Perfluorinated derivatives of phosphonic and phosphinic acids: Human health tier II assessment

05 February 2016

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Phosphonic acid, perfluoro-C6-12-alkyl derivatives	68412-68-0
Phosphinic acid, bis(perfluoro-C6-12-alkyl) derivatives	68412-69-1

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

Perfluoroalkyl phosphonic acids (PFPAs) and perfluoroalkyl phosphinic acids (PFPIAs) are chemicals with either one or two chains of 6 to 12 perfluorinated carbon atoms (C6-C12) attached through a carbon–phosphorous (C-P) bond to either a phosphonate or phosphinate functional group, respectively. These chemicals can be considered analogous to perfluoroalkyl sufonates (PFAS). However, the PFPAs and PFPIAs differ in that they contain two acidic hydrogens. Other than the potential transformation of PFPIAs to PFPAs, there are no known precursors to these two groups of chemicals (Lee et al., 2012). Both PFPAs and PFPIAs are high production volume commercial surfactants manufactured and offered for a range of consumer and industrial uses (Deon & Mabury, 2010; Buck et al., 2011; Danish EPA, 2015).

The chemicals belong to a larger group of industrial perfluorochemicals (PFCs). This group includes perfluoroalkylsulfonic acids and perfluoroalkyl carboxylic acids with six or more perfluorinated carbons in the chain which are known to be of high human health and environmental concern. The most concerning members of this group are perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA), and further information on these chemicals found in the IMAP Human Health Assessments (NICNAS, 2015a,b). The chemical PFOS is listed as a Persistent Organic Pollutant (POP) under Annex B of the Stockholm Convention on Persistent Organic Pollutants (the Stockholm Convention) and a proposal has been submitted to list PFOA, its salts and PFOA-related compounds in Annexes A, B and/or C. While it is currently unclear what influence the phosphonic or phosphinic acid moieties in the PFPAs and PFPIAs, respectively, have on their human health or environmental hazard characteristics, both PFPA and PFPIAs have been identified as persistent, bioaccumulative and toxic (PBT) chemical candidates due to their structural similarities to PFOS, their high-predicted bioconcentration factors and their long-range atmospheric transport (Howard & Meylan, 2007).

This assessment evaluates the available exposure and hazard data for PFPA and PFPIAs and considers whether it is currently possible to characterise the human health risks for these substances.

Import, Manufacture and Use

Australian

No specific Australian uses were identified. Manufacture of these chemicals in Australia is not expected.

However, due to high volume production as well as commercial use of these chemicals identified internationally, these chemicals are likely to be present in Australia.

International

Blends of C6-C12 PFPAs and PFPIAs, with CAS numbers 68412-68-0 and 68412-69-1, respectively, have been reported to have annual production volumes in the range of tonnes to hundreds of tonnes in 1998 and 2002 (Howard & Muir, 2010).

The PFPAs and PFPIAs are commercial fluorinated surfactants used as levelling and wetting agents in a range of consumer and industrial uses including carpet and upholstery cleaning products (Lee et al., 2012; Buck et al., 2011). A commercial wetting agent with the trade name Masurf-780 contained C6, C8, C10 and C12 substances (Deon & Mabury, 2010; Danish EPA, 2015). These chemicals may also have a use in polymer electrolyte membrane fuel cells for electronic devices (Idupulapati et al., 2011).

It is not clear to what extent the use of these chemicals has decreased over the time since concerns about the related perfluorocarboxylic acids and perfluoroalkyl sulfonates were identified.

The chemicals have reported non-industrial use as de-foaming agents in pesticides (Lee et al., 2012).

Restrictions

Australian

No known restrictions have been identified.

International

On 22 October 2013, the United States Environmental Protection Agency (US EPA) published a significant new use rule (SNUR) for perfluoroalkyl sulfonates (PFAS) and long-chain perfluoroalkyl carboxylates (LCPFACs) for use as part of stain resistant carpets or for treating carpet. However, the final SNUR contains an exception for these two substances (CAS Nos. 68412-68-0 and 68412-69-1) used as surfactants in carpet cleaning products (US EPA, 2013).

In August 2006, the US EPA cancelled the tolerance exemption for certain PFPAs, thereby no longer permitting their use as inert ingredients in pesticide products applied to food crops (US EPA, 2006).

These chemicals were identified as substances of concern as a result of Environment Canada’s New Substances notification process and through the Action Plan for the Assessment and Management of Perfluorinated Carboxylic Acids and their Precursors (Government of Canada, 2012).

