Perfluoroalkyl sulfonates (PFSA) (C5-C7) and their direct precursors: Human health tier II assessment

29 June 2018

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
1-Hexanesulfonyl fluoride, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-	423-50-7
1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-, potassium salt	3871-99-6
1-Pentanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,5-undecafluoro-, potassium salt	3872-25-1
1-Heptanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-, potassium salt	60270-55-5
1-Heptanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-, ammonium salt	68259-07-4
1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-, ammonium salt	68259-08-5
1-Pentanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,5-undecafluoro-, ammonium salt	68259-09-6

Chemical Name in the Inventory	CAS Number
1-Heptanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-, compound with 2,2'-iminobis[ethanol] (1:1)	70225-15-9
1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-, compound with 2,2'-iminobis[ethanol] (1:1)	70225-16-0

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group are perfluoroalkyl sulfonic acids, perfluoroalkyl sulfonic fluoride and salts of the perfluoroalkyl sulfonate (PFSA) anion, all of which contain 5–7 perfluorinated carbons terminated with a sulfonate group, and which have the potential to hydrolyse and/or dissociate into a range of environmentally persistent perfluorosulfonate anions.

NICNAS has developed an action plan to assess and manage chemicals which may degrade to perfluorinated carboxylic acids, perfluoroalkyl sulfonates and similar chemicals, which can be found in Appendix G of the Handbook for Notifiers on the NICNAS website (NICNASa). Under this action plan, perfluorooctane sulfonate (PFOS) hazard information is used to estimate the hazard of PFAS degradation products, apart from perfluorobutane sulfonate (PFBS). Data for the critical effects of bioaccumulation and hepatotoxicity, developmental toxicity and carcinogenicity would need to be provided to demonstrate that a lower toxicity profile applies.

This assessment will evaluate:

a) the relative hazard and risk of the chemicals in this group compared with PFOS; and

b) whether there are sufficient data to amend some or all of the default assumptions in the action plan.

Assessing these chemicals as a group also provides relevant information for the risk assessment of more complex derivatives of PFSA that contain 5–7 perfluorinated carbons that can degrade to the relevant perfluorinated anions in the environment (indirect precursors). These more complex derivatives of PFSA will be assessed separately under IMAP.

The focus of this assessment will be the chemicals' bioaccumulation potential and systemic long-term effects. Data for acute and local effects have been included where available. For certain endpoints such as irritation, sensitisation and genotoxicity, PFOS is considered a suitable analogue. For systemic end points, PFOS is considered to represent the worst case for toxicity of the chemicals in this group.

Import, Manufacture and Use

Australian

Information collected by NICNAS indicates that the chemicals in this group are not manufactured in Australia.

Whilst approximately 7.4 tonnes and 13.6 tonnes of PFSA (as technical grade and in products) were reported to be imported into Australia in 2006 and 2007, respectively, most were chemicals based on PFBS, a four-carbon PFSA. Various PFSA surfactants (chain length unspecified) were reported to be imported in fire fighting foams. In 2007, approximately 60 tonnes of fire fighting foams containing 1–5 % of PFSA substance were held in stock at sites around Australia (NICNAS).

It is noted that some of the chemicals in this group could be present in the environment due to historic use, due to release from articles or as breakdown products resulting from the use of indirect precursor chemicals not covered by this assessment.

International

The following international uses for chemicals of this group have been reported by the Organisation for Economic Co-operation and Development (OECD, 2011) or identified through Galleria Chemica (Galleria Chemica):

- as fluorinated anionic surfactants;
- as intermediates; and
- in anti-reflective coatings in photolithography.

The chemicals could potentially be used as paint additives and in fire fighting foams (OECD, 2013).

According to an OECD survey published in 2011, potassium perfluorohexane sulfonate (CAS No. 3871-99-6) and perfluorohexane sulfonyl fluoride (CAS No. 423-50-7) were reportedly produced in the United States (US) in 2008. They are mainly used as raw materials or precursors to produce PFSA-based products. Only one product containing the chemicals was reported. The concentration of the chemical in the product was <10% and its total residual quantity in the product was reported as approximately 0.5 tonnes (OECD, 2011).

No evidence of the presence of these chemicals in consumer products was found in available North American databases (Household Products Database and Personal Care Council), indicating that the chemicals are not likely to be widely available for domestic or cosmetic uses.

All chemicals in this group are pre-registered under the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) legislation, but none have been registered under the REACH legislation at the time of assessment.

Restrictions

Australian

No known mandatory restrictions have been identified.

