File No: EX/211 (STD/1409)

June 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Polyfluorinated Polymer in Capstone® FS-30

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment and Energy.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

This assessment report is for an extension of original assessment certificate for Polyfluorinated polymer in Capstone® FS-30. Based on the submission of new information by the extension notifier, some sections of the original assessment report have been modified. These modifications have been made under the heading 'Extension Application' in the respective sections.

SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
EX/211 (STD/1409)	Ricoh Australia Pty Ltd	Polyfluorinated polymer in Capstone® FS-30	Yes	≤ 3 tonnes per annum	Component of paints and coatings, floor care and cleaning products, stone and tile sealants and inks.

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified polymer is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the table below.

Hazard classification	*Hazard statement*
Acute toxicity (Category 4)	H302 – Harmful if swallowed

Based on the available information, the notified polymer is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:
R22: Harmful if swallowed

The environmental hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute Category 3	H402: Harmful to aquatic life

Human health risk assessment
Under the conditions of the occupational settings described, the notified polymer is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified polymer is not considered to pose an unreasonable risk to public health.

However, the notified polymer is a potential precursor of perfluorohexanoic acid (PFHxA), which is persistent in the environment. Due to the environmental distribution of PFHxA resulting from the use pattern of the notified polymer, secondary human exposure to PFHxA via the environment may occur. The notified polymer is replacing a long chain polyfluoroalkyl polymer, the latter of which will result in secondary human exposures to perfluorooctanoic acid (PFOA) and longer chain perfluorocarboxylic acids (PFCAs). PFOA and longer chain PFCAs are more hazardous to human health and have higher bioaccumulation potential, compared to PFHxA (Russell *et al*, 2013). The overall human health risk posed by the notified polymer is less than that of the substance it replaces.

Environmental risk assessment
On the basis of the PEC/PNEC and assessed use pattern, the notified polymer itself is not considered to directly pose an unreasonable short-term risk to the environment.

However, degradants of the notified polymer, along with associated impurities and residual monomers of the notified polymer, are potential precursors of the very persistent chemical, PFHxA. The assessed use pattern of the notified polymer does not control the release of breakdown products into the environment during use and after disposal and the long-term environmental risk profile of PFHxA is currently unknown. Consequently, the long-term risk profile for the notified polymer and its degradation products is unknown. This situation may change if further data on the environmental behaviour of the notified polymer and its poly- and perfluoroalkyl degradation products (including PFHxA) were to become available.

The notified polymer is a potential precursor for PFHxA in the environment. PFHxA is an environmentally persistent chemical that has potential to be globally distributed. However, the ecotoxicological profile and bioaccumulation potential of PFHxA is considered to be less problematic when compared with long chain (C8 and above) perfluorocarboxylic acids that PFHxA is expected to replace, noting that current evidence shows that PFHxA was not bioaccumulative in aquatic systems or humans (Russell *et al*, 2013). Nonetheless, the introduction and use of chemicals that degrade to release PFHxA and other very persistent poly- and perfluoroalkyl compounds should be considered a short-term measure until suitable alternatives, with less persistent chemistry, are identified.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- The notified polymer should be classified as follows:
  - Acute toxicity (Category 4): H302 – Harmful if swallowed*

  *Classification of products/mixtures containing the notified polymer should be considered based on the concentration of the notified polymer present.

CONTROL MEASURES
Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified polymer:
  - Local ventilation systems, where possible
  - Enclosed, automated processes, where possible

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified polymer:
  - Avoid contact with skin
  - Avoid breathing mists, vapours or sprays
  - Maintain good hygiene practices

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified polymer:
  - Coveralls
  - Impervious gloves
  - Respiratory protection if ventilation is inadequate

  Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified polymer are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals*

(GHS) as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Environment

- The notified polymer should only be introduced as part of a strategy to phase out the use of long chain perfluorinated chemicals.

- The notifier should seek ways to minimise the level of residual polyfluoroalkyl monomers and impurities in the notified polymer. Such levels should be as low as practicable: where possible, the total weight of these constituents should not exceed the levels attainable utilising international best practice.

- The following control measures should be implemented by users of the notified polymer, or products containing the notified polymer, to minimise exposure of the notified polymer to the environment:
  - Best practice on-site treatment of waste streams should be employed to maximise removal of the notified polymer from wastewaters.

Disposal

- If the notified polymer or products containing the notified polymer cannot feasibly be disposed using a technique that will destroy or irreversibly transform the perfluorinated components of the notified polymer, disposal should be to landfill.

Emergency procedures

- Spills or accidental release of the notified polymer should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified polymer is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
  - the importation volume exceeds three tonnes per annum notified polymer;
  - the function or use of the polymer is changed from a component of paints and coatings, floor care and cleaning products, stone and tile sealants, and inks;
  - the formulation of the product containing the notified polymer is changed;
  - additional information has become available on the repeat dose toxicity of the notified polymer;
  - additional information has become available to the person as to an adverse effect of the poly- or perfluoroalkyl degradation products of the notified polymer (such as PFHxA);
  - additional information has become available to the person as to the environmental fate of the polymer or its poly- or perfluoroalkyl degradation products (such as PFHxA) in relation to degradation or partitioning behaviour, including during water treatment processes;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of paints and coatings, floor care and cleaning products, stone and tile sealants and inks, or is likely to change significantly;
  - the amount of chemical being introduced has increased, or is likely to increase, significantly;

- the polymer has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the polymer on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

AICS Annotation

- When the notified polymer is listed on the Australian Inventory of Chemical Substances (AICS) the entry is proposed to include the following statement(s):
  - This polymer has been assessed by NICNAS and there are specific secondary notification obligations that must be met. Potential introducers should contact NICNAS before introduction.

(Material) Safety Data Sheet
The (M)SDS of the notified polymer provided by the notifier was reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

Extension Application (current):
The SDS of the notified polymer provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

This notification has been conducted under the cooperative arrangement with the United States Environmental Protection Agency (US EPA). Information pertaining to the assessment of the notified chemical by the US EPA was provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment, including the recommendations on safe use of the notified chemical, were carried out by NICNAS.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Holders of Original Assessment Certificates:

The Chemours Company (Australia) Pty Limited (ABN 90 169 142 750)
7 Eden Park Drive
MACQUARIE PARK NSW 2113

IMCD Australia Limited (ABN 44 000 005 578)
1st Floor, 372 Wellington Road
MULGRAVE VIC 3170

Avlo Australia Pty Ltd (ABN 44 154 403 399)
1-3 Jappady Street
MORDIALLOC VIC 3195

Laticrete Pty Ltd (ABN 57 069 067 992)
29 Telford Street
VIRGINIA QLD 4014

Applicant for a previous Extension (EX/209) of the Original Assessment Certificate:

PPG Industries Australia Pty Ltd (ABN: 82 055 500 939)
14-20 McNaughton Road
CLAYTON VIC 3168

Applicants for a previous Extension (EX/213) of the Original Assessment Certificate:

Axalta Coating Systems Australia Pty Ltd (ABN: 53 158 497 655)
15-23 Melbourne Road
RIVERSTONE NSW 2765

Carestream Health Australia Pty Ltd (ABN: 41 123 474 724)
Level 3, 176 Wellington Parade
EAST MELBOURNE VIC 3002

Applicant for the current Extension of the Original Assessment Certificate:

Ricoh Australia Pty Ltd (ABN: 30 000 593 171)
2 Richardson Place
NORTH RYDE NSW 2113

NOTIFICATION CATEGORY
Standard: Synthetic polymer with Mn < 1000 Da (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, polymer constituents, residual monomers, impurities, use details and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Repeat-dose toxicity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
China, Korea, USA, Taiwan and Japan

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
ELN101570-4, Capstone® FS-3100 (notified polymer up to 100% concentration)
Capstone® FS-30, Capstone® FS-31, Capstone® FS-34, Capstone® FS-35 (notified polymer up to 30% concentration)

MOLECULAR WEIGHT
> 500 Da

ANALYTICAL DATA
Reference IR spectra was provided.

3. COMPOSITION

DEGREE OF PURITY > 90%

LOSS OF MONOMERS, OTHER REACTANTS, ADDITIVES, IMPURITIES
Not expected to occur under normal conditions of use.

DEGRADATION PRODUCTS
Over time, the notified polymer is expected to ultimately degrade into perfluorohexanoic acid (PFHxA) - CAS name: Hexanoic acid, 2,2,3,3,4,4,5,5,6,6,6-undecafluoro-; CAS No. 307-24-4.

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 ºC AND 101.3 kPa: Yellow/tan solid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	40-50 ºC	Measured
Density	1,290 kg/m^3	Measured
Vapour Pressure	0.24 kPa at 25.176ºC	Measured
Water Solubility	0.168 g/L at 20 ºC	Measured.
Hydrolysis as a Function of pH	Not determined	Does not contain hydrolysable functionality
Partition Coefficient (n-octanol/water)	log Pow = 4.39 – 4.89 at 20 ºC	Measured. Based on its surface activity, the notified polymer is expected to partition between the octanol and water phases.
Adsorption/Desorption	log K_{oc} < 2.97	Calculated. The notified polymer may have low absorption based on its surface activity and the perfluorinated functionality that has hydro/lipophobic tendencies.
Dissociation Constant	Not determined	Not expected to dissociate based on lack of dissociable functionality.
Flash Point	Not determined	Expected to be high based on the partial fluorination.
Flammability	Not determined	Not expected to be flammable based on the partial fluorination.
Autoignition Temperature	Not determined	Expected to decompose prior to any

		autoignition.
Explosive Properties	Not expected to be explosive	Contains no explosophores.
Oxidising Properties	Not expected to be oxidising	Estimated based on structure.

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The notified polymer is expected to be stable under normal conditions of use.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified polymer is not recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified polymer will not be manufactured in Australia. The notified polymer will be imported into Australia in an aqueous dispersion (10 - 25%) or as the raw material (100%).

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	≤ 2	≤ 2	≤ 2	≤ 3	≤ 3

PORT OF ENTRY
Sydney, Melbourne and Brisbane

TRANSPORTATION AND PACKAGING
The notified polymer will be imported by sea in 3.79 kg, 24.64 kg and 199.76 kg phenolic lined steel containers. The notified polymer and products containing it will be transported by road within Australia.

USE
Original Application
The notified chemical is intended to be introduced in order to phase out the use of a partially fluorinated polymer containing fluorinated carbon chain lengths > 6 in various proportions (*i.e.*, existing chemical). The use categories of the notified polymer are identical to those of the existing polymer it replaces, as outlined below.

The notified polymer will be used as a component of paints and coatings (up to 0.2% concentration), floor care and cleaning products (up to 0.02% concentration), stone and tile sealants (up to 0.03% concentration), and ink formulations (up to 1.5% concentration). Paints and coatings and stone and tile products are expected to be used by professional and domestic users. Floor care products and inks are intended only for commercial/industrial settings.

Extension Application (EX/213)
Cleaning products will contain the notified chemical at concentrations of < 0.1%. The products will not be used by the public.

Extension Application (current)
There are no changes of the notified chemical use from the original application.

OPERATION DESCRIPTION
Reformulation
Drums containing the notified polymer (at up to 100% concentration apart from ink where the concentration will be up to 25%) will be received at reformulation sites and weighed manually or automatically pumped from drums into the mixing vessel (which may be heated) towards the end of the blending process. Once blending is complete, the finished products containing the notified polymer will be automatically dispensed into product containers. The blending and dispensing equipment will be cleaned periodically. Quality control staff may test

samples of the finished products.

Paints and coatings
The notified polymer (up to 100% concentration) will be formulated into paints and coatings (up to 0.2%). Paints and coatings will be applied by professionals by paint pad, brush, roller or low pressure spray. Domestic users will apply the paints and coatings by brush and roller, with spray use by the public not expected.

Floor care and cleaners
Original Application
Professional cleaners will manually dispense/load commercial floor care and cleaning products containing the notified polymer (up to 0.02% concentration) into floor polish machines for application to floors, usually in malls and shopping centres.

Previous Extension Application (EX/213)
Screen cleaner containing the notified polymer at concentrations < 0.1% will be used to clean intensifying screens and imaging plates in the lab and field. The cleaner will be applied with a cloth.

Stone and tile sealants
The notified polymer (up to 100% concentration) will be formulated into stone and tile sealants (up to 0.03% concentration). Professional and consumer users will apply finished stone and tile products containing the notified polymer by non-aerosol spray, brush, roller or sponge to stone and tile surfaces in public buildings or shopping malls.

Inks
The notified polymer (up to 25% concentration) will be formulated into ink products (up to 1.5% concentration). Ink products containing the notified polymer are expected to be used in thermal inkjet printers in commercial/industrial settings to produce high-end signs and advertisements.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

The notified polymer is not expected to undergo significant degradation during use. As such, most potential exposure to workers and the public is expected to be to the notified polymer itself, rather than to its degradation products. Exposure to the residual polyfluoroalkyl starting constituents and/or impurities of the notified polymer (discrete polyfluoroalkyl chemicals containing perfluoroalkyl carbon chain lengths ranging from four to ten) is also possible. Such exposure is limited by the relatively low concentration of polyfluoroalkyl impurities in the notified polymer in imported products (up to 1%) and end use products (up to 0.015%).