Existing Worker Health and Safety Controls

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Only limited information is currently available on the toxicity of these chemicals.

Toxicokinetics

The biological fate of these chemicals in rats suggests that, if exposure occurs, these chemicals may be persistent in the body.

In a toxicokinetic study, the absorption and elimination of PFPAs were determined by administering Masurf-780 (a commercial product containing a mixture of the PFPA and PFPIA with different fluorinated carbon chain lengths) to rats and determining the levels of PFPA and PFPIA in blood, urine and faeces at different time points (D'eon & Mabury, 2010).

To determine oral absorption, adult male Sprague Dawley (SD) rats (4) received 210 mg/kg body weight (bw) of Masurf-780 and for elimination kinetics and routes of excretion, adult male and female SD rats received 250 µg/kg bw of Masurf-780. The chemicals were completey absorbed from the gastrointestinal tract, although the absorption was slow, with the first peak appearing in blood within two days and another peak nine days after administration of the substance.

The chemical PFPA was excreted in urine and faeces, whereas PFPIA was excreted only in faeces. Renal elimination of the PFPA was slow and varied depending on the carbon chain length of the congener and the sex of the animals. Both sexes excreted the majority of the C6 PFPA in the urine over the 48 hours of urine collection, whereas the female rats excreted 96 % of C8 PFPA in 48 hours, and the males excreted only 11 %. Female rats excreted 10 %, and males less than 1 %, of the administered C10 PFPA in 48 hours.

Acute Toxicity

Oral

No data are available.

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

No data are available. However, as these chemicals are strong acids, both chemicals would be expected to have irritant properties if administered as pure chemicals.

Eye Irritation

No data are available. However, as these chemicals are strong acids, both chemicals would be expected to have irritant properties if administered as pure chemicals.

Sensitisation

Skin Sensitisation

No data are available.

Repeated Dose Toxicity

Oral

In experiment one, adult male CD-1 mice received 0 (control), 10.4 or 41.6 mg/kg bw of Masurf-780 once daily for seven days by oral gavage. In a second experiment, SV129 wild-type (WT) and peroxisome proliferator-activated receptor alpha (PPARa)-null male mice (null) were similarly dosed with Masurf FS-780 at 0 (control), 3.1 or 20.8 mg/kg bw/day. All mice were sacrificed 24 h after the last treatment. No deaths were reported. Dose-dependent increases in liver weight were found in CD-1 and SV129 WT mice but not in null mice. Hence, like other PFAAs, PFPAs appear to function as an activator of PPARa. These results suggest that PFPA-induced liver enlargement occurs specifically through activation of PPARa (Das et al, 2011).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

No data are available.

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Information on the effect of PFPA on reproduction in animals is not available. These chemicals were not toxic to development in mice.

In a developmental study in mice, full details are not available, pregnant CD-1 mice received 0, 5, 10, 20, 30 or 40 mg/kg body weight (bw) of Masurf-780 by oral gavage daily on gestation days (GD) 1–17. No effects on maternal body weight gain, number of live foetuses or foetus body weights were observed at GD 17, except at the highest dose level, which also caused some mortality. Foetal liver weight was significantly increased at doses 10 mg/kg bw/day and above and this effect persisted until postnatal day 42. In addition, neonatal survival and growth were affected only at the highest dose. These findings suggest that PFPA exposure during pregnancy did not compromise neonatal survival and postnatal growth to the same extent as seen with the extensively studied perfluorochemicals, PFOS and PFOA, but the hepatic effects appeared to be common to all classes of PFCs (Tatum et al., 2011).

Risk Characterisation

Critical Health Effects

Only limited information is available for the health effects of these chemicals. However, these chemicals belong to a larger group of industrial PFCs (including PFOS and PFOA) which are known to be of high human health and environmental concern (see ***Grouping Rationale***). In addition, the available studies suggest that the PFPAs and PFPIAs can have similar health hazards (as seen for hepatic toxicity) as observed for other PFCs.

Public Risk Characterisation

Use in consumer products

Although use of these chemicals in Australia is not known, internationally these are high volume chemicals used as surfactants in a variety of domestic products including carpet and upholstery cleaning products.

The general public may be exposed to the chemical via the dermal route if it is used in domestic products.

Secondary exposure to PFOS via the environment

Public exposure to these chemicals could occur through secondary exposure via the environment.