Measures taken to date to reduce the importation and use of PFSA compounds and their salts and precursors has largely been through NICNAS recommendations (published as alerts as part of NICNAS Factsheets) since 2002 and subsequent voluntary action by industry. NICNAS's first three alert Factsheets recommended that PFOS- and related PFSA-based chemicals be restricted to only essential uses for which no suitable or less hazardous alternatives were available (NICNAS).

International

In the United States of America (USA), all the chemicals in this group are subject to a Significant New Use Rule (SNUR). These SNURs allow the continuation of a few limited, highly technical uses of these chemicals for which no alternatives are available, and which are characterised by very low volume, low exposure, and low releases. Any other uses of these chemicals required prior notice to, and review by, the US Environmental Protection Agency (EPA) (US EPA, 2002; US EPA, 2007).

Whilst PFOS is restricted in several countries (NICNAS), the chemicals in this group are not covered by these restrictions.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available for the chemicals in this group.

International

No specific exposure standards are available for the chemicals in this group.

Health Hazard Information

The chemicals in this group have the potential to hydrolyse and/or dissociate into PFSA anions that contain 5–7 perfluorinated carbons.

Limited toxicological data are available for the majority of chemicals in this group. Hazard data for perfluorohexanesulfonate (PFHxS) can be used to estimate hazards for the members of this group that contain five and six perfluorinated carbons. In the absence of toxicological data, PFOS hazard information is used to estimate systemic hazards. Due to lack of available data for the chemicals in this assessment, the data for direct precursors of PFBS and PFOS have been used to estimate the direct irritation potential of the chemicals that is independent of toxicokinetics of distribution, metabolism and excretion of the chemical.

Toxicokinetics

Based on the available information, the chemicals in this group are expected to be rapidly absorbed after ingestion and, to a lesser extent, through inhalation. They are slowly eliminated, mainly in the urine. Elimination is substantially slower in humans than primates or rodents.

PFOS is well absorbed by the digestive tract and is mainly accumulated in the liver, followed by plasma, kidneys and lungs. It is mainly eliminated in urine, followed by faeces (NICNASb). PFHxS was shown to be mainly eliminated via urine in rats, with urinary excretion in males being dose-dependent. Mean daily faecal excretion was <0.5% of the administered dose at all time points (Sundstrom et al., 2012). PFHxS was shown to be distributed to the blood, liver and kidneys (Butenhoff et al., 2009; Sundstrom et al., 2012).

Once absorbed, PFOS is eliminated from the human body very slowly. The mean elimination half-life of PFOS in humans was estimated to be 5.4 years (3.9–6.9 years) based on the serum PFOS levels determined in retirees who had been exposed to PFOS during their working life (NICNASb). Much shorter serum half-lives were reported for PFOS in male and female monkeys (131 and 110 days, respectively) and rats (43 and 60 days, respectively).

Similarly for PFHxS, a long serum elimination half-life of 7–8 years was estimated in humans (estimate for the two females in the was 4,458 and 4,866 days) compared with shorter half-lives in male and female monkeys (141 and 87 days, respectively) and rats (30 and 1.5 days, respectively) (Sundstrom et al., 2012). In comparison, PFBS is eliminated substantially faster in humans than perfluoroalkyls with longer carbon chain lengths (e.g. PFHxS and PFOS) with serum half-lives of 28, 4 and 0.2 days in humans, monkeys and rats, respectively (OECD, 2013).

A comparative pharmacokinetic pro?le study of PFHxS across the three species (rat, mouse and monkey) showed that rats and mice (serum half-life of one month) are more effective at eliminating PFHxS than monkeys (half-life of four months). The authors concluded that this could be due to differences in expression of organic anion transporters between species. The study also demonstrated sex-speci?c elimination differences in the rat (females demonstrating faster elimination rates as also seen in the above study) but not in mice or monkeys (Sundstrom et al., 2012).

Biomonitoring studies have shown that exposure in the general population is widespread and that PFHxS and PFOS are the PFSAs commonly present in human serum (Calafat et al., 2006; Fromme et al., 2007; Kato et al., 2011). In pooled human sera from the Australian population, PFOS was the highest PFSA detected in concentrations ranging from 5.3–19.2 ng/mL (2008/2009) to 4.4–17.4 ng/mL (2010/2011). PFHxS levels ranged from 1.2–5.7 ng/mL (08/09) and 1.4–5.4 ng/mL (10/11). Median levels of PFHxS have not significantly changed from 2002 (Toms et al., 2014).