Over time, the notified polymer will break down and release PFHxA into the environment, which is likely to lead to secondary human exposure to PFHxA. This exposure is unquantifiable.

6.1.1. Occupational Exposure

EXPOSURE DETAILS
Transport and storage workers
Transport and storage workers will only come into contact with the notified polymer (up to 100% concentration) in the unlikely event of an accident.

Reformulation processes
Dermal and ocular exposure of workers to the notified polymer (up to 100% concentration) may occur when connecting and disconnecting hoses, and during cleaning and maintenance operations. Personal protective equipment (PPE) such as protective clothing, goggles and gloves are expected to be worn during these procedures. Inhalation exposures are not expected based on the low vapour pressure of the notified polymer and because aerosols are not expected during reformulation processes. The remainder of the formulation process, including packaging, is expected to be mostly automated and exposure is expected to be low.

Paints and coatings, floor care and cleaners, stone and tile sealants and inks
Dermal and ocular exposure to the notified polymer (up to 0.2% concentration) may occur when workers are applying paints and coatings, floor care and cleaning products or stone and tile sealants by paint pad, brush or

roller with some potential for inhalation exposure when applying by low pressure spraying methods. PPE is expected to be worn, including gloves, protective clothing, safety glasses and respiratory protection when aerosols may be present. Professionals may be exposed on a repeated basis.

Exposure of workers to the notified polymer (up to 1.5% concentration) during the use of ink products containing it in thermal inkjet printers is expected to be low due to the enclosed automated nature of the process. Workers required to intervene in the process may undergo dermal, ocular and inhalation exposure. Systemic exposures may result from dermal contact with substrates to which ink containing the notified polymer has been applied; however, based on the relatively low concentration in the end-use products and the fact that the majority of the polymer will remain bound to the substrate to which it was applied, exposure is expected to be low.

6.1.2. Public Exposure

Products containing the notified polymer (up to 0.2% concentration) will be used by the public. Dermal, ocular and inhalation exposure to the notified polymer may occur when paints and coatings or stone and tile sealants are used. The public is not expected to apply paints and coatings by spray; however, stone and tile products containing the notified polymer at up to 0.03% concentration may be applied by non-aerosol spray and the highest exposures will occur when products are sprayed in enclosed settings such as bathrooms. Consumer exposure is expected to be acute in nature, because repeated daily uses are considered unlikely, and of short duration (i.e., up to 15 minutes).

The public may make dermal contact with surfaces that have had the notified polymer applied in coatings, stone and tile sealants, floor care products or inks. This exposure may be on a long term repeated basis. However, once applied the notified polymer will adhere to the substrate and is not expected to be available for exposure in significant quantities.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified polymer and an analogue are summarised in the table below. Details of these studies can be found in Appendix B.

Endpoint	*Test substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Notified polymer – variation 2	LD50 = 1,030 mg/kg bw; harmful
Rat, acute oral toxicity	Notified polymer – variation 1	LD50 = 550 mg/kg bw; harmful
Rat, acute oral toxicity	Notified polymer – variation 3	LD50 = 1,030 mg/kg bw; harmful
Rat, acute dermal toxicity	Notified polymer – variation 3	LD50 > 5,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	Notified polymer – variation 1	LD50 > 5,000 mg/kg bw; low toxicity
Rat, acute inhalation toxicity	Notified polymer – variation 1	LC50 > 5.9 mg/L/4 hour; low toxicity
Rabbit, skin irritation	Notified polymer – variation 3	non-irritating
Rabbit, skin irritation	Notified polymer – variation 1	non-irritating
Rabbit, skin irritation	Notified polymer – variation 2	non-irritating
Rabbit, eye irritation	Notified polymer – variation 1	slightly irritating
Rabbit, eye irritation	Notified polymer – variation 2	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	Notified polymer – variation 1	no evidence of sensitisation
Mouse, skin sensitisation – Local lymph node assay	Notified polymer – variation 3	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	Notified polymer – variation 1	non mutagenic
Rat, Repeated dose toxicity – 90 day oral toxicity study with a one generation reproductive and developmental study	Analogue chemical	NOAEL (systemic) = 25 mg/kg bw/day NOAEL (reproductive and developmental) not established
Rat, one-generation reproductive toxicity study	Analogue chemical	NOAEL (systemic) > 25 mg/kg bw/day NOAEL (reproductive and developmental) > 25 mg/kg bw/day
*Mouse, Repeated dose toxicity – 28 day oral gavage toxicity	Notified polymer	NOAEL = 30 mg/kg bw/day

* The study is additional information which has become available on the notified polymer after the original assessment and is added/written under the *extension application* EX/209.

Toxicokinetics, metabolism and distribution.
The notified polymer has a molecular weight of ~500 – 1,000 Da and has between 1 and 6% of low molecular weight species, which would suggest low to moderate dermal absorption. A moderate water solubility of 0.168 g/L at 20 °C favours dermal absorption but the relatively high partition coefficient (log Pow = 4.39 – 4.89 at 20 °C) suggests the rate of dermal penetration may be limited by the rate of transfer between the stratum corneum and the epidermis. The toxicity studies suggest that the notified polymer is absorbed both dermally and orally with systemic effects seen in the acute oral and reproductive studies following oral exposure to rats and also in the LLNA following dermal exposure to mice.

Some accumulation in the respiratory tract may occur from respirable particles (< 10 μm), if present. Alternatively, larger inhalable particles (< 100 μm), if present, are likely to deposit in the nasopharyngeal region where some will be coughed or sneezed out with the balance swallowed.

Acute toxicity.
In three acute oral toxicity studies on different variations of the notified polymer it was found to be harmful, with LD50 values between 550 and 1,030 mg/kg bw.

There were no deaths or adverse test substance related effects in either of two acute dermal toxicity studies where the notified polymer was applied at a concentration of 5,000 mg/kg bw. In an LLNA study with the notified polymer, mice treated with a concentration of 100% lost 17-21% of their bodyweight by day 2 with clinical signs at lower concentrations including wet fur, dehydration and decreased faeces.

Inhalation toxicity
Perfluoroalkyl chemicals have been known to cause acute lung injury. Acute lung injury is characterised by respiratory problems ranging from mild to severe effects, including mortality, associated with acute or repeated exposures. Acute lung injury is generally considered to be of most concern when the compound has surface activity (Fischer et al., 2012).

In an acute inhalation toxicity study on the notified polymer no deaths occurred with the LD50 > 5.9 mg/L/4 hour and hence it is considered to be of low toxicity. At the high dose a number of clinical signs were noted, all of which had cleared by four days after dosing.

No repeated dose inhalation studies with the notified polymer have been submitted and thus uncertainties remain surrounding possible chronic respiratory tract effects following repeated exposures to the notified polymer.

Irritation and Sensitisation.
The notified polymer was non-irritating to the skin of rabbits in three separate tests on different variations of the polymer. In two separate eye irritation studies on two different variations of the notified polymer it was found to be slightly irritating to the eyes of rabbits with effects resolving in one study within 72 hours and in the other study within four days.

The potential for the notified polymer (up to 100% concentration) to cause skin sensitization was determined using two local lymph node assays. In one of the studies reductions in body weight and signs of toxicity necessitated euthanizing the animals treated with a concentration of 100% on day 2; however, in the other study at the same concentration signs of toxicity were not as severe and the animals could complete the study. No evidence of a positive lymphoproliferative response (relative stimulation index exceeding 3) was observed at any concentration in either of the studies. The notified polymer (up to 100% concentration) is unlikely to cause delayed contact hypersensitivity.

Repeated Dose Toxicity
In an oral repeated dose toxicity study combined with a one generation reproductive study, analogue 1 was administered to rats at doses of 0 (water), 25, 100 or 500 mg/kg bw/day for 90 days. Exposure to the test substance at doses of 100 or 500 mg/kg bw/day resulted in adverse treatment related effects. Adverse effects included changes in body weight and organ weight parameters, food efficiency, thyroid follicular hypertrophy, chronic progressive nephropathy, clinical signs, liver enzyme and red blood cell parameters. There were no adverse systemic effects on the parental animals at the lowest dose of 25 mg/kg bw/day, which was therefore

the NOAEL for the study.

A second one generation reproductive study with analogue 1 was conducted on rats at doses of 0 (water), 1, 10 or 25 mg/kg bw/day to investigate the effects seen in the above study. In this study statistically significant test substance related increases in the liver weight relative to body weight were seen in both male and female animals dosed with 25 mg/kg bw/day of the test substance. Compared to the control group, the increase in the liver weight relative to body weight was 110 and 114% for male and female rats in the 25 mg/kg bw/day group, respectively. In the absence of histopathological or clinical chemical changes indicative of liver injury the study authors considered the liver weight increases to be a physiologic response to metabolism of a xenobiotic and not toxicologically adverse. Therefore, the NOAEL for systemic effects in both male and female animals was set at the highest dose tested of 25 mg/kg bw/day.

Previous Extension Application (EX/209)
In a 28day repeat oral (gavage) dose study in mice one male dosed at 250 mg/kg bw/day, which was the maximum dose tested, was found dead on Day 14. In addition, adverse clinical signs consisting of non-sustained convulsions at ≥ 125 mg/kg bw/day and sustained convulsions at 250 mg/kg bw/day were noted following dosing, and functional observation battery changes were evident in male animals dosed at 250 mg/kg bw/day males. Centrilobular hypertrophy in the liver and correlating increases in liver weights were noted in animals dosed at ≥ 125 mg/kg bw/day. Erythropoiesis in the spleen and associated increases in spleen weight were evident in males at 250 mg/kg bw/day. Single occurrences of hunched posture and decreased activity were noted at 30 mg/kg bw/day. Therefore, the NOAEL for both male and female animals was established at 30 mg/kg bw/day.

Mutagenicity.
A bacterial reverse mutation assay was conducted according to the plate incorporation method. The notified polymer did not induce a toxicologically significant increase in the number of revertant colonies of *Salmonella typhimurium* (TA1535, TA1537, TA98, TA100) or *Escherichia coli* WP2uvrA, in the presence or absence of metabolic activation (Aroclor 1254 induced rat liver S9 fraction), at concentrations ranging from 33.3 to 5000 µg/plate in dimethyl sulfoxide. The standard positive control substances induced clear increases in the number of revertant colonies, confirming the sensitivity of the test system to known mutagens and the activity of the S9 fraction. The notified polymer was not mutagenic under the conditions of this in vitro assay.

Toxicity for reproduction.
In an oral repeated dose toxicity study combined with a one generation reproductive study, analogue 1 was administered to rats at doses of 0 (water), 25, 100 or 500 mg/kg bw/day. Reproductive effects included a significant reduction in the number of implantation sites in the 500 mg/kg bw/day dose group in comparison to the control group and a reduction in the fertility index at all doses in comparison to the control group. Adverse effects in the F1 generation were seen in the 100 and 500 mg/kg bw/day dose groups and consisted of reductions in the mean litter size, number of pups born and born alive, pup survival and pup weight. Based on the presence of adverse reproductive effects at all of the doses tested in this study a NOAEL for reproductive and neonatal toxicity could not be set.

A second one generation reproductive study with the analogue chemical was conducted on rats at doses of 0 (water), 1, 10 or 25 mg/kg bw/day to investigate the effects seen in the above study. Based on the absence of adverse effects on any reproductive parameters or on the F1 offspring the NOAEL for reproductive and neonatal toxicity in this study was 25 mg/kg bw/day, which was also the NOAEL for systemic toxicity in the parental animals.

Health hazard classification
Based on the available information, the notified polymer is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the table below.

Hazard classification	***Hazard statement***
Acute toxicity (Category 4)	H302 – Harmful if swallowed

Based on the available information, the notified polymer is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:
R22: Harmful if swallowed

Toxicology of break down products

The notified polymer contains perfluoroalkyl side-chains that are potential precursors of PFHxA in the environment (PFHxA; CAS No. 307-24-4), a perfluorinated chemical consisting of 5 perfluorinated carbons (a short chain perfluorinated chemical). The polymer that is proposed for replacement by the notified polymer is expected to break down to perfluorooctanoic acid (PFOA; CAS No. 335-67-1) (consisting of 7 perfluorinated carbons) and other per- and polyfluorocarboxylic substances with longer perfluoroalkyl carbon chain lengths. The toxicokinetic and toxicological properties of the long chain break down products are generally less favourable compared to the short chain break down products, with properties becoming less favourable with increasing perfluoroalkyl carbon chain length. In addition, it has been established that the bioaccumulation potential of perfluorocarboxylic acids increases with perfluoroalkyl carbon chain length (Conder, 2008; Giesy 2010).

