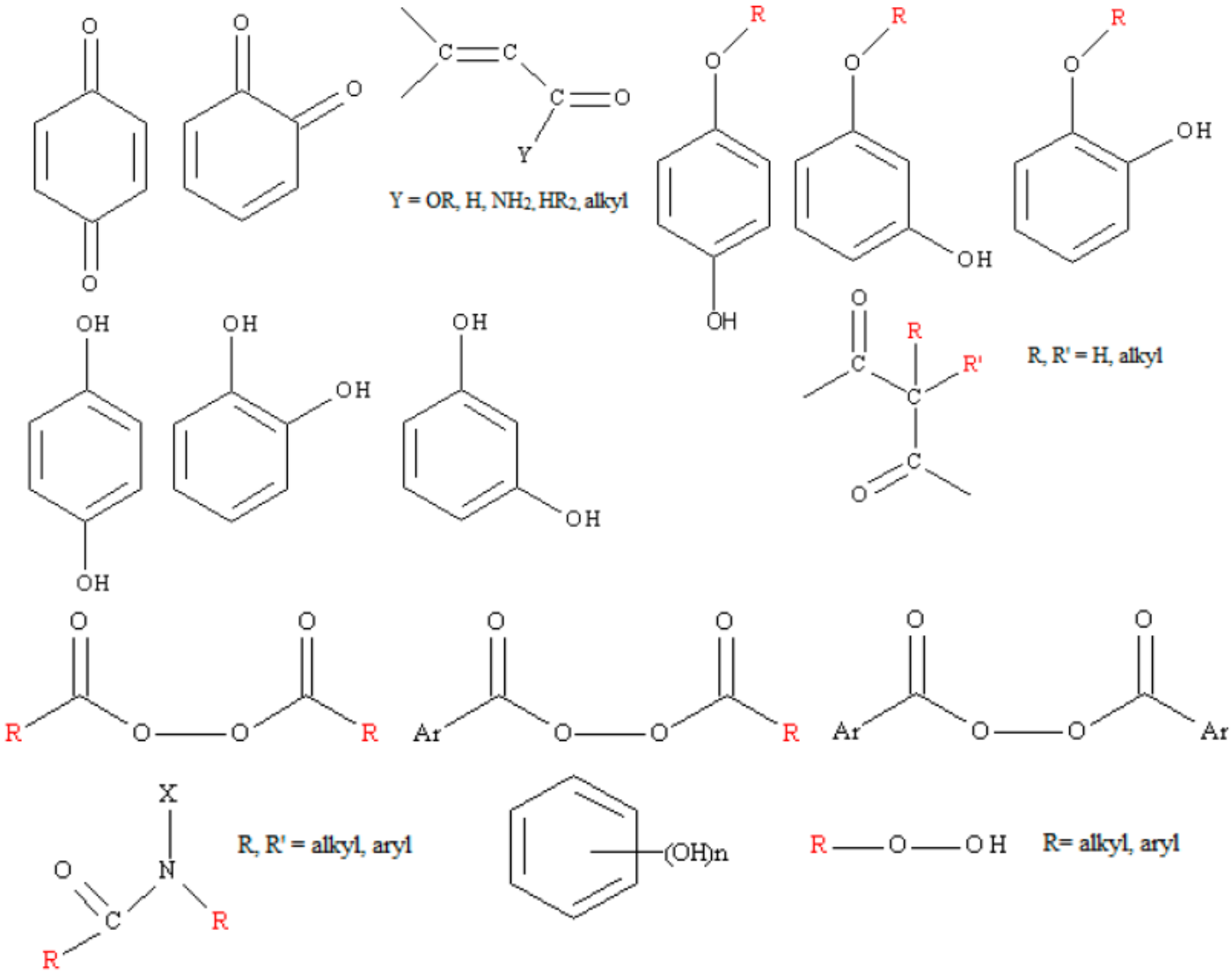
## APPENDIX C: Pharos Output for Perfluorohexanoic Acid (CAS #307-24-4)