World wide, PFHxS is found in umbilical cord blood, human milk and child serum (ATSDR, 2009).

Perfluoroalkyl compounds have been found in human breast milk, but there are no studies that looked at whether a baby's health was affected by drinking this milk. Levels of perfluoroalkyls in breast milk are much lower than in the mother’s blood, indicating that these substances are not concentrated during milk production (ATSDR, 2009).

A study of Chinese women (n = 19) detected PFHxS (100 ng/L) and PFOS (45–360 ng/L) in breast milk (So et al., 2006). These levels of PFOS and PFHxS were far less than those reported in human blood or serum samples (PFOS: 5400–26000 ng/L and PFHxS: 370 ng/L) in a separate study in the Chinese population (Yeung et al., 2006).

Little variation was found in PFOS and PFHxS in composite milk samples collected each year between 1996 and 2003–2004 from four different regions in Sweden, indicating that the levels have been constant during the span of this study. The chemicals, PFOS (0.201 ng/mL) and PFHxS (0.085 ng/mL) levels in human milk were about 1 % of the corresponding level in serum. Mean maternal serum concentrations were 20.7 ng/mL (8.2–48 ng/mL) for PFOS and 4.7 ng/mL (1.8–11.8 ng/mL) for PFHxS (Karrman et al., 2007). While no clear temporal trend was established by Karrman et al (2007), a recent comprehensive study by Sundstrom and co-workers (2011) demonstrated that the PFOS and PFHxS levels in human milk samples showed increasing trends from 1972 to 2000, with a plateau in the 1990s and a decreasing trend during 2001–2008 (Sundstrom et al (2011).

Sundstrom et al (2011). A temporal trend study (1972–2008) of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in pooled human milk samples from Stockholm, Sweden. Environ Int 37(1):178-183.

The chemical, PFHxS was detected in 88 % of samples of maternal sera (n = 20) and umbilical cord sera (n = 20) taken from the general population of Seoul, South Korea. Concentrations between paired maternal (0.55 ng/mL) and cord (0.34 ng/mL) sera were significantly correlated. Within the same study, PFHpS and PFOS were also detected in maternal (0.09 and 2.93 ng/mL, respectively) and umbilical cord (0.06 and 1.26 ng/mL, respectively) sera (Kim et al., 2011).

Acute Toxicity

Oral

No data are available for the chemicals in this group.

Based on the data for PFOS (oral median lethal dose (LD50) of 252 mg/kg bw for rats) (NICNASb), the chemicals in this group are expected to have moderate acute toxicity following oral exposure. Classification is considered warranted (see **Recommendation** section). If data become available for the individual group members, they should be used to determine individual classifications.

Dermal

No data are available for the chemicals in this group or PFOS.

Inhalation

No data are available for the chemicals in this group.

Based on the data for PFOS (median lethal concentration (LC50) of 5.2 mg/L for rats) (NICNASb), the chemicals in this group are expected to have low acute toxicity following inhalation exposure. If data become available for the individual group members, they should be used to determine individual classifications.

Corrosion / Irritation

Skin Irritation

No data are available for the chemicals in this group.

Based on data for the potassium salt of PFOS and PFBS, which are non-irritating (NICNASb; NICNASd), the majority of chemicals in this group could be, at most, slight skin irritants. However, skin irritant/corrosive effects cannot be ruled out for perfluorohexane sulfonyl fluoride (which is reactive and could possibly hydrolyse to PFHxS). If data become available for the individual group members, they should be used to determine individual classifications.

Eye Irritation

No data are available for the chemicals in this group.

Whilst the potassium salt of PFOS was a slight irritant in rabbits, with effects that were not sufficient for classification (NICNASb), potassium PFBS is classified as hazardous with the risk phrase 'Irritating to eyes' (Xn; R36) in the HSIS (Safe Work Australia).

Eye irritant or corrosive effects cannot be ruled out for perfluorohexanesulphonyl fluoride (which could possibly hydrolyse to PFHxS). In the absence of additional information, based on potassium PFBS, a classification is considered warranted for all the chemicals in the group. If data become available for the individual group members, they should be used to determine individual classifications.

Sensitisation

Skin Sensitisation

No data are available for the chemicals in this group or PFOS. Direct precusors of PFBS are considered non-sensitisers (NICNASd).

Repeated Dose Toxicity

Oral

Based on the available data, toxicity for PFHxS, following repeated exposure, was dose dependent. Similar to PFOS, the liver was considered the target organ. Overall, the data support classification for all the chemicals in the group (see **Recommendation** section). If data become available for the individual group members, they should be used to determine individual classifications.