A review of the literature indicates that PFHxA has a less hazardous human health profile, compared to PFOA (refer to Appendix D for details). It is therefore inferred that the human health hazards associated with the expected break down product of the notified polymer (PFHxA) are likely to be similar or less than the human health hazards associated with the expected break down products (PFOA and longer chain perfluorocarboxylic acids) of many per- and polyfluoroalkyl chemicals currently on the market and that are intended for replacement by the notified polymer.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

The notified polymer is harmful if swallowed, with all other toxicology studies on the notified polymer indicating low hazard. An analogue of the notified polymer was shown to have a NOAEL of 25 mg/kg bw/day after repeated oral exposure.

The notified polymer is expected to be absorbed dermally and therefore workers exposed to the polymer at a 100% concentration during reformulation could be at risk of systemic toxicity. However, reformulation is expected to be a mostly automated and enclosed process with workers using PPE and hence the possibility for exposure will be low. Based on the automated and enclosed nature of the process and the use of PPE the risk of systemic toxicity to workers during reformulation of products containing the notified polymer is not considered to be unreasonable.

Slight eye irritation may occur during reformulation of the notified polymer but automated processes are expected to be in place and PPE (clothing, gloves and goggles) will be worn, which will further minimise exposure. The risk of slight eye irritation is not considered to be unreasonable.

Repeated dermal and accidental ocular exposure to the notified polymer (up to 0.2% concentration) may occur when workers are applying paints and coatings, floor care and cleaning products or stone and tile sealants by paint pad, brush or roller with some potential for inhalation exposure when applying by low pressure spraying methods. Workers may also be exposed, mainly via the dermal route, to the notified polymer at concentrations up to 1.5% when using ink cartridges in thermal inkjet printers. The repeated dose toxicity of the notified polymer has not been investigated; however, repeat dose oral toxicity studies on an analogue showed toxicity with a NOAEL of 25 mg/kg bw/day. Therefore, as a precaution it should also be assumed that the notified polymer may be toxic following repeated exposure. The relatively low concentration of the notified polymer in the end use products, the automation of some processes, and the use of PPE will lower exposure to the notified polymer. Overall, due to the relatively low concentrations, the automation of some processes, and the use of PPE the risk of repeat dose toxicity to workers resulting from repeated exposure is not considered to be unreasonable.

Repeated inhalation exposure to the notified polymer is not of concern to workers during reformulation as aerosols are not expected to be generated, but may be of concern when spraying the reformulated notified polymer (up to 0.2% concentration). However, the use of low-pressure spray and the low concentration of the notified polymer are expected to further minimise exposure. The lack of repeat dose inhalation toxicity data is considered to be a data deficiency given the potential for lung injury and/or particle overloading. This is of particular concern for workers who may use products containing the notified polymer every day. The notified polymer was of low acute toxicity following a 4 hour exposure with no deaths in the study at concentrations up to 5.9 mg/L and therefore has a reduced possibility of inducing lung waterproofing following repeated inhalation exposure. Due to the low acute inhalation toxicity and the expected low exposure the risk of inhalation toxicity resulting from repeated exposure to the notified polymer is not considered to be

unreasonable.

Workers may also be exposed to per- and polyfluoroalkyl impurities of the notified polymer at relatively low concentrations (< 1%), during reformulation. It is expected that the engineering controls and personal protective equipment utilised during these operations (as outlined above) will act to mitigate any risk associated with such exposure.

6.3.2. Public Health

The public may be exposed to the notified polymer (up to 0.2% concentration) when paints and coatings or stone and tile sealants containing it are used. Consumer exposure is expected to be acute in nature because repeated daily uses are unlikely. The notified polymer was found to be harmful following acute oral exposure with the lowest LD50 being 550 mg/kg bw, but was of low acute inhalation and dermal toxicity. Acute dermal or inhalation exposure to products containing the notified chemical is unlikely to produce any systemic toxicity, considering the low hazard and the low concentration. Acute oral exposure to the notified chemical is expected to be far below that required for systemic toxicity to occur. Based on the relatively low acute toxicity of the notified polymer and its low concentration in paints and coatings or stone and tile products the risk to public health when using these products is not considered to be unreasonable.

The public may also be exposed to the notified polymer and low levels of per- and polyfluoroalkyl impurities from direct dermal contact with articles that have either been coated or cleaned with products containing the notified polymer. This exposure may be on a long term repeated basis. However, dermal transfer from the treated article is expected to be low as the notified polymer will be present at low concentrations and will predominantly remain absorbed to the substrate to which it was applied. Thus the risk to public health from repeated dermal exposure to the notified polymer from treated articles is not considered to be unreasonable. The risk to public health from long term repeated dermal exposure to per- and polyfluoroalkyl impurities of the notified polymer from treated articles may be mitigated by the relatively low concentrations at which they are present in end use products.

The public may be exposed indirectly to the ultimate break down product of the notified polymer, PFHxA, via the environment. Such exposure may increase over time due to the persistence of PFHxA in the environment. A quantitative risk assessment for this exposure was not conducted. However, the available data indicates that PFHxA has a more favourable toxicological profile and bioaccumulation potential than the long chain per- and polyfluoroalkyl substances that are the ultimate break down products of the majority of polyfluoroalkyl polymers currently in Australian commerce (such as PFOA). In particular, it is noted that the polymer being replaced contains perfluorinated carbon chain lengths > 6. It is concluded that the risks to human health from indirect exposure to breakdown products of polyfluoroalkyl substances will decrease following introduction of the notified polymer, on the basis that the notified polymer is intended to replace a currently available “long” chain polyfluoroalkyl polymer.

It should also be noted that the notified polymer has been approved for the same uses in the USA for a manufacture/import volume greater than the volume under consideration in Australia.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified polymer will not be manufactured in Australia. Therefore, releases to the environment are not expected from this activity. Releases to the environment may occur following accidental spills during import, transport or storage. Any notified polymer that is spilled is expected to be adsorbed onto a suitable material and collected for disposal in accordance with local regulations.

The notified polymer may either be imported in ready-to-use products or in products for further reformulation in Australia. The notified polymer may enter the wastewater stream during reformulation as a result of rinsing empty import containers, mixing equipment, transfer lines and the filling machine. The exact volume of notified polymer released per annum due to reformulation activities is not known. However, using conservative assumptions using notifier estimates and considering emission scenarios, a total of up to 11.3 kg/year is expected to be released during reformulation, as outlined in the table below.

Use	Paints	Floor wax and polish	Stone and tile treatment	Ink
Estimate of the notified polymer annual import volume for each use	45%	30%	15%	10%
Estimate of release to wastewater from use	0.32%	0.35%	< 0.5%	0.5%
Annual release to wastewater based on a 3 tonne annual import volume	4.3 kg	3.2 kg	< 2.3 kg	1.5 kg

Reformulation wastes will be disposed of via wastewater treatment facilities at the site of reformulation and/or be disposed of by hazardous waste disposal contractors. It is assumed that treated water will subsequently be discharged to sewers. The notifier indicates that reformulation wastes containing the notified polymer may be disposed of by high temperature incineration, in accordance with local regulations.

Notified polymer residues remaining in empty import containers are expected to be minimal as containers will be rinsed prior to disposal. Residues in import containers may be thermally decomposed during metals reclamation of metal containers or enter the wastewater streams following plastic container recycling. Alternately, empty containers with residues of the notified polymer may be disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

When used in paints and stone and tile treatments, the notified polymer may enter wastewater as residues in application equipment washings or rinsings from empty product containers. Wastewater containing the notified polymer that is generated by professional and consumer users may be disposed of to sewers. The notified polymer may also enter sewers from the disposal of water in spray booths when products containing the notified polymer are applied by spray by industrial users, such as original equipment manufacturers.

When used in floor wax and polish, the notified polymer may enter wastewater as residues in spent cleaning solution drained from waxing machine tanks, which are expected to be disposed of to sewers by professional users.

Limited release to sewer is expected during use of the notified polymer in inks. Filled cartridges will be placed directly into printing equipment. Ink will be applied to vinyl, plastics and paper in a closed system and dried and cured thermally before exiting the printer. Accidental spills of ink are expected to be absorbed onto appropriate material and disposed of to landfill.

The notifier's estimates for release of the notified polymer to sewer are summarised in the table below:

Use	Paints		Floor wax and polish	Stone and tile treatment	Ink
User	*Professional*	*Domestic*	*Professional*	*Professional*	*Professional*
Estimate of the notified polymer annual import volume for each use	40%	5%	30%	15%	10%
Estimate of release to wastewater from use	1%	25%	45%	1%	Limited release during use
Annual release to wastewater based on a 3 tonne annual import volume	12 kg	37.5 kg	405 kg	4.5 kg	0 kg

Therefore, the total release of the notified polymer from use is estimated to be 459 kg (15.3% of the total annual import volume).

It is expected that all uses will also generate solid wastes containing the notified polymer. These include residues on rags used to wipe drips, on old applicators (brush, roller, mop heads) and in empty product containers for paints, stone and tile treatments and floor and wax polish. Spent ink cartridges are also expected to contain residues of the notified polymer (up to 10%). Solid wastes generated during use are expected to be disposed of in accordance with local regulations, most likely to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

The notified polymer applied to painted surfaces is expected to be physically bound within the inert polymer matrix adhering to the surface of the articles and is expected to remain associated with the painted articles. The notified polymer applied to treated stone and tile surfaces and polished and waxed floors is expected to adhere to the surface to which it has been applied. However, abrasion of the floor surface by foot traffic is expected to result in some relocation of the notified polymer. Estimates for losses due to abrasion from these uses are not available. The notified polymer that remains associated with painted surfaces, stone, tile and flooring is expected to share the fate of articles. The majority of articles are expected to ultimately be disposed of to landfill.

The majority of the notified polymer used in inks is expected to be cured onto vinyl and plastics and is expected to share the fate of the article, most likely disposed of to landfill at the end of their useful life. Approximately 30% (90 kg) of the ink containing the notified polymer is expected to be applied to paper. It is assumed that 50% (45 kg) of the printed paper will end up in landfill and the rest will undergo paper recycling processes. During recycling processes, waste paper will be repulped using a variety of chemical agents, which, amongst other things, enhance detachment of inks from the fibres. Therefore, based on the percentage of ink that is applied to paper, up to approximately 1.5% (45 kg) of the annual total import volume of the notified polymer is expected to be released to sewer from its use in ink.

The notified polymer applied to surfaces may also degrade as a result of weathering upon being exposed to environmental conditions after use and after disposal. Degradation may result in the widespread release of degradation products such as perfluorohexanoic acid (PFHxA) to surface waters, landfill and landfill leachates, soils, and other regions where release is not foreseen.

7.1.2. Environmental Fate

For details of the environmental fate studies please refer to Appendix C.

The majority of the notified polymer is expected to adhere to the surface to which it is applied. Treated articles and other dried residues containing the notified polymer are expected to ultimately be disposed of to landfill. When associated with the article to which the product containing the notified polymer has been applied, the notified polymer is not likely to be mobile or bioavailable in landfill.

Some of the notified polymer may be released to sewer during reformulation, use and disposal. In general, surfactants have the potential to be removed from influent in sewage treatment plants (STP) via partitioning to phase boundaries. Predictions of the environmental partitioning behaviour of polyfluoroalkyl surfactants such as the notified polymer remain uncertain based on current knowledge because of limited data and their unique properties. In particular, the usual predictive models for partitioning during sewage treatment are inapplicable for chemicals containing perfluorinated functionality as they assume lipophilicity for hydrophobic functionality, whereas the perfluorinated functionality is both hydrophobic and lipophobic. The assumption that surface activity and/or high molecular weight results in efficient removal by sorption to sludge during conventional wastewater treatment has not been verified by supporting data for this class of chemical. Thus, noting its potential to disperse in water, a significant proportion of the notified polymer, and any associated impurities/residual monomers of poly- and perfluoroalkyl compounds, may well remain in the aqueous phase following wastewater treatment. As such, the notified polymer and the poly- and perfluoroalkyl impurities/residual monomers in wastewater have the potential to be released in STP effluent directly to surface waters or reused in the irrigation of agricultural soils throughout Australia.

Over time, the notified polymer is expected to become dissociated from the articles. The notified polymer has the potential to disperse in water but it is not expected to hydrolyse under environmental conditions (pH 4 to 9, 25 ºC) based on structural considerations. A test study indicates that the notified polymer is rapidly degradable, achieving 62% degradation in 28 days but failing the 10-day window criteria. Degradation products are not known for certain as no characterisation of the degradation products was undertaken in the biodegradation test. A recent paper found that close analogues of the notified polymer undergo rapid biotransformation via a chain shortening mechanism (see Exempt Information). However, the notified polymer is not expected to completely mineralise and degradation products may include more stable lower molecular weight polymers with per- and polyfluoroalkyl functionality or the very persistent perfluorinated degradation product PFHxA. Therefore, the notified polymer has the potential to release the PFHxA after only a short period of time.

In surface waters, agricultural soils and landfill, the notified polymer is expected to eventually degrade to form water, oxides of carbon and nitrogen and degradation products containing per- and polyfluoroalky

functionality. The expected initial per- and polyfluoroalkyl degradation products are assumed to undergo further degradation to form, among other compounds, the very persistent perfluorinated degradation product, PFHxA. It is noted that some volatile degradation intermediates have the potential to undergo long range atmospheric transport and thus may result in translocation of PFHxA in the environment. The notified polymer also contains impurities that may degrade to form perfluorooctanoic acid (PFOA) and other long-chain per- and polyfluorocarboxylic acids.