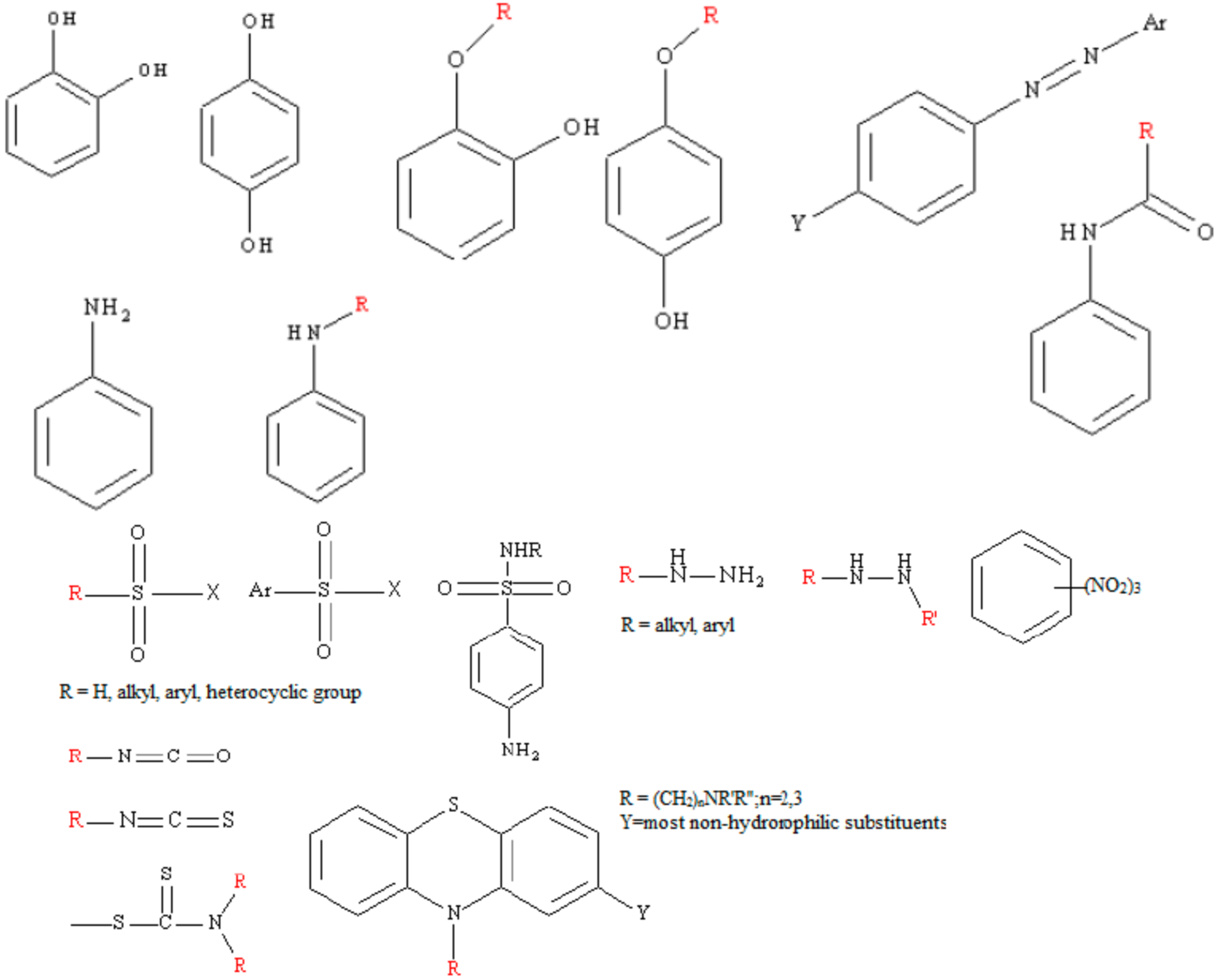


## APPENDIX D: Known Structural Alerts for Skin Sensitization

Below are known structural alerts for skin sensitizers (Payne and Walsh 1994). Perfluorohexanoic acid does not possess any known structural alerts for skin sensitization.