Sprague Dawley (SD) rats (15 rats/sex/group) were administered potassium PFHxS at 0, 0.3, 1, 3 or 10 mg/kg bw/day via oral gavage in a combined repeated dose study with a reproduction/developmental toxicity screening test (modified OECD Test Guideline (TG) 422). The male rats were treated for a total of 42 days; females were treated prior to mating through to postnatal day (PND) 22. The F1 generation pups were exposed in utero and potentially during lactation via milk, and were euthanised on PND 22. The effects in parental males included:

1) reduced serum cholesterol (all doses);

2) decreased prothrombin time (doses of 0.3, 3 and 10 mg/kg bw/day);

3) increased liver-to-body and liver-to-brain weight ratio, centrilobular hypertrophy, hyperplasia of thyroid follicular cells, decreased haematocrit (at 3 and 10 mg/kg bw/day); and

4) decreased triglycerides and increased albumin, urea nitrogen, alkaline phosphatase, Ca^{2+} and albumin/globulin ratio (at 10 mg/kg bw/day), but there were no significant gross or microscopic alterations in the kidneys (Butenhoff et al., 2009).

There were no treatment-related changes in dams or offspring. No significant gross or microscopic alterations were reported for the spleen, thymus, or mesenteric lymph nodes. Although no comprehensive neurological testing was conducted, tests for motor activity (autonomic functions; reactivity and sensitivity; excitability; and gait and sensorimotor coordination etc.) provided no indication of adverse neurological effects. No significant effects were noted in parental females (Butenhoff et al., 2009).

The chemicals, PFHxS and PFOS, administered (6 and 3 mg/kg bw/day, respectively, daily for 4–6 weeks) to male mice (APOE*3-Leiden.CETP) caused significant reductions in triglycerides, total cholesterol, non-high density lipoprotein, high density lipoprotein, plasma ApoA1, low density lipoprotein, apoB production, free fatty acids and glycerol, and significantly increased

liver weights, lipase activity and clearance of triolein. These effects were dependent on the alkyl chain length as PFBS had no significant effects in this study (Bijland et al., 2011).

PFOS had adverse health effects following repeated oral exposure. In general, oral exposure to PFOS and its salts resulted in hepatotoxicity and mortality; the dose-response curve for mortality was found to be very steep for rats and primates (NICNASb).

In comparison, direct precursors of PFBS are not considered to cause serious systemic effects from repeated oral exposure (NICNASd).

Dermal

No data are available for the chemicals in this group.

Inhalation

No data are available for the chemicals in this group.

Genotoxicity

No data are available for the chemicals in this group. Based on results from negative in vitro and in vivo genotoxicity and mutagenicity studies for direct precursors of PFOS and PFBS (NICNASb; NICNASd), the chemicals in this group are not expected to be genotoxic.

Carcinogenicity

No data are available for the chemicals in this group.

PFOS is classified as hazardous—Category 3 carcinogenic substance—with the risk phrase ‘Limited evidence of carcinogenic effect’ (Xn; R40 in the HSIS, Safe Work Australia). The chemicals induced benign tumours of the liver and the thyroid gland (Sibinski, 1987; Biegel et al., 2001). Tumours of mammary glands were also observed in these studies; however, it has been argued that since the morphologic appearance, overall incidence, and distribution of the tumours observed in treated groups were similar to historical control data for mammary-gland tumours in untreated animals (Giknis and Clifford, 2004), the incidence of mammary gland tumours is not a result of chronic dietary administration of APFO (Hardisty et al., 2010).

Histopathological changes in the liver and thyroid were observed in a repeated dose oral toxicity study with PFHxS.

In the absence of information, the chemicals in this group are recommended for classification (see **Recommendation** section). If data become available for the individual group members, they should be used to determine individual classifications.

Reproductive and Developmental Toxicity

In the only available animal study, PFHxS did not have an adverse effect on reproductive or developmental parameters in rats.

Some effects were seen in epidemiological studies in humans, but the significance of the observations is not clear. In these studies, levels of PFOS were typically an order of magnitude higher than those seen in human populations for PFHxS. Based on the weight of evidence from the available information, the chemicals in this group with <6 perfluorinated carbon chains are not considered to be reproductive/developmental toxins at low dose levels. However, in the absence of information for the chemicals with >6 perfluorinated carbons (CAS Nos. 60270-55-5, 68259-09-6 and 70225-15-9), developmental effects observed with PFOS cannot be ruled out and classification is warranted for these chemicals. If data become available for the individual group members, they should be used to determine individual classifications.