PFHxA is expected to be recalcitrant in the environment, and potentially undergo long range transport while mainly staying in the water column. In water, it is expected to be very persistent and will not hydrolyse, photolyse or biodegrade.

High-temperature incineration is the preferred method of disposal of poly- and perfluoroalkyl compounds due to the environmental persistence characteristics, when it results in mineralisation of the perfluoralkyl functionality to oxides of carbon and hydrofluoric acid. Incomplete combustion of perfluoralkyl functionality may produce an array of partially oxidised fluorocompounds such as perfluoroacetic acid, fluorinated dioxins and furans. Therefore, disposal of the notified polymer and its degradation products by incineration should only take place at facilities that demonstrate complete combustion of the perfluoroalkyl functionality and have adequate measures in place to control release of hydrofluoric acid.

The notified polymer has the potential to bioaccumulate based on its molecular weight and n-octanol/water partition coefficient. Generally, a log Pow of > 4.2 indicates a potential for bioaccumulation as high values indicate a tendency to partition to lipids while a low value indicates a tendency to partition to water. However, this also assumes lipophilicity of the hydrophobic functionality which does not apply to perfluoroalkyl functionality. Certain perfluoroalkyl compounds are known to accumulate in the blood and liver rather than lipids in biological systems (Danish EPA, 2008). As perfluoroalkyl compounds do not follow the usual mechanism for bioaccumulation and are not expected to bioaccumulate in lipids, and because of the notified polymer's surface-active properties, the n-octanol-water partition coefficient is not considered to be a reliable indicator of bioaccumulation potential for the notified polymer. Further, the notified polymer has the potential to undergo degradation and biotransformation in the environment, reducing its potential to bioaccumulate.

The available laboratory (Higgins *et al*., 2007; Martin *et al*., 2003ab; Woodcroft *et al*., 2010) and field (Falandysz *et al*., 2006; Falandysz *et al*., 2007, Furdui *et al*., 2007) evidence indicates that PFHxA is expected to be less bioaccumulative than PFOA and other long chain perfluoroalkyl compounds, which PFHxA-chemistry is replacing (although PFHxA and PFOA are not considered bioaccumulative). However, both are bioavailable and can be detected in wildlife as demonstrated by monitoring studies (Kumar *et al*., 2009; Ye *et al*., 2008ab; Wang *et al*., 2008). In aquatic biota, there is little evidence of increased bioconcentration of PFOA compared with PFHxA although PFOA may generally be expected to be found in aquatic organisms more often than PFHxA. In general, the available evidence indicates that the bioaccumulation potential of perfluorinated compounds is correlated with increasing fluorinated carbon chain length (Giesy *et al*., 2010). Therefore, PFHxA has a lower bioaccumulation potential than PFOA and other long chain perfluorinated compounds, which PFHxA-based chemistry is replacing.

7.1.3. Predicted Environmental Concentration (PEC)

The notified polymer may be released to the aquatic compartment through the disposal of wastewater generated during its reformulation, use or disposal. Under a worst-case scenario, it is assumed that there is no removal of the notified polymer during STP processes.

The predicted environmental concentration (PEC) due to releases from reformulation of paints, floor wax and polish, stone and tile treatments, and ink is calculated assuming release to an STP in Sydney with a daily effluent flow rate of 456 ML. For this scenario, it is assumed that for a worst-case, 1% of the total import volume of the notified polymer will be released during reformulation over 260 working days per year. The concentration of the notified polymer in STP effluent from point-source releases is estimated as follows:

Predicted Environmental Concentration (PEC) for release to the aquatic compartment during reformulation		
Total Annual Import Volume	3,000	kg/year
Proportion expected to be released to sewer	1%	
Annual quantity of chemical released to sewer	30	kg/year
Days per year where release occurs	260	days/year
Daily chemical release:	0.115	kg/day
Individual Sewage Treatment Plant Average Daily Flow:	456	ML/day

Removal within STP	0%	
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
Effluent concentration	0.25	µg/L

The PEC due to releases from use in paints, stone and tile treatments, floor polishes and waxes, and inks is calculated assuming nationwide release over 260 working days per year. Under a worst-case scenario, it is estimated that 5% of the notified polymer used in paint and stone and tile treatments will be released to sewer during use and 45% of floor polishes and waxes will be released during use. For this scenario, it will be assumed that 100% of the import volume of the notified polymer used in inks will be printed on paper and 50% of this paper will be recycled. The resulting concentration in sewage effluent on a nationwide basis is estimated as follows:

Predicted Environmental Concentration (PEC) for release to the aquatic compartment during use		
Total Annual Import Volume	3,000	kg/year
Portion used in paints and stone and tile treatments	60	%
Portion expected to be released to sewer from use in paints and stone and tile treatments	5	%
Annual quantity of polymer released to sewer from use in paints and stone and tile treatments	90	kg/year
Portion used in floor polish and wax	30	%
Portion expected to be released to sewer from use in floor polish and wax	45	%
Annual quantity of polymer released to sewer from use in floor polish and wax	405	kg/year
Portion used in ink	10	%
Portion expected to be released to sewer from use in ink	50	%
Annual quantity of polymer released to sewer from use in ink	150	kg/year
Total annual quantity of polymer released to sewer	645	kg/year
Days per year where release occurs	260	days/year
Daily chemical release:	2.48	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Effluent concentration	0.55	µg/L

Based on the above calculations, the worst-case concentration for the notified polymer in effluent due to the combined releases to STP from reformulation and use is 0.82 µg/L. Therefore, the PEC for the aquatic compartments are calculated as follows:

Predicted Environmental Concentration (PEC) for release to the aquatic compartment during use		
Combine effluent concentration	0.82	µg/L
Dilution Factor – River	1	
Dilution Factor – Ocean	10	
PEC – River	0.82	µg/L
PEC – Ocean	0.082	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified polymer in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.82 µg/L may potentially result in a soil concentration of approximately 5.5 µg/kg. Assuming accumulation of the notified polymer in soil for 5 and 10 years under repeated irrigation, the concentration of notified polymer in the applied soil in 5 and 10 years may be approximately 28 µg/kg and 55 µg/kg, respectively.

PEC for PFHxA and long chain perfluoroalkyl substances

The notified polymer is assumed to degrade and ultimately form the persistent degradant, PFHxA. However, the yield and rate of conversion of the notified polymer to PFHxA has not been established as characterisation

of the degradation products was not undertaken in the biodegradation study. Environmental monitoring data shows that PFHxA, and PFOA which PFHxA-chemistry is replacing, is widely found in the environment, particularly in fresh water close to industrial sources, but also in some biota. Water appears to be the main compartment where PFHxA is found. High measured concentrations of both PFHxA and PFOA in surface waters in Germany have been associated with the legal application of waste materials to agricultural soils (Skutlarek *et al*., 2006) indicating that these chemicals have the potential to enter the aquatic compartment following initial release into the soil compartment.

Some larger available data sets from the literature (McLachlan *et al*., 2007; Skutlarek *et al*., 2006; Nakayama *et al*., 2007; So *et al*., 2007; Ahrens *et al*., 2009) include monitoring from a range of rivers in Europe, the USA and China, along with data from the Atlantic Ocean. Using these data ($n \geq 60$), the 10th, 50th and 90th percentile concentrations for PFHxA are 1.0, 6.15 and 22.5 ng/L respectively, while those for PFOA are 2.94, 11.85 and 231.9 ng/L respectively. As use of chemicals that degrade to form PFHxA increases, levels of PFHxA may build up further in the environment.

PFHxA and other poly- and perfluoroalkyl substances have also been found in landfill leachate, with concentrations of PFHxA ranging from 270 – 790 ng/L (Huset *et al*., 2011). As landfills are reservoirs of solid waste, and receive waste water treatment plant sludge, which may contain poly- and perfluoroalkyl substances, landfills have the potential to continue to release PFHxA and homologues well into the future.

Historically, release of poly and perfluoroalkyl substances into the environment has been linked to direct releases of low molecular weight poly- and perfluoroalkyl compounds, such as poly- and perfluoroalkyl monomers during polymer manufacture and reformulation processes, rather than breakdown of the polymers themselves. In order to limit the extent of direct release of potential PFHxA precursors to the environment, it is recommended that control measures be implemented to minimise the residual weight percentage of unreacted poly- and perfluoroalkyl monomer constituents and impurities in the notified polymer to the extent practicable. Zhao *et al*. (2013) report that fluorotelomer alcohol (FTOH) residual raw material content in FTOH-based polymeric products is generally less than 0.1%. Efforts have also been made globally to control releases of perfluoroalkyl acids, such as PFOA and potential precursors, by reducing the presence of residual poly- and perfluoroalkyl monomers and impurities in polymers. It is recommended that the total weight of residual monomers and impurities in the notified polymer containing polyfluoroalkyl functionality should not exceed the levels attainable utilising international best practice and the levels are further reduced using available technological advances, to the extent practicable.

By reducing the presence of residual poly- and perfluoroalkyl monomers and impurities in polymers, it is expected that indirect releases from the degradation of polyfluoroalkyl substances will become a significant source of persistent poly- and perfluoroalkyl substances in the environment in the future. PFHxA is already being detected in the environment and as the long chain poly- and perfluoroalkyl substances are phased out in preference for short-chain polyfluoroalkyl chemistry containing a six-carbon perfluorohexyl moiety, the environmental levels of PFHxA are expected to increase.

Half-lives of polyfluoroalkylated polymers in aerobic soil have so far been found to be indeterminate (Russell *et al*., 2008; Russell *et al*., 2010; Washington *et al*, 2009). The half-lives of PFHxA in various environmental media are also unknown and its partitioning behaviour is uncertain. Further, degradation products of the notified polymer are unknown as characterisation was not undertaken in the biodegradation study. Therefore, a PEC for indirect releases of PFHxA arising from proposed use and disposal of the notified polymer in Australia cannot be determined.

7.2. Environmental Effects Assessment

Ecotoxicological data for the notified polymer are summarised in the table below. Details of the studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity		
Rainbow trout	96 h LC50 = 36.7 mg/L	Harmful to fish
Rainbow trout	96 h LC50 = 33.5 mg/L	
Invertebrate Toxicity		
Daphnia magna	48 h EC50 = 28.8 mg/L	Harmful to aquatic organisms

Algal Toxicity		
Green algae	72 h EC50 = 88.3 mg/L 72 h NOEC = 27.5 mg/L	Harmful to algae

Based on the measured data, the notified polymer is considered harmful to fish, aquatic invertebrates and algae on an acute basis. The notified polymer is formally classified under the Globally Harmonised System of Classification of Chemicals (GHS; United Nations, 2009) as "Acute Category 3: Harmful to aquatic life". The long-term hazard has not been measured for the notified polymer, therefore the notified polymer is not formally classified under the GHS. Based on the rapid degradability of the notified polymer, it is not classified under the GHS for long term hazard.

Effects of PFHxA and long chain perfluorocarboxylic acids
There are only limited available toxicity data for PFHxA to organisms, and these are limited to aquatic organisms. Based on the available literature, the most sensitive trophic level is algae. Latala *et al*., (2009) reported the 72-hour median effect concentrations (72 h EC50) for three marine species as follows: 1.0 mg/L for blue green algae (*Geitlerinema amphibium*); 1.4 mg/L for diatom (*Skeletonema marinoi*); and, 4.0 mg/L for green algae (*Chlorella vulgaris*). The data indicates that PFHxA is toxic to algae on an acute basis. The study also investigated the toxicity of PFOA to the three marine species: 0.25 mg/L for blue green algae; 0.37 mg/L for diatom; and, 0.98 mg/L for green algae. The data indicates that PFOA is very toxic to algae on an acute basis and demonstrate decreased toxicity of PFHxA compared with PFOA to three species tested.

Other data indicate that PFOA is not harmful to fish and aquatic invertebrates on an acute basis with median lethal or effect concentrations (L(E)C50) of greater than 100 mg/L (US FDA, 2009). The majority of the available data for the ammonium salt of PFOA (US EPA, 2002) show this substance is largely expected to be not harmful to fish and aquatic invertebrates, although one reported endpoint (fathead minnow 96 h LC50 = 70 mg/L) is below 100 mg/L.

Giesy *et al*. (2010) reported the relationship between increasing carbon chain length and increasing toxicity. Therefore, PFHxA is expected to have a less problematic ecotoxicological profile than PFOA and other long chain perfluorocarboxylic acids it is expected to replace. Long-term effects data that reflect or model the periods over which perfluorocarboxylic acids are present in the environment are not available for PFHxA or long chain perfluorocarboxylic acids. Therefore, the long-term hazard to aquatic organisms has not been adequately established and is unknown.