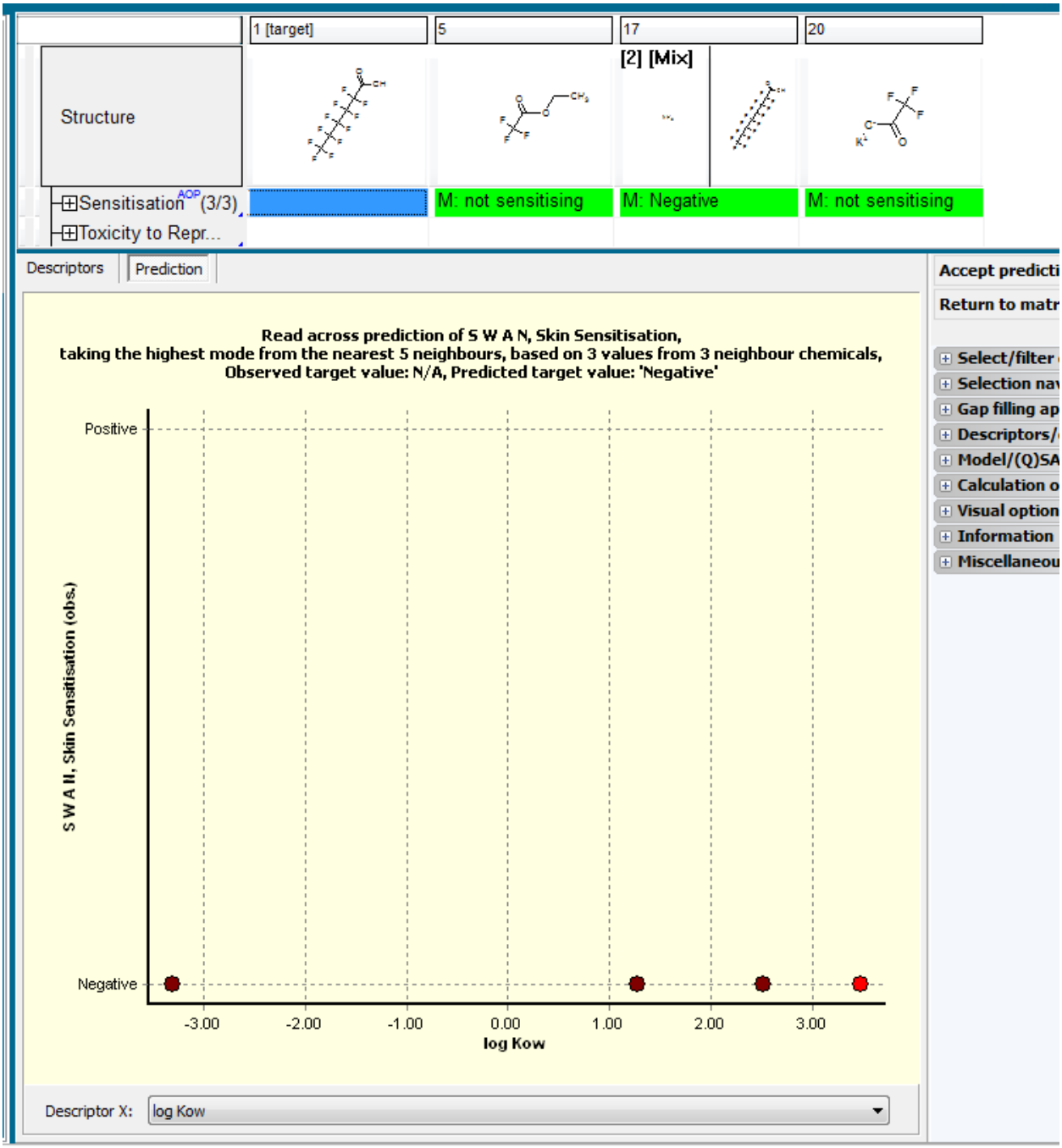




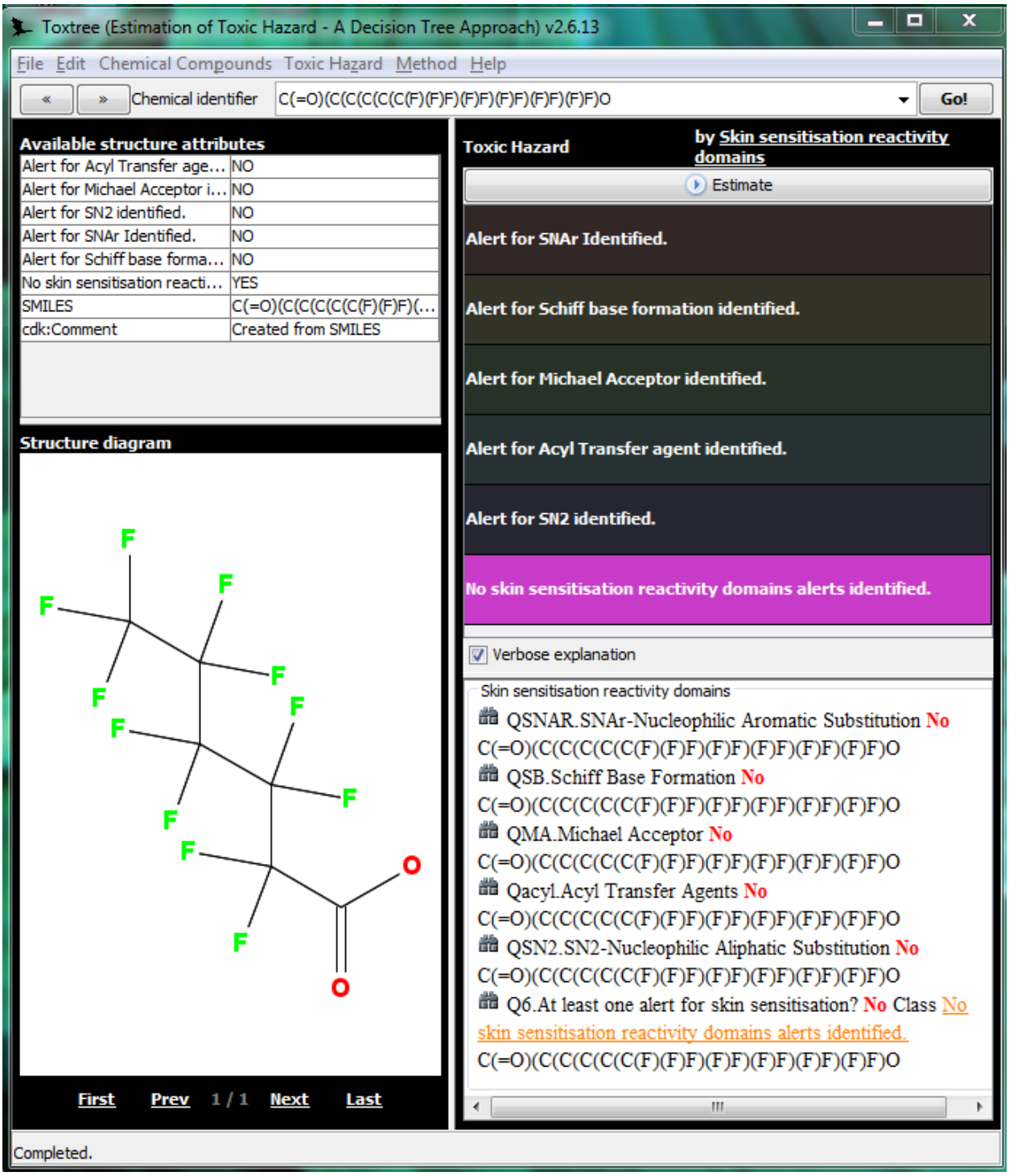


## APPENDIX E: OECD Toolbox Skin Sensitization Results for Perfluorohexanoic Acid (CAS #307-24-4)

Read across chemicals were identified by categorization using "OECD HPV Chemical Categories".



## APPENDIX F: Toxtree Skin Sensitization Results for Perfluorohexanoic Acid (CAS #307-24-4)

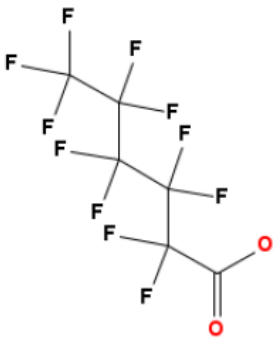


## APPENDIX G: VEGA Skin Sensitization Results for Perfluorohexanoic Acid (CAS #307-24-4)



### 1. Prediction Summary

**Prediction for compound Molecule 0**

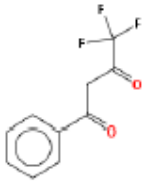


Prediction: Reliability:

**Prediction is Sensitizer, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues:**
**- only moderately similar compounds with known experimental value in the training set have been found**
**- accuracy of prediction for similar molecules found in the training set is not adequate**
**- a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 unknown fragments and 2 infrequent fragments found)**

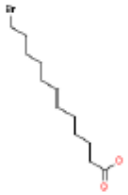
Compound: Molecule 0
Compound SMILES: O=C(O)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F
Experimental value: -
Predicted skin sensitization activity: Sensitizer
O(Active): 1
O(Inactive): 0
Reliability: the predicted compound is outside the Applicability Domain of the model
Remarks:
none

## 3.1 Applicability Domain:
### Similar Compounds, with Predicted and Experimental Values



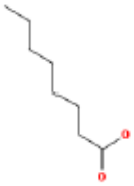
CAS: 326-06-7
Dataset id: 203 (Training set)
SMILES: O=C(c1ccccc1)CC(=O)C(F)(F)F
Similarity: 0.611

Experimental value: Sensitizer
Predicted value: NON-Sensitizer



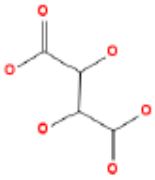
CAS: 73367-80-3
Dataset id: 26 (Test set)
SMILES: O=C(O)CCCCCCCCCCCBr
Similarity: 0.594