PFHxS was not a reproductive or developmental toxicant in rats (SD), exposed via gavage to up to 10 mg/kg bw/day as potassium PFHxS, for a period that included premating, gestation, and lactation (Butenhoff et al., 2009, see **Repeated dose toxicity** section). The offspring were potentially exposed via placental transfer in utero and through post-natal exposure via milk. There were no treatment-related reproductive (mating, fertility parameters in both males and females, birth outcome, gestation index, pregnancy rates and necroscopic examinations) or developmental effects in either the parents or offspring. The reproductive no observed adverse effect level (NOAEL) was 10 mg/kg bw/day, the highest dose tested.

Following a single treatment of potassium PFHxS (at 0, 0.61, 6.1 or 9.2 mg/kg bw) on PND 10 via gavage to NMRI mice, animals in the highest dose group exhibited changes in both spontaneous and nicotine-induced behaviour as adults (Viberg et al., 2013). This was similar to observations in similar experiments using PFOS, but the significance of these findings is not clear.

A recent study in 588 men from Greenland, Poland and Ukraine evaluated the possible association between PFC exposure and male semen quality. PFOS and PFHxS could be detected in >97 % of the samples. As for PFOS, a 35 % lower proportion of normal sperm was found at the highest tertile for PFHxS compared with the first, and a non-significant decrease in the proportion of normal sperm was also observed at the second tertile. However, PFHxS-induced effects could have been driven by effects of PFOS, which was measured at an ~20-fold higher concentration in the studied men (Toft et al., 2012).

A British study found that girls born to mothers with maternal serum concentrations of PFHxS in the upper tertile (>2.0 ng/mL) weighed significantly less at birth compared with girls born to mothers with serum concentrations in the lower tertile (<1.3 ng/mL). Birth length was also significantly lower. The models were adjusted for maternal smoking during pregnancy, maternal BMI, previous live births and gestational age. The babies weighed heavier at 20 months, but this was not statistically significant. Levels of PFOS were typically an order of magnitude higher than PFHxS. The magnitude of the differences in babies' birth weight, at 20 months and length by tertile was similar for PFOS (Maisonet et al., 2012). The study drew positive associations between maternal serum concentrations and markers of foetal and postnatal growth in girls.

Two other smaller Canadian studies did not find any significant associations between maternal PFHxS levels and foetal weight and length of gestation (Monroy et al., 2008; Hamm et al., 2010).

Taylor et al., (2014) observed a monotonic association between PFHxS exposure and menopause age using the National Health and Nutrition Examination Survey (NHANES) data, with women having higher concentrations after natural menopause. A positive association was also observed with the rate of hysterectomies. Levels of PFOS were typically an order of magnitude higher than PFHxS. Other studies have shown that association between perfluoroalkyl concentration and the menstrual cycle, whether delayed menarche or early onset menopause (including hysterectomies) are likely due to the underlying pharmacokinetics (clearance from the body) of perfluoroalkyls (Wu et al., 2015). Using PBPK models, Verner et al (2015) have shown that associations reported in epidemiological studies between perfluoroalkyl concentrations and birth weights are likely attributable to confounding by the maternal glomerular filtration rate.

PFOS did not have an adverse effect on the reproductive parameters in rats, but was toxic to development. Based on reduced birth weights, the NOAEL and the lowest observed adverse effect level (LOAEL) for the second generation of rodents (F2) were determined to be 0.1 mg/kg bw/day and 0.4 mg/kg bw/day, respectively (NICNASb). Based on animal data, PFBS was found not to be a reproductive or a developmental toxin (NICNASd).

Risk Characterisation

Critical Health Effects

The chemicals in this group are slowly eliminated from the body following absorption. The critical health effects for risk characterisation include systemic long-term effects (hepatoxicity and developmental toxicity and benign tumours of the liver and the thyroid) from oral exposure. The chemicals can also cause eye irritation. The chemicals in this group with ≤6 perfluorinated carbon chains are not considered to be reproductive/developmental toxins at low dose levels. However, in the absence of information for the chemicals with >6 perfluorinated carbons (CAS Nos. 60270-55-5, 68259-09-6 and 70225-15-9), developmental effects similar to those observed for PFOS cannot be ruled out.

Public Risk Characterisation

Use in consumer products

Based on the available use information, the chemicals are not likely to be available for domestic or cosmetic uses. Hence, the public risk from direct use of these chemicals is not considered to be unreasonable.