7.2.1. Predicted No-Effect Concentration

The most sensitive ecotoxicological endpoint for the notified polymer was the 48-hour median effect concentration (48 h EC50) for daphnia. This endpoint was used to calculate the predicted no-effect concentration (PNEC). An assessment factor of 100 was used as measured data was available for three trophic levels.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (*Daphnia*; 48 h)	28.8	mg/L
Assessment Factor	100	
PNEC:	288	µg/L

7.3. Environmental Risk Assessment

Risk assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.82	288	< 0.01
Q - Ocean	0.082	288	< 0.01

Based on a worst-case scenario, the risk quotients (Q) for river and marine waters are much less than 1, indicating the notified polymer will not be present at ecotoxicologically significant concentrations in surface waters. The available data indicates that the notified polymer is not harmful to aquatic life. The polymer itself is rapidly degradable. It is not expected to persist in the environment therefore reducing its potential to bioaccumulate. However, the notified polymer is assumed to degrade to form PFHxA which may be delocalised from points of release.

Perfluoroalkyl substances are expected to be very persistent in the environment (for example, PFOA:

$t_{½}$ (hydrolysis) > 200 years; US EPA 2002) but PFHxA is considered to have low potential for bioaccumulation. There is limited evidence in the published literature of PFHxA toxicity to aquatic organisms on an acute basis, although it is reported to be toxic to marine algae. There is no available data on the long-term aquatic effects of PFHxA.

The main environmental risks associated with polyfluoroalkyl polymers relate to the release of perfluoroalkyl degradation products such as PFHxA. However, it is not possible to quantify the long-term risks of PFHxA to the environment due to knowledge gaps both in predicting environmental concentrations from indirect sources of release and its long-term environmental effects. . To date, the available data on environmental concentrations of PFHxA indicate a low risk of environmental toxicity. However, the long-term environmental risk profile of PFHxA is currently unknown, and further long term research should ideally be undertaken to characterise this risk.

PFHxA is already wide-spread in surface waters and biota. Continuing release of PFHxA which has no known breakdown mechanism (at least in soil and water) could result in increasing environmental concentrations over time. Hence, there is potential for ecotoxicologically significant concentrations to eventually be reached following its accumulation in the environment. In this eventuality, precursors of PFHxA such as the notified polymer cannot be recalled after release and are a potential source of PFHxA in the environment even long after their use ceases. Thus, use and disposal of the notified polymer increases the environmental risk profile of PFHxA. The notified polymer also contains impurities which are assumed to degrade to form PFHxA. Therefore, considering the dispersive use pattern of the notified polymer, it is recommended to reduce the impurities in the notified polymer that breakdown to form PFHxA, to the extent possible.

Conclusions
On the basis of the PEC/PNEC ratio and assessed use pattern, the notified polymer itself is not considered to directly pose an unreasonable short-term risk to the aquatic environment.

However, degradants of the notified polymer, along with associated impurities and residual monomers of the notified polymer, are potential precursors of the very persistent chemical, PFHxA. The assessed use pattern of the notified polymer does not control the release of breakdown products into the environment during use and after disposal and the long-term environmental risk profile of PFHxA is currently unknown. Consequently, the long-term risk profile of the notified polymer and its degradation products is unknown. This situation may change if further data on the environmental behaviour of the notified polymer and its poly- and perfluoroalkylated degradation products (including PFHxA) were to become available.

The notified polymer is a potential precursor for PFHxA in the environment, PFHxA, is environmentally persistent and has potential to be globally distributed. However, the ecotoxicological profile and bioaccumulation potential of PFHxA is considered to be less problematic when compared with long chain (C8 and above) perfluoroalkyl acids that PFHxA is expected to replace. Nonetheless, it is recommended that the introduction and use of chemicals that degrade to release PFHxA and other very persistent poly- and perfluoroalkyl compounds should be considered a short-term measure until suitable alternatives, with less persistent chemistry, are identified.

In order to limit the extent of direct release of potential PFHxA and long chain perfluorocarboxylic acid precursors to the environment, it is recommended that control measures be implemented to minimise the residual weight percentage of unreacted polyfluoroalkyl monomer constituents and impurities in the notified polymer to the extent practicable. Where possible, the total weight of residual monomers and impurities in the notified polymer containing polyfluoroalkyl functionality should not exceed the levels attainable utilising international best practice. It is recommended that the levels remain within this range and are further reduced using available technological advances, to the extent practicable.

8. RISK ASSESSMENT FOR PREVIOUS EXTENSION APPLICATION (EX/209)

There are no changes under the proposed extension to the introduction volume, the use, or the occupational, public and environmental exposure. However, the additional 28-day repeated dose oral (gavage) toxicity in mice study report which was provided with this extension application showed that the notified polymer produced significant health effects (target organs: liver/spleen) in mice at concentrations of ≥ 125 mg/kg bw/day, with the NOAEL being 30 mg/kg bw/day. The NOAEL in the 28-day study is similar to that observed in the previous 90 day oral toxicity study with a one generation reproductive and developmental study in rats where the NOAEL

was 25 mg/kg bw/day. Subsequently the extension application is not expected to impact on the original human health and environmental risk assessment and recommendations.

9. RISK ASSESSMENT FOR PREVIOUS EXTENSION APPLICATION (EX/213)

There are no changes under the proposed extension to the introduction volume, the use, or the occupational, public and environmental exposure. However, the concentration of the notified chemical in the imported cleaning products will be < 0.1% but only for professional use with a total imported volume of < 1kg per annum. Therefore, the extension application is not expected to impact on the original human health and environmental risk assessment and recommendations.

10. RISK ASSESSMENT FOR CURRENT EXTENSION APPLICATION

There are no changes under the proposed extension to the introduction volume, the use, or the occupational, public and environmental exposure. Therefore, the extension application is not expected to impact on the original human health and environmental risk assessment and recommendations.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Vapour Pressure 0.24 kPa at 25.176 ºC

Method In house method
Remarks A sample was loaded into a static cell which was degassed at 0 °C before being heated to 150 °C whilst measuring the pressure.
Test Facility Not specified

Water Solubility 0.168 g/L at 20 ºC
0.142 g/L at 12 ºC

Method In-house method
Remarks Six separate 100 – 104 mg samples of test substance were added to 200 mL of Haskell Well Water (HWW) and stirred for 25 hours at 12 and 20 ºC. The samples were centrifuged and aliquots of the supernatant were analysed by LC/MS resulting in well-resolved peaks. The initial study produced a higher than expected solubility of the test substance at 12 ºC, likely due to the difficulty separating the solution and test substance after centrifuging. An additional solubility study was performed at 12 ºC by adding approximately 35 mg of test substance to 200 mL of HWW in triplicate. The resulting solubility from the additional study was determined to be more representative of the solubility of the test substance.
Test Facility DuPont (2012)

Partition Coefficient (n-octanol/water) log Pow = 4.39 to 4.89 at 20 ºC

Method OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks HPLC Method. The test substance was eluted as a series of peaks. Minimal peak tailing was observed at the end of the series.
Test Facility DuPont (Unspecified date)

Adsorption/Desorption $\log K_{oc} < 2.97$

Method Calculated using the Chiou equation and Kenaga equation
Remarks The Chiou equation is used for halogenated molecules and the Kenaga equation is used for a variety of organic molecules. Both equations rely on knowledge of the solubility of the molecule. The equations are as follows:

Chiou equation: $\log Koc = -0.557 \times \log S + 4.277$ (where S = solubility in µmol/L)

Kenaga equation: $\log Koc = -0.55 \times \log S + 3.64$ (where S = solubility in mg/L)

Test Facility Calculated by DuPont

Stability Stable up to 96 hours at 6 ºC and 20 ºC

Method In-house method
Remarks 25.3 mg of the test substance was added to 500 mL of Haskell Well Water (HWW). After stirring the solution, stability solutions were prepared in HWW up to nominal concentrations of 1.00 mg test substance/L. One solution was refrigerated at 6 ºC for 96 hours and the other was kept at a temperature of 20 ºC for 96 hours.
Test Facility DuPont (2012)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified polymer – variation 2

METHOD
- Species/Strain: Rat/Sprague-Dawley
- Vehicle: None
- Remarks - Method: No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1 female	5000	1/1
2	1 female	175	0/1
3	1 female	550	0/1
4	1 female	1750	1/1
5	1 female	550	0/1
6	1 female	1750	1/1
7	1 female	550	0/1
8	1 female	1750	1/1

- LD50: 1030 mg/kg bw
- Signs of Toxicity: No signs of toxicity were observed in the animal treated at 175 mg/kg bw. Hypoactivity and piloerection were observed on the first day in animals treated at 550 and 1750 mg/kg bw, with abnormal gait observed in animals treated at 1750 mg/kg bw. The 550 mg/kg bw animals appeared healthy for the remainder of the study period and a weight gain was observed. Mortalities occurred within 3 days for the animals treated at 1750 mg/kg bw and on day 1 for the 5000 mg/kg bw animal.
- Effects in Organs: Red intestines were observed in animals treated at 1750 and 5000 mg/kg bw.

CONCLUSION: The notified polymer is harmful via the oral route.

TEST FACILITY: Eurofins (2010a)

B.2. Acute toxicity – oral

TEST SUBSTANCE: Notified polymer – variation 1

METHOD
- Species/Strain: Rat/Sprague-Dawley
- Vehicle: Administered as recieved
- Remarks - Method: No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1 female	5,000	1/1
2	2 female	175	0/2
3	4 female	550	1/4
4	3 female	1,750	3/3

- LD50: 550 mg/kg bw
- Signs of Toxicity: In the animals treated at 175 mg/kg bw, hypoactivity, hunched posture

	and reduced faecal volume were observed. In the 550 mg/kg bw dose group one animal died on the first day with hypoactivity and piloerection noted prior to death. Clinical signs noted in the surviving rats in the 550 mg/kg bw dose group were hypoactivity, piloerection, hunched posture, ano-genital staining and reduced faecal volume. In the 1,750 and 5,000 mg/kg bw groups all animals died within 1 day of dosing, with clinical signs prior to death including hypoactivity, abnormal posture and gait and piloerection.
Effects in Organs	No gross abnormalities were noted in animals that survived to the end of the study. In animals that died prematurely red discoloration of the intestines was noted.
Remarks - Results	All surviving animals gained weight over the course of the study.
CONCLUSION	The notified polymer is harmful via the oral route.
TEST FACILITY	Eurofins (2010b)

B.3. Acute toxicity – oral

TEST SUBSTANCE	Notified polymer – variation 3
METHOD	OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure.
Species/Strain	Rat/Crl:CD(SD)
Vehicle	Test substance administered as supplied.
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1 female	175	0/1
2	3 female	550	0/3
3	3 female	1,750	3/3

LD50	1,030 mg/kg bw
Signs of Toxicity	In the animal treated at 175 mg/kg bw, ataxia, decreased muscle tone, low posture, pupil mydriasis (prolonged dilation), curled toes, splayed limbs, bobbing head and abnormal gait were observed for up to 1 day after dosing. In the animals treated at 550 mg/kg bw, ataxia, decreased muscle tone, high or low posture, pupil mydriasis (prolonged dilation), fast breathing, stained skin/fur, splayed limbs, bobbing head, paralysis and abnormal gait were observed for up to 2 days after dosing. All 3 rats dosed at 1,750 mg/kg bw died on the first day, with clinical signs including ataxia, cold to touch, immobility, moribundity decreased muscle tone, paralysis, low posture, pupil mydriasis (prolonged dilation), abnormal breathing, wet fur, salivation, splayed limbs and abnormal gait were observed.
Effects in Organs	No gross abnormalities were noted in animals that survived to the end of the study. In one animal that died prematurely red discoloration of the intestines and nose and a white substance in the esophagus was noted.
Remarks - Results	All surviving animals gained weight over the course of the study.
CONCLUSION	The notified polymer is harmful via the oral route.
TEST FACILITY	DuPont (2010a)

B.4. Acute toxicity – dermal

TEST SUBSTANCE	Notified polymer – variation 3

METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test
Species/Strain	Rat/Crl:CD(SD)
Vehicle	None
Type of dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5000	0/10

LD50	> 5,000 mg/kg bw
Signs of Toxicity - Local	None
Signs of Toxicity - Systemic	None
Effects in Organs	A single incidence of kidney dilation was observed at necropsy but was considered to be a common finding in rats and was not considered to be treatment related.

CONCLUSION The notified polymer is of low toxicity via the dermal route.

TEST FACILITY DuPont (2010b)

B.5. Acute toxicity – dermal

TEST SUBSTANCE Notified polymer – variation 1

METHOD	OECD TG 402 Acute Dermal Toxicity.
Species/Strain	Rat/Sprague-Dawley
Vehicle	Test substance administered as supplied
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5,000	0/10

LD50	> 5,000 mg/kg bw
Signs of Toxicity - Local	There were no test substance related dermal reactions.
Signs of Toxicity - Systemic	There were no deaths or test substance related clinical signs.
Effects in Organs	No gross abnormalities were noted upon necropsy at the end of the study.
Remarks - Results	All animals gained weight during the course of the study.