Experimental value: Sensitizer
Predicted value: Sensitizer



CAS: 124-07-2
Dataset id: 167 (Test set)
SMILES: O=C(O)CCCCCCC
Similarity: 0.594

Experimental value: NON-Sensitizer
Predicted value: Sensitizer

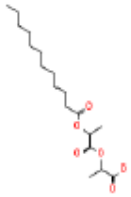


CAS: 87-69-4
Dataset id: 196 (Test set)
SMILES: O=C(O)C(O)C(O)C(=O)O
Similarity: 0.59

Experimental value: Sensitizer
Predicted value: Sensitizer

CAS: 10520-81-7
Dataset id: 38 (Test set)
SMILES: O=C(O)C(CCCCCCCCCCCC)Br
Similarity: 0.583

Experimental value: Sensitizer
Predicted value: Sensitizer



CAS: 13557-75-0
Dataset id: 171 (Training set)
SMILES: O=C(O)C(OC(=O)C(OC(=O)CCCCCCCCCCC)C)C
Similarity: 0.576

Experimental value: Sensitizer
Predicted value: Sensitizer

## 3.2 Applicability Domain:
### Measured Applicability Domain Scores

| | |
|---|---|
| ✖ | **Global AD Index**<br>AD index = 0.33<br>Explanation: the predicted compound is outside the Applicability Domain of the model. |
| ⚠ | **Similar molecules with known experimental value**<br>Similarity index = 0.602<br>Explanation: only moderately similar compounds with known experimental value in the training set have been found. |
| ✖ | **Accuracy of prediction for similar molecules**<br>Accuracy index = 0.486<br>Explanation: accuracy of prediction for similar molecules found in the training set is not adequate. |
| ✔ | **Concordance for similar molecules**<br>Concordance index = 1<br>Explanation: similar molecules found in the training set have experimental values that agree with the predicted value. |
| ✔ | **Model's descriptors range check**<br>Descriptors range check = True<br>Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set. |
| ✖ | **Atom Centered Fragments similarity check**<br>ACF index = 0.51<br>Explanation: a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 unknown fragments and 2 infrequent fragments found). |

Symbols explanation:

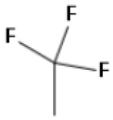
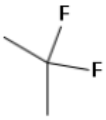
✔ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✖ The feature has a bad assessment, model is not reliable regarding this aspect.

## 4.1 Reasoning:
### Relevant Chemical Fragments and Moieties

(Molecule 0) Reasoning on rare and missing Atom Centered Fragments.
The following Atom Centered Fragments have been found in the molecule, but they are not found or rarely found in the model's training set:

| | |
|---|---|
|  | Fragment defined by the SMILES: FC(F)(F)C<br>The fragment has less than 3 occurrences in the model's training set |
|  | Fragment defined by the SMILES: FC<br>The fragment has less than 3 occurrences in the model's training set |
|  | Fragment defined by the SMILES: FC(F)(C)C<br>The fragment has never been found in the model's training set |

## APPENDIX H: EPISuite Modeling Results for Perfluorohexanoic Acid (CAS #307-24-4)

CAS Number: 307-24-4
SMILES : O=C(O)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F
CHEM : Hexanoic acid, undecafluoro-
MOL FOR: C6 H1 F11 O2
MOL WT : 314.06
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log Kow (octanol-water): ------
Boiling Point (deg C) : ------
Melting Point (deg C) : ------
Vapor Pressure (mm Hg) : ------
Water Solubility (mg/L): ------
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.68 estimate) = 3.48

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 165.08 (Adapted Stein & Brown method)
Melting Pt (deg C): 23.07 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 1.98 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) : 263 (Mean VP of Antoine & Grain methods)

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 27.12
log Kow used: 3.48 (estimated)
no-melting pt equation used

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 0.85273 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Neutral Organics-acid

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 3.29E-003 atm-m3/mole (3.33E+002 Pa-m3/mole)
Group Method: Incomplete
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 3.017E-002 atm-m3/mole (3.057E+003 Pa-m3/mole)
VP: 1.98 mm Hg (source: MPBPVP)
WS: 27.1 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:

Log Kow used: 3.48 (KowWin est)
Log Kaw used: -0.871 (HenryWin est)
Log Koa (KOAWIN v1.10 estimate): 4.351
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : -0.5854
Biowin2 (Non-Linear Model) : 0.0000
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 1.5083 (recalcitrant)
Biowin4 (Primary Survey Model) : 2.8920 (weeks )
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.4206
Biowin6 (MITI Non-Linear Model): 0.0000
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): -0.3141
Ready Biodegradability Prediction: NO