Secondary exposure via the environment

Public exposure to the chemicals in this group could occur through secondary exposure via the environment. The chemicals in this group are not likely to be used in significant quantities in Australia. It is noted that the chemicals in this group could be present in the environment due to historic use, or due to release from articles or the use of chemicals not covered by this assessment. Median levels of PFHxS in Australian blood sera have not significantly changed from 2002 (Toms et al., 2014). In addition, PFHxS was not detected in a survey of 65 foods and beverages packaged in glass, paper, plastic or cans conducted by Food Standards Australia New Zealand (FSANZ, 2010). Currently, it is recommended that the chemicals in this group be restricted to only essential uses for which no suitable or less hazardous alternatives are available. Further risk management will be determined as part of the IMAP Tier II Environment assessment report on these chemicals.

Occupational Risk Characterisation

Based on the available use information, the chemicals in this group are not likely to be used in significant quantities in Australia. Therefore, the chemicals are not considered to pose an unreasonable risk to the health of workers.

The data available support amendment to the hazard classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section).

NICNAS Recommendation

Currently, it is recommended that the chemicals in this group be restricted to only essential uses for which no suitable or less hazardous alternatives are available. Further risk management will be determined as part of the IMAP Tier II Environment assessment report for these chemicals.

It is recommended that this assessment be included in Appendix G **(see NICNAS Handbook for Notifiers)** as an additional source of toxicity data for chemicals that degrade to short-chain PFASs containing 5,6, and 7 perfluorinated carbons.

Any changes to the assessment outcomes under the action plan for chemicals that degrade to C5-C7 PFSA, will be considered as part of the IMAP assessment on the indirect precursors of these chemicals.

Regulatory Control

Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Note 1: The developmental toxicity classification applies to only the chemicals with carbon chain lengths greater than >6 (CAS Nos. 60270-55-5, 68259-07-4 and 70225-15-9).

Note 2: If data become available for the individual group members, they should be used to determine individual classifications.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)	Toxic if swallowed - Cat. 3 (H301)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Repeat Dose Toxicity	Toxic: Danger of serious damage to health by prolonged exposure if swallowed (T; R48/25)	Causes damage to organs through prolonged or repeated exposure if swallowed - Cat. 1 (H372)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)	Suspected of causing cancer - Cat. 2 (H351)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May cause harm to the unborn child (T; R61) May cause harm to breastfed babies (Xn; R64)	May damage the unborn child - Cat. 1B (H360D) May cause harm to breast-fed children (H362)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

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Last Update 29 June 2018

Chemical Identities

Chemical Name in the Inventory and Synonyms	**1-Hexanesulfonyl fluoride, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-** 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-1-hexanesulfonyl fluoride perfluorohexanesulfonyl fluoride
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	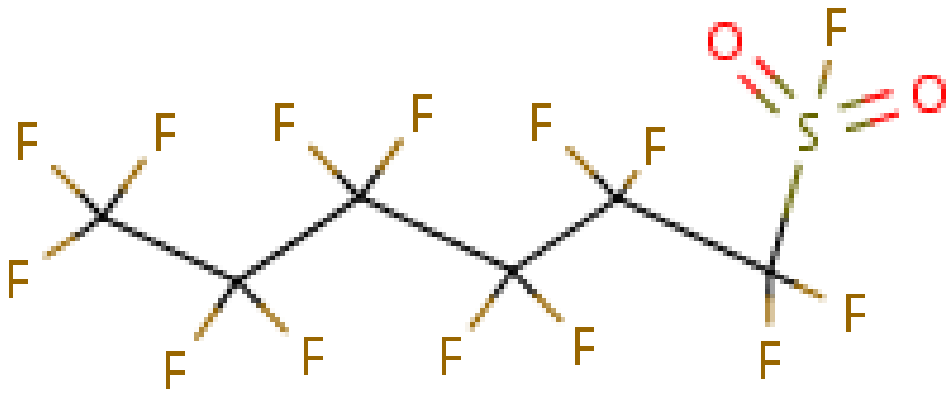
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Molecular Weight	402.1

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	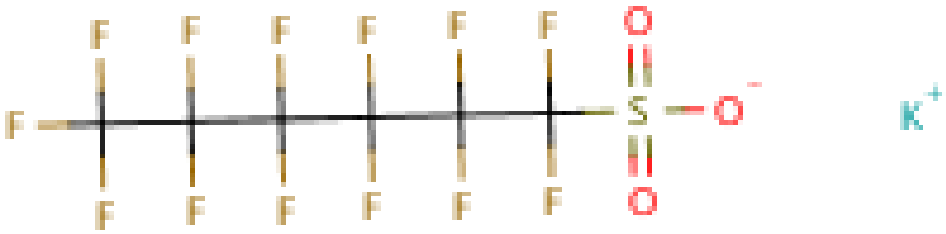
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Molecular Weight	438.2