CONCLUSION The notified polymer is of low toxicity via the dermal route.

TEST FACILITY Eurofins (2010c)

B.6. Acute toxicity – inhalation

TEST SUBSTANCE Notified polymer – variation 1

METHOD	Equivalent to OECD TG 403 Acute Inhalation Toxicity
Species/Strain	Rat/Crl:CD(SD)
Vehicle	None
Method of Exposure	Nose-only exposure
Exposure Period	4 hours
Physical Form	liquid aerosol
Particle Size	MMAD = 1.1-1.8 μm (GSD = 2.0)

Remarks - Method Necropsy was not conducted for this study.

RESULTS

Group	*Number and Sex of Animals*	*Concentration (mg/L)*	*Mortality*
1	5 male	0.61 ± 0.29	0/5
2	5 male	5.9 ± 1.0	0/5

LC50 > 5.9 mg/L

Signs of Toxicity There were no mortalities in the study. Just after exposure, red discharge from the nose and eyes, and a clear discharge from the mouth were observed in animals treated at 0.61 mg/L but were considered to be related to nose-only administration and therefore not related to treatment. Slight weight loss (1-7 g) was observed over the first day in the group but body weight increases were observed on day 2.

Lethargy, laboured breathing and lung noise were observed in the animals treated at 5.9 mg/L but resolved within one day. Additional signs of toxicity include red discharge from the nose, ruffled fur, irregular respiration, wet perineum and red stain on the face, resolving by day 4. Animals in this group lost body weight (41-42 g) after exposure with body weight gains occurring on day 3.

CONCLUSION The notified polymer is of low toxicity via inhalation.

TEST FACILITY DuPont (2010c)

B.7. Irritation – skin

TEST SUBSTANCE Notified polymer – variation 3

METHOD
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 Females
- Vehicle: None
- Observation Period: 72 Hours
- Type of Dressing: Semi-occlusive
- Remarks - Method: No significant protocol deviations

RESULTS

Remarks - Results Erythema and oedema scores were zero for all animals at all observation points.

CONCLUSION The notified polymer is non-irritating to the skin.

TEST FACILITY Eurofins (2010d)

B.8. Irritation – skin

TEST SUBSTANCE Notified polymer – variation 1

METHOD
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 (1 Male and 2 females)
- Vehicle: Test substance administered as supplied
- Observation Period: 72 Hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviations.

RESULTS

Remarks - Results	There were no deaths or test substance-related clinical signs or remarkable body weight changes during the study period. No signs of erythema or oedema were observed at any time.

CONCLUSION The notified polymer is non-irritating to the skin.

TEST FACILITY Eurofins (2010e)

B.9. Irritation – skin

TEST SUBSTANCE Notified polymer – variation 2

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 Females
Vehicle	Test substance administered as supplied.
Observation Period	72 Hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

Remarks - Results	There were no deaths or test substance-related clinical signs or remarkable body weight changes during the study period. No signs of erythema or oedema were observed at any time.

CONCLUSION The notified polymer is non-irritating to the skin.

TEST FACILITY Eurofins (2010f)

B.10. Irritation – eye

TEST SUBSTANCE Notified polymer – variation 1

METHOD OECD TG 405 Acute Eye Irritation/Corrosion

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 male
Observation Period	72 hours
Remarks - Method	Prior to instillation of the test substance, two to three drops of ocular anaesthetic (tetracaine hydrochloride 0.5%) were placed into both eyes of each animal.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	1.0	1.0	1.0	2	< 72 hours	0
Conjunctiva: chemosis	0.3	0.3	0	1	< 48 hours	0
Conjunctiva: discharge	1.0	0.7	0.7	2	< 72 hours	0
Corneal opacity	0	0	0	0	no effect	no effect
Iridial inflammation	0	0	0	0	no effect	no effect

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results	Irritant effects observed were reversible within 3 days and were below levels required for classification.

CONCLUSION	The notified polymer is slightly irritating to the eye.
TEST FACILITY	Eurofins (2010g)

B.11. Irritation – eye

TEST SUBSTANCE	Notified polymer – variation 2
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Observation Period	4 days
Remarks - Method	Prior to instillation of the test substance, two to three drops of ocular anaesthetic (tetracaine hydrochloride 0.5%) were placed into both eyes of each animal.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	1	1.7	1	2	< 4 days	0
Conjunctiva: chemosis	0.3	0.7	0.3	1	< 72 hours	0
Conjunctiva: discharge	1	1	0.7	3	< 72 hours	0
Corneal opacity	0	0	0	1	< 24 hours	0
Iridial inflammation	0	0.7	0.3	1	< 72 hours	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results	A single application of the test material to the non-irrigated eye of three rabbits produced iridial inflammation and moderate conjunctival irritation in all animals and corneal opacity in two animals. Two treated eyes appeared normal at the 72 hour observation with the remaining treated eye appearing normal at the 4 day observation. There were no deaths or test substance-related clinical signs or remarkable body weight changes during the study period.
CONCLUSION	The notified polymer is slightly irritating to the eye.
TEST FACILITY	Eurofins (2010h)

B.12. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified polymer – variation 1
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay (2002 version)
Species/Strain	Mouse/CBA/JHsd (female)
Vehicle	N,N-dimethylformamide
Remarks - Method	An irritation screening study was not conducted and 100% was selected as the highest concentration based on the lack of severe irritant effects observed with the test substance. The main study was conducted using 5 mice/group at 0, 5, 25, 50 or 100% concentration. A concurrent positive control was conducted using 25% hexylcinnamaldehyde (HCA) in the vehicle (5 mice/group).

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	743	n/a
5	1140	1.54
25	1560	2.10
50	1357	1.83
100	-	-
Positive Control		
25 (HCA)	5494	7.40

Remarks - Results

The animals treated at 100% concentration lost 17-21% of the initial body weights by day 2. Clinical signs in this group included wet fur, dehydration and decreased faeces. This group was sacrificed on day 2 due to excessive toxicity and were not evaluated for lymphocyte proliferation potential.

Dehydration was observed in one mouse treated at 50% concentration on day 2. Wet fur was observed in one mouse treated at 25% and in all mice treated at 50%. Mice treated at 50% concentration lost 7-12% of the initial body weight by day 2 but gained weight by day 5. One control group mouse lost body 18% of the initial body weight by test day 2 but gained weight by day 5.

The disintegrations per minute (dpm) value for one animal in the vehicle control group was higher than the range of historical controls, and was considered an outlier. This value was not included in the data analysis.

There were no increases in stimulation index indicative of a positive response in concentrations up to 50%. Results were not available for the 100% group as the animals were sacrificed early due to clinical signs and weight loss. A positive response was observed in the positive control group using hexylcinnamaldehyde (HCA).

CONCLUSION

There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified polymer.

TEST FACILITY

DuPont (2010d)

B.13. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE

Notified polymer – variation 3

METHOD

OECD TG 429 Skin Sensitisation: Local Lymph Node Assay (2002 version)

Species/Strain: Mouse/CBA/JHsd (female)

Vehicle: N,N-dimethylformamide

Remarks - Method

An irritation screening study was not conducted and 100% was selected as the highest concentration based on the lack of severe irritant effects observed with the test substance.

The main study was conducted using 5 mice/group at 0, 5, 25, 50 or 100% concentration. A concurrent positive control was conducted using 25% hexylcinnamaldehyde (HCA) in the vehicle (5 mice/group).

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	1233.4	n/a
5	1621.8	1.31
25	2080.2	1.69
50	2988.8	2.42
100	2630.8	2.13
Positive Control		
25 (HCA)	8641.0	7.01

Remarks - Results

Three animals treated at 100% concentration exhibited wet fur for 2 days after the test substance was applied. The average body weight of this group decreased slightly over the time of the study.

Statistically significant increases in cell proliferation measurements compared to the control group were seen in the 25, 50 and 100% concentration groups. However, the stimulation index remained below 3 for the test substance at all of the concentrations.

A positive response was observed in the positive control group using hexylcinnamaldehyde (HCA).

CONCLUSION

There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified polymer.

TEST FACILITY

DuPont (2010e)

B.14. Genotoxicity – bacteria

TEST SUBSTANCE

Notified polymer – variation 1

METHOD

OECD TG 471 Bacterial Reverse Mutation Test – Plate Incorporation Procedure

Species/Strain

S. typhimurium: TA1535, TA1537, TA98, TA100
E. coli: WP2uvrA

Metabolic Activation System

S9 fraction from Aroclor 1254 induced rat liver

Concentration Range in Main Test

a) With metabolic activation: 333-5000 µg/plate
b) Without metabolic activation: 333-5000 µg/plate

Vehicle

Dimethyl sulfoxide

Remarks - Method

No significant protocol deviations.

A cytotoxicity assay was conducted in all strains (in duplicate) in the presence and absence of metabolic activation between 33.3-5000 µg/plate. These plates subsequently became test 1. Vehicle and positive controls were used in parallel with the test substance. Plates in test 2 were conducted in triplicate.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	>5000	>5000	>5000	negative
Test 2	-	>5000	>5000	negative
Present				
Test 1	>5000	>5000	>5000	negative

Test 2	-	>5000	>5000	negative

Remarks - Results: The negative controls were within historical controls, and the positive controls showed large increases in revertants, confirming the validity of the test system.

CONCLUSION: The notified polymer was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY: DuPont (2010f)

B.15. Toxicity to reproduction – 90-day gavage study with one generation study

TEST SUBSTANCE: Analogue 1

METHOD: 90-Day Gavage Study with One-Generation Reproduction Toxicity Study
- Species/Strain: Rat/Crl:CD®(SD)IGS BR
- Route of Administration: Oral – gavage
- Exposure Information: Oral toxicity study: 90 - 96 days dosing
  Reproductive toxicity study: 72 days prior to cohabitation until weaning (postnatal day 21).
- Vehicle: Water
- Remarks – Method: A range-finding study was conducted at concentrations up to 1,000 mg/kg bw/day. Due to body weight loss and reductions in body weight gain the maximum dose level in the main study was set at 500 mg/kg bw/day.

  10 Rats/sex/group were used in the 90 day exposure evaluation and were necropsied after 95 or 96 days of exposure for male and female rats respectively. 5 Rats/sex/group were used for biochemical, clinical, anatomic and fluorine evaluations and were used for recovery evaluations 3 months after administration of the test substance had ended. 20 Rats/sex/group were used for reproductive evaluations and lastly 10 rats/sex in each of the high dose and control groups were used in a 1-month recovery. An additional 5 rats/sex/dose were dosed for 10 days and used for evaluation of hepatic biochemical analysis.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	45 per sex	0	2/90
2	35 per sex	25	0/70
3	35 per sex	100	1/70
4	45 per sex	500	2/90

Mortality and Time to Death

1 Male rat in the 100 mg/kg bw/day group and 1 female rat in the control group died of trauma secondary to the bleeding process. 1 Male rat in the control group and 2 male rats dosed with 500 mg/kg bw/day died of kidney inflammation and/or obstruction.

Effects on adult animals:

Clinical Observations

Compared to control animals lower body weight and lower body weight gain were generally observed in the 100 and 500 mg/kg bw/day dose groups. In the 500 mg/kg bw/day dose groups reductions were statistically significant during most test days and weekly intervals of the study. Male rats in the 100 mg/kg bw/day group had mean body weights lower than the control over the entire dosing phase and the reduction was statistically significant on days 35-70. No effects on body weight or body weight gain were seen in female rats in the 100 or 25 mg/kg bw/day dose groups. Weight effects were more readily reversible in males than females over the three month recovery period.

Male rats dosed with 500 mg/kg bw/day exhibited reduced mean food consumption and food efficiency compared to controls. Males dosed with 100 mg/kg bw/day also showed reductions in mean food efficiency. These changes tended to be reversible over the recovery period. Female rats did not display changes in mean food consumption though there were reductions in mean food efficiency in females dosed at 500 mg/kg bw/day.

There were statistically significant increases in the incidences of wet fur (chin/perineum), clear discharge from the mouth, hair loss and stained fur/skin in male and female animals in the 500 mg/kg bw/day dose group. Statistically significant increases in clear discharge from the mouth (both sexes) and in hair loss (females) was observed in the 100 mg/kg bw/day dose group.