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 240 Pa (1.8 mm Hg)
Log Koa (Koawin est ): 4.351
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 1.25E-008
Octanol/air (Koa) model: 5.51E-009
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 4.51E-007
Mackay model : 1E-006
Octanol/air (Koa) model: 4.41E-007

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 0.5200 E-12 cm3/molecule-sec
Half-Life = 20.569 Days (12-hr day; 1.5E6 OH/cm3)
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
7.26E-007 (Junge-Pankow, Mackay avg)
4.41E-007 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 1306 L/kg (MCI method)
Log Koc: 3.116 (MCI method)
Koc : 120.4 L/kg (Kow method)
Log Koc: 2.081 (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = 0.7588 days (HL = 5.739 days)
Log BCF Arnot-Gobas method (upper trophic) = 2.448 (BCF = 280.3)
Log BAF Arnot-Gobas method (upper trophic) = 2.450 (BAF = 281.6)
log Kow used: 3.48 (estimated)

Volatilization from Water:
Henry LC: 0.00329 atm-m3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 2.124 hours
Half-Life from Model Lake : 171.8 hours (7.157 days)

Removal In Wastewater Treatment:
Total removal: 60.34 percent
Total biodegradation: 0.10 percent
Total sludge adsorption: 9.21 percent
Total to Air: 51.03 percent
(using 10000 hr Bio P,A,S)

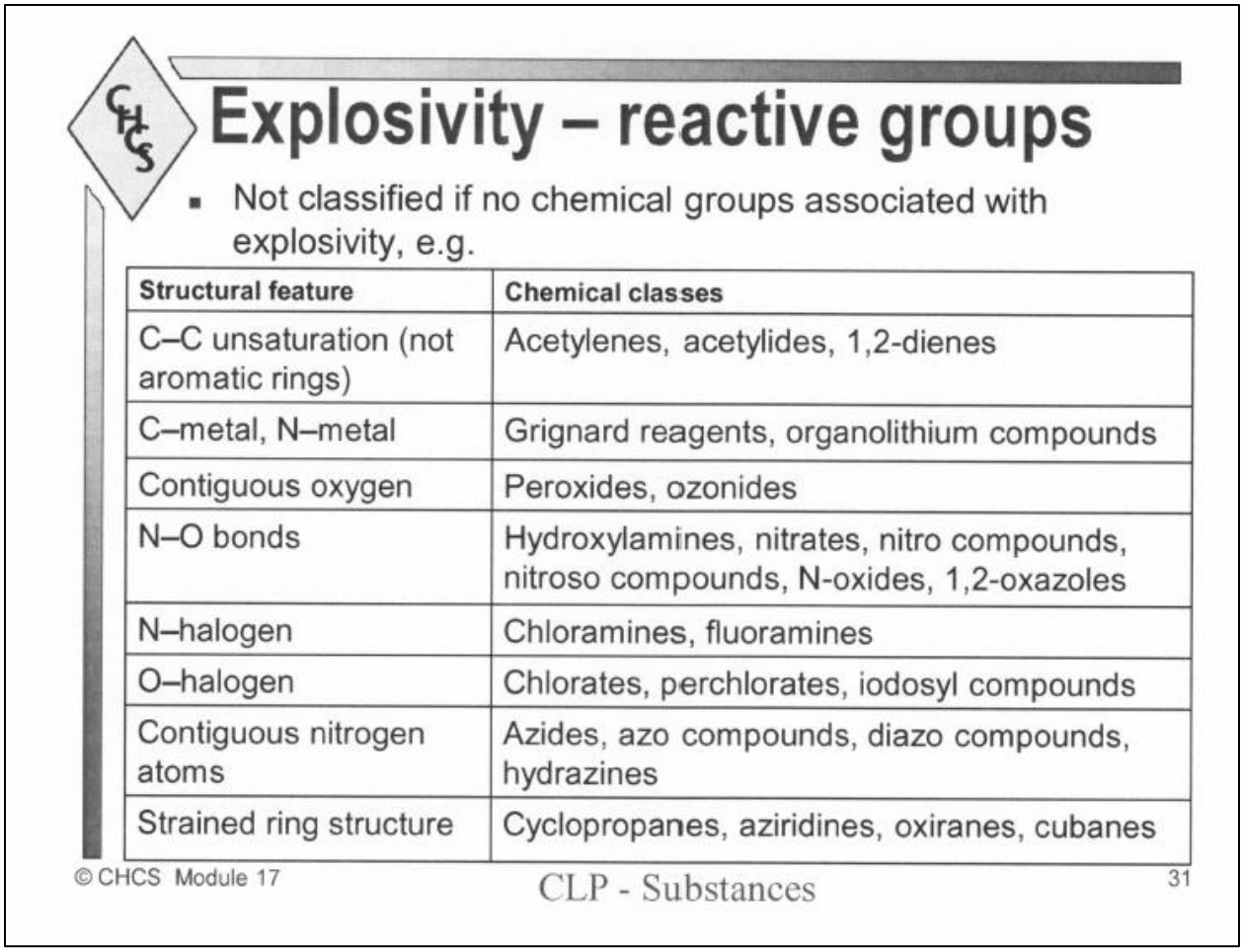
Level III Fugacity Model:

| | Mass Amount (percent) | Half-Life (hr) | Emissions (kg/hr) |
|---|---|---|---|
| Air | 8.77 | 494 | 1000 |
| Water | 11.7 | 4.32e+003 | 1000 |
| Soil | 78.2 | 8.64e+003 | 1000 |
| Sediment | 1.29 | 3.89e+004 | 0 |

Persistence Time: 834 hr

## APPENDIX I: Known Structural Alerts for Reactivity

### Explosivity – Abbreviated List



# Explosivity – reactive groups

- Not classified if no chemical groups associated with explosivity, e.g.

| Structural feature | Chemical classes |
|---|---|
| C–C unsaturation (not aromatic rings) | Acetylenes, acetylides, 1,2-dienes |
| C–metal, N–metal | Grignard reagents, organolithium compounds |
| Contiguous oxygen | Peroxides, ozonides |
| N–O bonds | Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles |
| N–halogen | Chloramines, fluoramines |
| O–halogen | Chlorates, perchlorates, iodosyl compounds |
| Contiguous nitrogen atoms | Azides, azo compounds, diazo compounds, hydrazines |
| Strained ring structure | Cyclopropanes, aziridines, oxiranes, cubanes |

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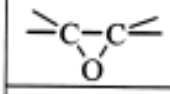
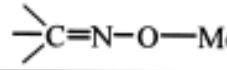
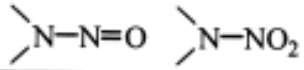
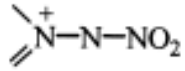
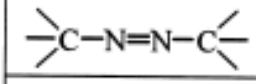
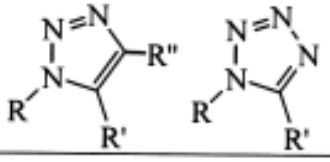
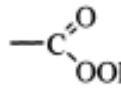
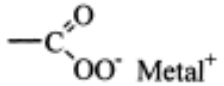
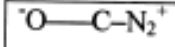
## Explosivity – Full List