The PFPAs have been detected in surface waters and wastewater samples at ng/L levels in Canada and in Europe (Deon et al, 2009; Esparza et al., 2011; Ullah et al., 2011; Llorca et al, 2012). The PFPAs and PFPIAs were also detected in indoor dust samples (De Silva et al., 2012). The PFPAs were not detected in a recent human serum study, but PFPIAs were above detection limits (LOD). The levels of most prevalent congeners were above 3.7 ± 1.3 pg/mL (Lee & Mabury, 2011). The PFPIAs were also detected in fish fillet from the Great Lakes (United States), suggesting that fish consumption may be a source of human exposure to these compounds (De Silva et al., 2012; Guo et al., 2012).

While the current measured levels of PFPA and PFPIA are considerably lower than for PFOS and PFOA, the findings demonstrate that these chemicals contribute to the environmental fluorochemical contamination and may bioaccumulate in food chain.

Occupational Risk Characterisation

Based on the available information, the chemicals are not expected to be manufactured in Australia. However, although unknown, these chemicals are likely to be present in Australia. Further assessment of the chemicals in this group may be necessary to determine the risk to workers if information becomes available indicating that these chemicals are introduced into Australia in significant quantities. The available data are not sufficient to determine appropriate hazard classifications.

Long-term occupational exposure to these chemicals could occur while using the formulated products. However, epidemiological studies in workers exposed to PFOS and PFOA, the most well studied members of the perfluorochemicals, did not provide clear evidence of effects in humans at normal occupational exposure levels (NICNASa). Therefore, the chemicals are not considered to pose an unreasonable risk to the health of workers.

NICNAS Recommendation

The absence of domestic use and exposure data for the substances in this group precludes a more complete assessment of their industrial uses in Australia. The potential consequences of ongoing emissions of these chemicals also cannot be fully evaluated due to the lack of human health hazard data available.

NICNAS will continue to monitor the availability of toxicological and use information for these chemicals to enable characterisation of the hazards. If sufficient information becomes available, a Tier III assessment may be undertaken.

Regulatory Control

Advice for consumers

Products containing the chemicals should be used according to the instructions on the label.

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 that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- 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.

References

Buck RC, Franklin J, Berger U, Conder JM, Cousins IT, de Voogt P, Jensen AA, Kannan K, Mabury SA, van Leeuwen SP 2011. Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classification, and origins. Integr Environ Assess Manag 7(4), pp. 513-541. doi: 10.1002/ieam.258.

Danish Ministry of the Environment, Environmental Protection Agency (Danish EPA), 2015. Short-chain Polyfluoroalkyl Substances (PFAS). A literature review of information on human health effects and environmental fate and effect aspects of short-chain PFAS. Environmental project No. 1707, 2015. Accessed at **http://www2.mst.dk/Udgiv/publications/2015/05/978-87-93352-15-5.pdf**

Das K, Rosen P, Mitchell B, Wood CR, Abbot BD, Lau C, 2011. Perfluorophosphonic acid activates peroxisome proliferator-activated receptor-alpha but not constitutive androstane receptor in the murine liver. In: Presented at Society of Toxicology (SOT) Annual Meeting, Washington, DC, United States. Accessed January 2016 at **http://cfpub.epa.gov/si/si_public_record_report.cfm?dirEntryId=230824** .

De Silva AO, Allard CN, Spencer C, Webster GM, Shoeib M, 2012. Phosphorus-containing fluorinated organics: polyfluoroalkyl phosphoric acid diesters (diPAPs), perfluorophosphonates (PFPAs), and perfluorophosphinates (PFPIAs) in residential indoor dust. Environ Sci Technol 46(22), pp.12575-82. doi: 10.1021/es303172p.

D'eon JC, Mabury SA, 2010. Uptake and elimination of perfluorinated phosphonic acids in the rat. Environ Toxicol Chem 29(6), pp.1319-29. doi: 10.1002/etc.167.

D'eon, JC, Crozier, PW, Furdui, VI, Reiner, EJ, Libelo, EL, Mabury, SA 2009. Perfluorinated phosphonic acids in Canadian surface waters and wastewater treatment plant effluent: discovery of a new class of perfluorinated acids. Environ. Toxicol. Chem.

Esparza X, Moyano E, De Boer J, Galceran MT, Van Leeuwen SPJ, 2011. Analysis of perfluorinated phosponic acids and perfluorooctane sulfonic acid in water, sludge and sediment by LC–MS/MS. Talanta 86, pp. 329–336.