Statistically significant reductions in forelimb (25 %) and hindlimb (18 %) strength were observed in male animals in the 500 mg/kg bw/day group at the end of the 90 day dosing period but were partially reversible with only the reduction in hindlimb (15 %) strength being still significantly lower at the end of the recovery period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Male and female animals in the 500 and 100 mg/kg bw/day dose groups had reductions in parameters relating to red blood cell mass (haemoglobin, haematocrit, and/or red cell count), all findings were completely reversed after three months of recovery. Male rats in the 500 mg/kg bw/day group had increased alanine aminotransferase and sorbitol dehydrogenase during the dosing period, which persisted during the recovery period, but these were not present in female animals at this dose at the end of the study. Alkaline phosphatase and total bilirubin were increased in male and female animals in the 500 mg/kg bw/day group during the dosing period with the effects not present during the recovery period. Minimal but statistically significant increases in parameters reflecting glomerular filtration (urea nitrogen, creatine and inorganic phosphorus) were present in male and female animals, which correlate with histologic evidence of renal failure in animals in the 500 mg/kg bw/day group. The effects were not observed at the end of the recovery period. Decreased sodium and chloride levels were seen in male (500 mg/kg bw/day) and female (100 and 500 mg/kg bw/day) animals. Statistically significant and dose dependent increases in total protein and albumin were observed in both male and female animals during the dosing period. Total protein and albumin levels were not significantly elevated at the end of the 3 month recovery period. Globulin levels were only significantly increased during the recovery period suggesting this change may not be treatment related. Male and female animals in the 100 and 500 mg/kg bw/day dose groups had increased calcium and cholesterol levels and decreased triglyceride concentrations during the dosing period, which reverted to levels similar to the control values by the end of the 3 month recovery period. Male and female animals dosed with 500 mg/kg bw/day of the test substance had decreased urine specific gravity/osmolality, urine pH and urine protein concentration with the effects reversed during the recovery period. Plasma and urine fluoride levels in males and females showed a dose dependent increase and urine fluoride values were still elevated at the end of the recovery period although they had decreased considerably compared to the end of the study.

The rate of β-oxidation, which is a measure of peroxisome proliferation, was statistically significantly increased in male rats at the 10 day point (171 and 286% in dose groups 100 and 500 mg/kg bw/day respectively) and at the 90 day point (181% in the 500 mg/kg bw/day dose group) and 1 month recovery (195% in the 500 mg/kg bw/day dose group) but had returned to control values by the end of the 3 month recovery. The increases in the rate of β-oxidation was accompanied by an increase in the liver weights of animals in the same dose groups. There was a decrease in the rate of β-oxidation in female rats dosed with 25 mg/kg bw/day of the test substance at the 10 day point and an increase (131 %) in animals dosed with 500 mg/kg bw/day of the test substance at the 1 month recovery test point. The changes in the rate of β-oxidation in female rats was considered to be incidental by the study authors due to the lack of dose response in the decrease and the small difference in the increase over the controls.

Effects in Organs
Increased mean liver weights and/or microscopic hepatocellular hypertrophy were present in male animals in all the dose groups and female animals in the two highest dose groups at 90 days and in male and female animals in the 500 mg/kg bw/day dose group at the 1 and 3 month recovery (with the exception of the absence of hepatocellular hypertrophy at the three-month recovery point).

Mean kidney weights (absolute and relative to the body or brain weight) were significantly higher than controls for female animals in the 100 or 500 mg/kg bw/day dose groups. The mean kidney weights (relative to the body) were significantly higher in the 1 and 3 month recovery groups in female animals dosed with

500 mg/kg bw/day. In male animals mean kidney weights (relative to the body) were significantly higher in the 100 and 500 mg/kg bw/day dose groups and in the 500 mg/kg bw/day 1 month recovery group. The incidence of chronic progressive nephropathy was significantly increased in both sexes at the higher doses and may partially explain the higher liver weights seen. This effect was still observed in females at the 3 month recovery, though not in males.

The mean spleen weight and spleen weight relative to the brain was significantly decreased in males in the 500 mg/kg bw/day dose group. The mean spleen weight relative to the brain was significantly increased in females in the 100 and 500 mg/kg bw/day dose groups. The mean spleen weight relative to the body weight was significantly increased in female animals in the 500 mg/kg bw/day dose group both at the end of the 13 week dosing period and at the 3 month recovery, but not in the 1 month recovery. Significantly increased incidences of extramedullary hematopoiesis were observed in both sexes in the 100 and 500 mg/kg bw/day dose groups at the 90 day sacrifice. The incidence of extramedullary hematopoiesis remained significantly increased in male and female animals in the 500 mg/kg bw/day dose group at the 1 month recovery; there were no significant increases in any of the treatment groups at the 3 month recovery. Increased pigment in the spleen was observed in male animals in the 100 and 500 mg/kg bw/day dose group at the 90 day sacrifice and in the 500 mg/kg bw/day dose group at the 1 month recovery. In female animals significantly increased pigment in the spleen was observed in the 500 mg/kg bw/day dose group at the 90 day sacrifice and in the 100 and 500 mg/kg bw/day dose groups at the 3 month recovery.

Other changes in organ weights were predominantly decreases in mean organ weights in male animals in the 500 mg/kg bw/day dose group at the 90 day sacrifice and was significant in the heart, brain, thymus, adrenal glands and epididymis.

Follicular hypertrophy in the thyroid glands was present in numerous male and female rats in the 100 and 500 mg/kg bw/day dose groups at the 90 day sacrifice and in 1 male rat in the 25 mg/kg bw/day dose group. At the 1 month recovery follicular hypertrophy was still present in the 500 mg/kg bw/day dose group (the only dose group measured at this time point) in both sexes, but at the three month recovery was only present in male animals in the 500 mg/kg bw/day dose group. In the absence of hormonal data to demonstrate maintenance of normal hormonal levels, the thyroid hypertrophy was considered to be potentially adverse by the study authors. Stippled, granular, clumped and/or diffusely basophilic colloid was found in follicles in thyroids from both the controls and all treated groups with an increased incidence and severity in the treated groups. The alterations in the colloid were not associated with adverse cellular morphologic changes and hence not considered to be of toxicological significance.

Reproductive Effects

The mean estrous cycle length was significantly greater in treated animals. However, there was no dose response relationship and values were within historical controls and hence the changes are considered to be of uncertain toxicological significance. In addition there were no differences between the treated and control groups on the percent of days in estrus, diestrus or proestrus or the mean precoital interval.

There were statistically significant decreases in the number of epididymal sperm (88%, 91% and 88% of controls for the 25, 100 and 500 mg/kg bw/day dose groups respectively), however, there was no dose response relationship and the values were within the historical control range for the testing facility and hence are considered to be of no toxicological significance. There was a statistically significant increase (108% of the control) in the number of testicular spermatids per testis in the 500 mg/kg bw/day dose group, however this change was not observed on per gram of testis basis and hence is considered to be of no toxicological significance. There were no significant changes in the percent of motile sperm or sperm with normal morphology.

There were no test substance related effects on the mating index (females with evidence of mating/females cohoused with males × 100), gestation length or implantation efficiency. In the 500 mg/kg bw/day group there was a significant reduction in the number of uterine implantation sites (10.7 vs 15.3 for the control). The fertility index (no. of females with litters/no. of females with evidence of mating × 100) was reduced in the treatment groups (55.0%, 57.9% and 65.0% for the 25, 100 and 500 mg/kg bw/day dose groups respectively) in comparison to the control group (85.0%).

Effects on 1st Filial Generation (F1)

The number of pups born and born alive (72% and 66% of the control respectively) was significantly reduced in rats in the 500 mg/kg bw/day dose group. The number of pups surviving at any stage of the study was

significantly lower in the 500 mg/kg bw/day dose group with only 10% of the number of pups left alive in comparison to the controls 21 days after birth. Due to this the number of litters in the 500 mg/kg bw/day dose group with at least 1 pup surviving at day 21 was also significantly reduced (25%) in comparison to the control group. In the 100 mg/kg bw/day dose group survival was similar to controls up until 14 and 21 days after birth where it was 79% and 76% of the control respectively.

At all measurements of the mean pup weight at birth and on days 4, 7, 14 and 21 in the 500 mg/kg bw/day dose group there were significant decreases (90%, 71%, 54%, 56% and 57% respectively) in comparison to the control. In the 100 mg/kg bw/day dose group the mean pup weight was only significantly decreased in comparison to the control on days 4, 7 and 14 with decreases of 94%, 86% and 94% respectively.

Apart from one partially cannibalised pup in the control group, clinical signs in the F1 generation during lactation were limited to the 500 mg/kg bw/day dose group and consisted of lethargy, weakness and stained or wet perineum. The clinical signs in the 500 mg/kg bw/day dose group were present in only 1 out of a total of 12 litters and hence are considered to be of no toxicological significance. Clinical signs at day 21 were limited to isolated incidences of alopecia.

Due to the poor survival in the 500 mg/kg bw/day dose group there was insufficient data to evaluate post weaning in life parameters or post weaning anatomical pathology. In the 25 and 100 mg/kg bw/day dose groups there were no test substance related effects in any of the in life parameters measured. A significant decrease was seen in mean absolute liver weights (91% of control) and also relative to the body or brain and an increase in the mean brain weight relative to the body was seen in male animals in the 100 mg/kg bw/day dose group. The difference in the organ weights in the 100 mg/kg bw/day dose group is considered secondary to the lower body weight at this dose. There were no test substance related effects noted in the gross and microscopic observations on the organs of the F1 animals.

Remarks - Results

In the parental animals, 90 days of exposure to the test substance at doses of 100 or 500 mg/kg bw/day resulted in adverse treatment related effects. Adverse effects included changes in body weight and organ weight parameters, food efficiency, thyroid follicular hypertrophy, chronic progressive nephropathy, clinical signs, liver enzyme and red blood cell parameters. There were no adverse systemic effects on the parental animals at the lowest dose of 25 mg/kg bw/day.

Reproductive effects included a significant reduction in the number of implantation sites in the 500 mg/kg bw/day dose group in comparison to the control group and a reduction in the fertility index at all doses in comparison to the control group. Adverse effects in the F1 generation were seen in the 100 and 500 mg/kg bw/day dose groups and consisted of reductions in the mean litter size, number of pups born and born alive, pup survival and pup weight.

CONCLUSION

Based on the presence of adverse reproductive effects at all of the doses tested a NOAEL for reproductive and neonatal toxicity could not be set.

Due to a range of adverse effects in the parental animals dosed at 100 or 500 mg/kg bw/day the NOAEL for systemic effects in both male and female animals is the next lowest dose of 25 mg/kg bw/day.

TEST FACILITY DuPont (2002a)

B.16. Toxicity to reproduction – one generation study

TEST SUBSTANCE	Analogue 1
METHOD	Similar to OECD 415 One-Generation Reproduction Toxicity Study
Species/Strain	Rat/Crl:CD®(SD)IGS BR
Route of Administration	Oral – gavage
Exposure Information	Exposure period - female: 72 days before mating, during mating period (max. 15 days), during pregnancy, and until final sacrifice (after day 4 post-partum). Exposure period - male: 72 days before mating, during mating period (max. 15 days), and until final sacrifice (day 96/97).

Vehicle	Water
Remarks – Method	The dose levels were based on a previous 90-day subchronic toxicity and one-generation reproduction study where adverse reproductive effects were seen down to the lowest dose tested which was 25 mg/kg bw/day.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	24 per sex	0	0/48
2	24 per sex	1	0/48
3	24 per sex	10	0/48
4	24 per sex	25	0/48

Mortality and Time to Death

There were no unscheduled deaths in any group during the study.

Effects on Parental (P) animals:

There were no test substance related effects on body weight, body weight gain or food consumption in either male or female animals.

There were no test substance related effects on estrous cycle parameters, mating, precoital interval, fertility, gestation length, number of implantation sites, implantation efficiency and number of *corpora lutea* at each dose level.

Statistically significant test substance related increases in the liver weight and liver weight relative to body weight were seen in both male and female animals dosed with 25 mg/kg bw/day of the test substance. The increase in the liver weight relative to body weight was 110 and 114% for male and female rats respectively in comparison to the control group. The following effects were noted in a microscopic examination of the liver in animals dosed with 25 mg/kg bw/day: minimal hepatocellular vacuolation in 1 male, minimal focal necrosis in 1 male, minimal inflammation in 8 males and 4 females and minimal increased extramedullary haematopoiesis in 2 females. A similar level of microscopic observations was seen in the livers of the animals in the control group. In the absence of histopathological or clinical chemical changes indicative of liver injury the study authors considered the liver weight increases to be a physiologic response to metabolism of a xenobiotic and not toxicologically adverse.

Effects on 1st Filial Generation (F1)

There were no test substance related effects on the number of pups born, whether they were born alive, their sex ratio, survival to the end of the study (lactation day 4), birth weight and weight at the end of the study. Clinical signs in the F1 generation were limited to 1 pup from the 25 mg/kg bw/day displaying a subcutaneous haemorrhage.

Remarks - Results

There were no test substance related adverse effects on any parental animals or on the F1 offspring.

CONCLUSION

Based on the absence of adverse effects on any parental animals or on the F1 offspring the NOAEL is the highest dose tested at > 25 mg/kg bw/day.

TEST FACILITY DuPont (2010g)

Previous Extension Application (EX/209)

B.17. Repeat dose toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.