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	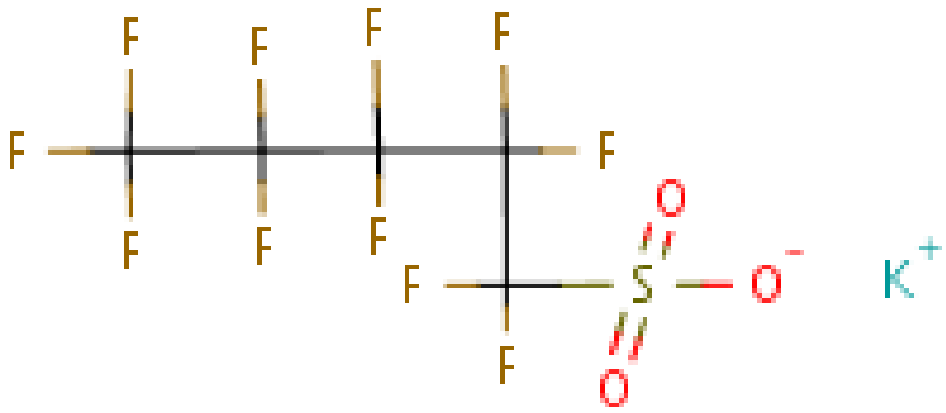
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Molecular Weight	388.2

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	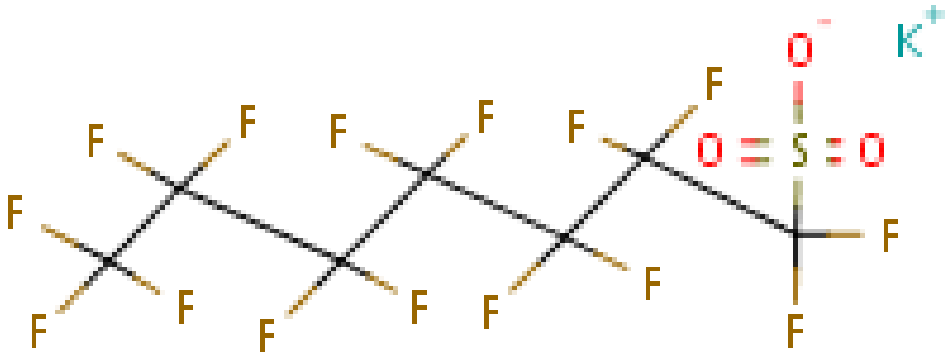
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	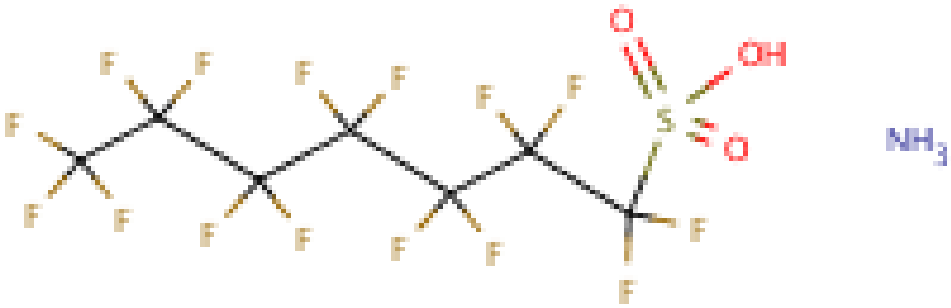
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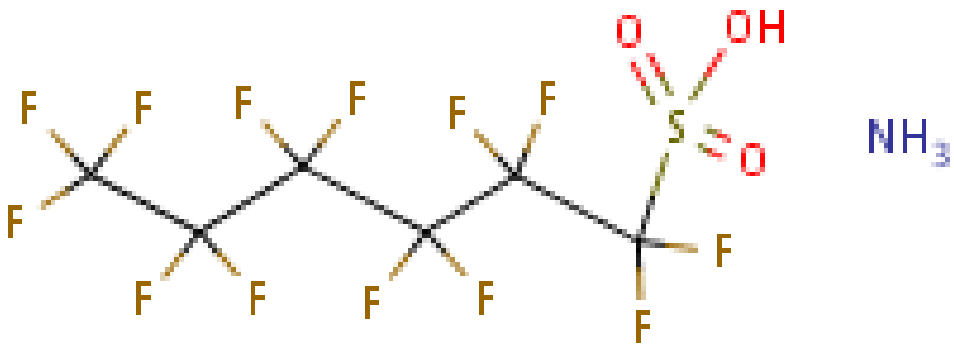