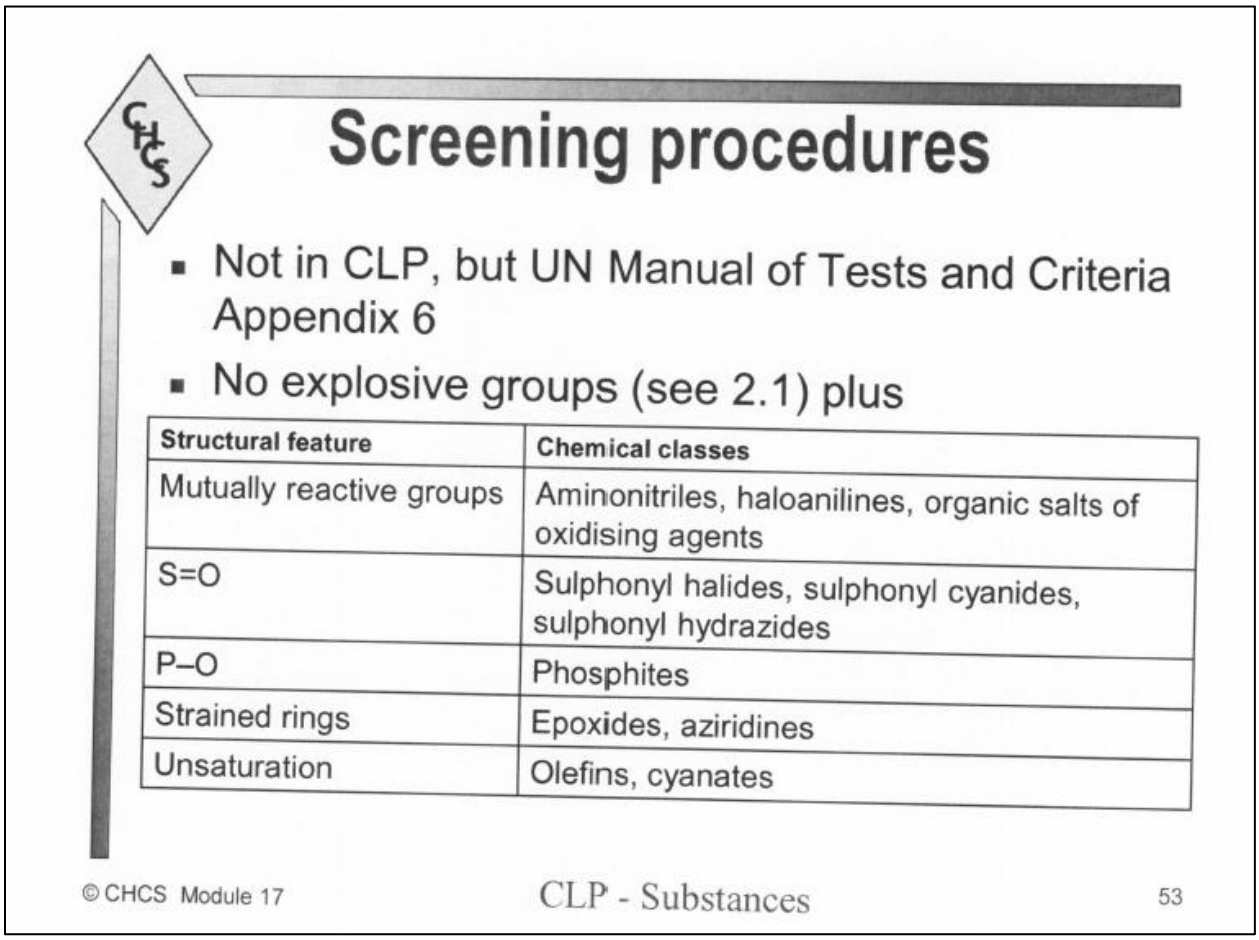
**Table R.7.1-28 Chemical groups associated with explosive properties**

| Chemical group | Chemical Class |
|---|---|
| -C≡C-<br>-C≡C-Metal<br>-C≡C-Halogen | Acetylenic Compounds<br>Metal Acetylides<br>Haloacetylene Derivatives |
|  | Diazo Compounds |
| -N=O -$NO_2$ | Nitroso and Nitro Compounds, |
| R-O-N=O<br>R-O-$NO_2$ | Acyl or Alkyl Nitrites and Nitrates |
|  | 1,2-Epoxides |
|  | Metal Fulminates or *aci*-Nitro Salts |
|  | N-Metal Derivatives (especially heavy metals) |
|  | N-Nitroso and N-Nitro Compounds |
|  | N-Azolium Nitroimidates |
|  | Azo Compounds |
| Ar-N=N-O-Ar | Arene Diazoates |
| $(ArN=N)_2O$, $(ArN=N)_2S$ | Bis-Arenediazo Oxides and Sulfides |
| RN=N-NR'R'' | Triazines |
|  | High-nitrogen Compounds: e.g. Triazoles, Tetrazoles |

| Chemical group | Chemical Class |
|---|---|
| [1] ROOR',<br>[2]  | Peroxy Compounds:<br>[1] Alkyl hydroperoxides (R'=H), Peroxides (R'=organic);<br>[2] Peroxo acids (R'=H), Peroxyesters (R'=organic) |
| [1] ROOMetal,<br>[2]  | Metal peroxides, Peroxoacids salts |
| $-N_3$ | Azides e.g. $PbN_6$, $CH_3N_3$ |
|  | Arenediazonium oxides i.e. inner diazonium salts in which the counter ion is an oxide |
| Ar-N=N-S-<br>Ar-N=N-S-Ar | Diazonium sulfides and derivatives, Arenediazo Aryl Sulfides |
| $XO_n$ | Halogen Oxide: e.g. percholrates, bromates, etc |
| $NX_3$ e.g. $NC1_3$, $RNC1_2$ | N-Halogen Compounds |

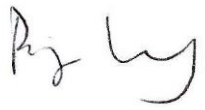
Adapted from Bretherick (Bretherick's Handbook of Reactive Chemical Hazards 6th Ed., 1999, Butterworths, London)

**Self-Reactive Substances**



**Licensed GreenScreen® Profilers**

**Perfluorohexanoic Acid GreenScreen® Evaluation Prepared by:**



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