Government of Canada, 2012. Proposed Risk Management Approach for Perfluorooctanoic Acid (PFOA), its Salts, and its Precursors and Long-Chain (C9-C20) Perfluorocarboxylic Acids (PFCAs), their Salts, and their Precursors. Environment Canada and Health Canada. Accessed January 2012 at **http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=451C95ED-1**.

Guo R, Reiner EJ, Bhavsar SP, Helm PA, Mabury SA, Braekevelt E, Tittlemier SA, 2012. Determination of polyfluoroalkyl phosphoric acid diesters, perfluoroalkyl phosphonic acids, perfluoroalkyl phosphinic acids, perfluoroalkyl carboxylic acids, and perfluoroalkane sulfonic acids in lake trout from the Great Lakes region. Anal Bioanal Chem 404(9): pp. 2699-709. doi: 10.1007/s00216-012-6125-1.

Howard PH, Muir DCG, 2012. Identifying new persistent and bioaccumulative organics among chemicals in commerce. Environ Sci Technol 44, pp. 2277–2285.

Howard, PH, Meylan W, 2007. EPA Great Lakes Study for Identification of PBTs to Develop Analytical Methods: Selection of Additional PBTs - Interim Report. EPA Contract No. EP-W-04-019. Syracuse Research Corporation. Syracuse, NY.

Idupulapati N, Devanathan R, Dupuis M, 2011. Atomistic simulations of perfluoro phosphonic and phosphinic acid membranes and comparisons to Nafion. J Phys Chem B 115(12), pp. 2959-69. doi: 10.1021/jp111972h.

Lee H, De Silva AO, Mabury SA 2012. Dietary bioaccumulation of perfluorophosphonates and perfluorophosphinates in juvenile rainbow trout: evidence of metabolism of perfluorophosphinates.Environ Sci Technol 46(6), pp. 3489-3497. doi: 10.1021/es204533m. Epub 2012 Feb 29.

Lee H, Mabury SA, 2011. A pilot survey of legacy and current commercial fluorinated chemicals in human sera from United States donors in 2009. Environ Sci Technol 45(19): pp. 8067-74. doi: 10.1021/es200167q.

Llorca M, Farre M, Pico Y, Muller J, Knepper TP, Barcelo D, 2012. Analysis of perfluoroalkyl substances in waters from Germany and Spain. Sci. Total Environ. 431, pp. 139–150.

National Industrial Chemicals Notification and Assessment Scheme (NICNASa). Human Health Tier II Assessment for Perfluorooctanoic Acid (PFOA) and its direct precursors.. Accessed May 2015 at **http://www.nicnas.gov.au**

National Industrial Chemicals Notification and Assessment Scheme (NICNASb). Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for perfluorooctane sulfonate (PFOS) and its direct precursors. Accessed March 2015 at **http://www.nicnas.gov.au**

Tatum KR, Das K, Grey BE, Lau C, 2011. Effects of perfluorinated phosphonic acids exposure during pregnancy in the mouse. In: Presented at Society of Toxicology (SOT) Annual Meeting, Washington, DC, United States. Accessed January 2016 at **http://cfpub.epa.gov/si/si_public_record_Report.cfm?dirEntryId=235687&CFID=30006325&CFTOKEN=94239073**.

Ullah S, Alsberg T, Berger U, 2011. Simultaneous determination of perfluoroalkyl phosphonates, carboxylates, and sulfonates in drinking water. J. Chromatogr A 1218 (37), pp. 6388-6395.

United States Environmental Protection Agency (US EPA), 2006. Inert ingredient; revocation of the tolerance exemption for mono- and bis-(1H,1H,2H,2H-perfluoroalkyl) phosphates where the alkyl groupis even numbered and in the C6–C12 range. US EPA Public Docket OPP-2006-0253. Washington, DC.

United States Environmental Protection Agency (US EPA), 2013. Significant New Uses: Perfluoroalkyl Sulfonates and Long-Chain Perfluoroalkyl Carboxylate Chemical Substances. Accessed January 2016 at **http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2012-0268-0034**

Last Update 05 February 2016

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Phosphonic acid, perfluoro-C6-12-alkyl derivatives** Perfluoro-C6-12-alkylphosphonic acid PFPA mono-PFPA
CAS Number	68412-68-0
Structural Formula	

	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	

Chemical Name in the Inventory and Synonyms	**Phosphinic acid, bis(perfluoro-C6-12-alkyl) derivatives** Diperfluoro-C6-12-alkylphosphinic acid PFPIA di-PFPA
CAS Number	68412-69-1
Structural Formula	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	

Share this page