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	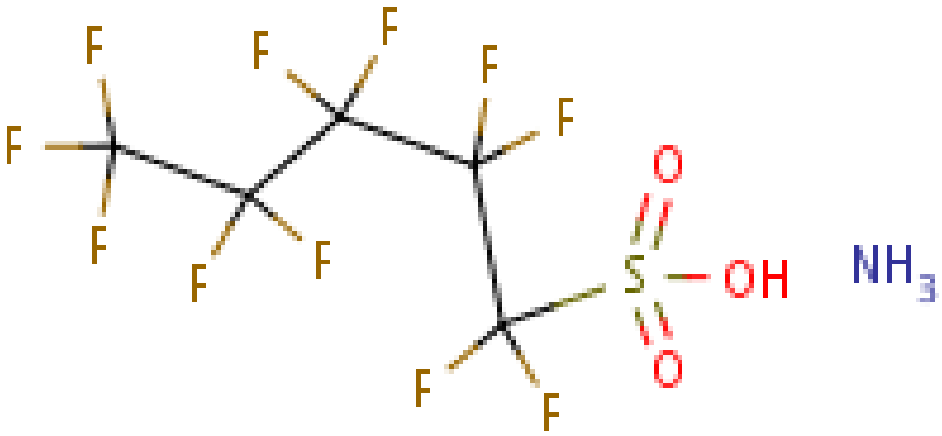
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Molecular Weight	367.1

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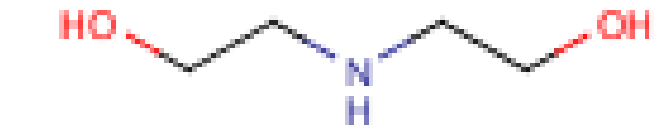
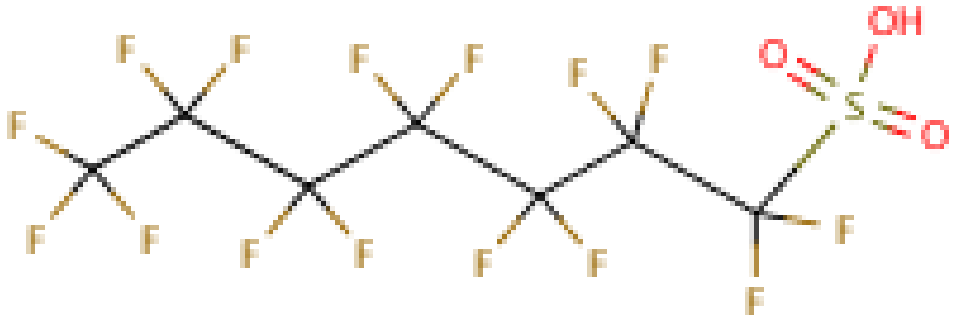
CAS Number	70225-15-9
Structural Formula	

	 
Molecular Formula	C7HF15O3S.C4H11NO2
Molecular Weight	555.3

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	 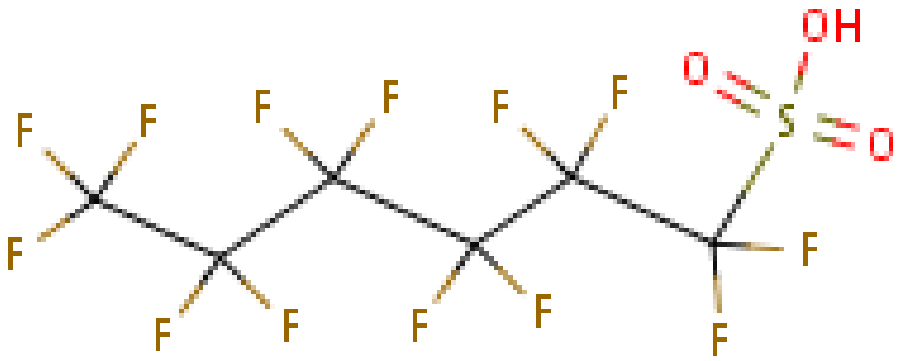
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Molecular Weight	505.2

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