Species/Strain	Mouse/CD-1
Route of Administration	Oral – gavage

Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Reverse Osmosis Deionized (RODI) Water
Remarks - Method	The test substance was tested in a 7 day oral repeat dose study at dose levels of 0, 30, 250, and 500 mg/kg/day (unpublished report). Clinical observations such as low posture and increased muscle tone (which resolved by Day 4 in all animals) were limited to the mid and high dose groups. Effects on body weight gain and changes in histopathology, primarily in the liver were observed. There were no adverse effects observed at 30 mg/kg/day. In a discontinued study, a dose level of 500 mg/kg/day resulted in lethality following a single oral dose.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10M, 10F	0	0/20
low dose	10M, 10F	30	0/20
mid dose	10M, 10F	125	0/20
high dose	10M, 10F	250	1/20
control recovery	5M, 5F	0	0/10
low dose recovery	5M, 5F	30	0/10
mid dose recovery	5M, 5F	125	0/10
high dose recovery	5M, 5F	250	0/10

Mortality and Time to Death

One unscheduled death, test substance-related, was noted during the study and occurred on Day 14 at 250 mg/kg bw/day dose level in one male animal. There were no gross or microscopic findings observed.

Clinical Observations

Test substance related clinical signs were observed throughout the dosing phase and consisted of transient abnormal gait, decreased activity, hunched posture, laboured breathing, prostration, and non-sustained convulsions in males and females administered at ≥ 125 mg/kg bw/day dose levels. Transient sustained convulsions, tremors, incoordination, lateral recumbency, shallow breathing, locomotory stereotypy, and dehydration effects were observed in males and females administered at 250 mg/kg bw/day dose levels. An occurrence of erect fur was observed at 125 mg/kg bw/day. Single occurrences of hunched posture and decreased activity were noted at 30 mg/kg bw/day.

During Week 4 of the study, the 250 mg/kg bw/day male groups showed changes in functional observation battery such as slow respiration, and changes in body posture such as flattened limbs spread out, and some other effects such as eyelid closure, impaired mobility (body drags or is flattened or is flattened against the surface), moderately abnormal gait, decreased righting ability, and decreased body temperature (2.2 °C lower than control groups). No test substance-related clinical signs or effects on functional observation battery parameters were observed during the recovery phase.

Loss and/or decreases in body weight gain were noted in males administered at 250 mg/kg bw/day of the test substance during the dosing phase. Mean body weight loss of 5.52% less than that of the control groups, occurred during Week 1 of treatment, with recovery by Week 3.

During Week 1of the study, decreases in mean food consumption of 12% in the treated male groups and 18% in the treated female groups were noted at 250 mg/kg bw/day dose level. Recovery was noted by the following week.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

The study authors considered there to be no test substance related changes in haematology parameters, clinical chemistry, or coagulation parameters during the study.

Effects in Organs

There were no gross pathology findings that the study authors considered test substance related during the study.

There was a trend for increasing liver weights and decreasing spleen weights. Test substance-related effects on organ weights were statistically significant in males and females at ≥ 125 mg/kg bw/day in the liver and in males at 250 mg/kg bw/day in the spleen. Microscopic findings showed that the increased liver weights were likely due to the centrilobular hypertrophy in the liver and the decreased spleen weights were likely due to the decreased erythropoiesis in the spleen. Complete recovery of the liver and spleen organ weight changes and liver microscopic findings and near complete recovery of the spleen microscopic findings were noted following the 28-day dose-free period.

Remarks – Results

Adverse clinical signs consisting of non-sustained convulsions at ≥ 125 mg/kg bw/day and sustained convulsions at 250 mg/kg/day were noted in males and females during the dosing phase. Functional observation battery changes were evident in males dosed at 250 mg/kg bw/day. Centrilobular hypertrophy in the liver and correlating increases in liver weights were noted in ≥ 125 mg/kg/day male and female groups and erythropoiesis in the spleen and associated increases in spleen weight were evident in males at 250 mg/kg bw/day. All findings recovered during the 28-day dose-free period except the decreased erythropoiesis in the spleen.

CONCLUSION

The NOAEL was established as 30 mg/kg bw/day in this study, based on the adverse effects seen at doses ≥ 125 mg/kg/day.

TEST FACILITY Unpublished report (2017)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Variation 2 of the notified polymer
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Dissolved organic carbon (DOC), inorganic carbon (IC), total carbon (TC)
Remarks - Method	The method was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
9	26.2	9	64.1
20	54.3	20	83.3
28	62	28	90.1

Remarks - Results

All test validity criteria were met. A toxicity control indicated the inoculum was active and the test substance is not toxic to microorganisms. Under the constraints of the test guidelines, the test substance passed the 60% TCO_2 production within the 28 day timeframe. However, the test substance failed to exceed 60% degradation within a ten day period, therefore failing the criteria to be classified as readily biodegradable. Since the test substance is still degraded within the 28 days, it can be considered to be rapidly degradable.

Characterisation of the degradants was not undertaken. The entire carbon content of the notified polymer is not expected to completely mineralise. The perfluorinated portion is expected to remain at the completion of the test. A recent study on perfluorinated polymers with similar structures also indicated that after shortening of the non-perfluorinated portion of the polymer, the resulting polymer is expected to be stable (see Exempt Information). Therefore, degradation products may include more stable lower molecular weight polymer with perfluorinated functionality.

CONCLUSION	The notified polymer is rapidly degradable.
TEST FACILITY	Wildlife International, Ltd. (2010)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish (Test 1)

TEST SUBSTANCE	Variation 1 of the notified polymer
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Static.
Species	*Oncorhynchus mykiss* (Rainbow trout)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	139 to 157 mg $CaCO_3$/L
Analytical Monitoring	HPLC

Remarks – Method The method was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations. The test substance formed a slightly foamy solution after stirring with the water.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*			
Nominal	*Actual*		*24 h*	*48 h*	*72 h*	*96 h*
0	0	7	0	0	0	0
7.5	6.66	7	0	0	0	0
15	13.0	7	0	0	0	0
30	29.0	7	0	0	0	0
60	46.5	7	7	7	7	7
120	112	7	7	7	7	7

LC50 36.7 (29.0 to 46.5) mg/L at 96 hours.
NOEC 13.0 mg/L at 96 hours (based on DSEWPaC interpretation)
Remarks – Results All relevant test validity criteria were met. The geometric mean of the measured concentrations was used to calculate the LC50. The 95% fiducial limits are 29.0 to 46.5 mg/L. Sublethal effects were observed at 29.0 mg/L including erratic swimming, lethargy, rapid respiration and lying on the bottom of the test vessel.

CONCLUSION The notified polymer is harmful to fish

TEST FACILITY DuPont (2010h)

C.2.2. Acute toxicity to fish (Test 2)

TEST SUBSTANCE Variation 3 of the notified polymer

METHOD OECD TG 203 Fish, Acute Toxicity Test - Static.
Species *Oncorhynchus mykiss* (Rainbow trout)
Exposure Period 96 hours
Auxiliary Solvent None
Water Hardness 177 to 184 mg $CaCO_3$/L
Analytical Monitoring HPLC
Remarks – Method The method was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations. The test substance formed a slightly foamy solution after stirring with the water.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*			
Nominal	*Actual*		*24 h*	*48 h*	*72 h*	*96 h*
0	0	7	0	0	0	0
7.5	6.64	7	0	0	0	0
15	12.8	7	0	0	0	0
30	26.5	7	0	0	0	0
60	42.4	7	5	7	7	7
120	105	7	7	7	7	7

LC50 33.5 (26.5 to 42.4) mg/L at 96 hours.
NOEC 12.8 mg/L at 96 hours (based on DSEWPaC interpretation)
Remarks – Results All relevant test validity criteria were met. The geometric mean of the measured concentrations was used to calculate the LC50. The 95% fiducial limits are 26.5 to 42.4 mg/L. Sublethal effects were observed at 26.5 mg/L including erratic swimming, lethargy, loss of equilibrium and lying on the bottom of the test vessel.

CONCLUSION	The notified polymer is harmful to fish
TEST FACILITY	DuPont (2011)

C.2.3. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Variation 1 of the notified chemical
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test - Static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	140 to 150 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	The method was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	0	4 × 5	0	0
2.5	2.4	4 × 5	0	0
5	4.92	4 × 5	0	2
10	10.3	4 × 5	0	2
20	21.6	4 × 5	0	7
40	45.1	4 × 5	9	17

EC50	28.8 (23.9 to 35.5) mg/L at 48 hours
NOEC	2.4 mg/L at 48 hours (based on DSEWPaC interpretation)
Remarks - Results	All relevant test validity criteria were met. The geometric mean of the measured concentrations was used to calculate the EC50. The 95% fiducial limits are 23.9 to 35.5 mg/L. No immobilisation was observed at 2.4 mg/L however one daphnid was floating on the surface. No other sublethal effects were observed at any concentration. Therefore this is likely to be an anomaly.
CONCLUSION	The notified polymer is harmful to aquatic invertebrates
TEST FACILITY	DuPont (2010i)

C.2.4. Algal growth inhibition test

TEST SUBSTANCE	Variation 1 of the notified polymer
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Pseudokirchneriella subcapitata* (Green algae)
Exposure Period	72 hours
Concentration Range	Nominal: 0, 7.5, 15, 30, 60, 120 mg/L Actual: 0, 7.47, 14.7, 27.5, 54.8, 114 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	HPLC
Remarks - Method	The study was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Biomass		*Growth*	
E_bC50 *mg/L at 72 h*	*NOEC* *mg/L at 72 h*	*E_rC50* *mg/L at 72 h*	*NOEC* *mg/L at 72 h*
50.1 (48.8 to 51.3)	27.5	88.3 (87.8 to 88.8)	27.5

Remarks - Results

All relevant test validity criteria were met. The geometric mean of the measured concentrations was used to calculate the EC50. The 95% fiducial limits are 48.8 to 51.3 mg/L for biomass and 87.8 to 88.8 mg/L for growth rate.

A recovery test was conducted for test concentrations where greater than 50% inhibition of growth was observed. The effects on growth and reproduction of the algae were found to be algistatic within 4 days at the mean measured concentrations that were ≤ 114 mg/L.

CONCLUSION

The notified polymer is harmful to algae.

TEST FACILITY

DuPont (2010j)

APPENDIX D: TOXICOLOGY OF PERFLUOROHEXANOIC ACID (PFHXA)

The following conclusions can be drawn from the data on PFHxA to assess health effects:

1. Absorption of PFHxA in mice and rats was rapid, with C_{max} achieved within 1 hour. Systemic exposure (AUC) was higher in males than in females in both mice and rats, probably as a result of the more rapid clearance in females than in males. Low levels of PFHxA were found in various rat tissues; these decreased rapidly and could not be detected in most tissues by 24 hours. Excretion of unchanged PFHxA was rapid and was largely via the urine. Most of the PFHxA was excreted via the urine within 24 hours, indicating almost 100% bioavailability. There was no evidence of bioaccumulation following repeat exposure in rats. Similar kinetics were observed in monkeys, with rapid absorption, similar exposure for males and females, and rapid and comprehensive urinary excretion of unchanged PFHxA. The volume of distribution in rats and monkeys indicates distribution mainly to extracellular fluid. The serum half-lives were 2.4/5.3 hours (male/female) in monkeys and 1/0.42 hours (male/female) in rats (Chengelis *et al*., 2009a; Gannon *et al*., 2011).
2. In a study comparing the toxicokinetics of PFHxA to PFOA following repeated oral exposure for 10 days, results indicate that the AUC was 9 times lower for PFHxA, which is attributed to the more rapid excretion of PFHxA. The half-life for PFHxA was 3 times lower than PFOA and persistence in the liver was much lower for PFHxA than PFOA (DuPont, 2003).
3. During seasonal use of ski wax, PFHxA levels in the blood of workers increased during the ski season, then decreased to below the detection limit following cessation of exposure. PFOA levels in blood were also monitored and were found at mostly stable concentrations before, during and after the ski season (elevated compared to the general population). These data suggest that clearance of PFHxA from blood occurs soon after cessation of exposure (Nilsson *et al.*, 2010).
4. The acute toxicity of PFHxA was low, with an LD_{50} value of > 1750 mg/kg bw and < 5000 mg/kg bw in female rats. Males are expected to be more sensitive to PFHxA based on higher exposure (AUC) and an expected lower LD_{50} for males (Loveless *et al*., 2009). No information was available to assess acute dermal toxicity or acute inhalation toxicity.
5. In repeat dose oral toxicity studies in rats (14 days, 90 days), there was evidence of effects on the liver and decreased haematological parameters at 500 mg/kg bw/day, with liver effects in males at 100 mg/kg bw/day. Nasal lesions (degeneration and atrophy of the olfactory epithelium) were observed at 100 mg/kg bw/day and above in the 90-day study and the NOAEL was 20 mg/kg bw/day in both sexes (DuPont, 2006k; DuPont, 2007c, Chengelis *et al.*, 2009b).
6. In a 2-year chronic toxicity/carcinogenicity study in rats, there were treatment-related systemic effects (increased incidence of struggling, and papillary necrosis and tubular degeneration of the kidneys) at 100/200 mg/kg bw/day (male/female). The NOAEL for non-neoplastic effects was 15/30 mg/kg bw/day (male/female). There was no evidence of carcinogenicity in either male or female rats (AGC Chemicals, 2010).
7. NaPFHx showed no effect on fertility parameters in a one-generation reproduction study in rats. The NOAEL for maternal systemic toxicity in the P1 animals was 100 mg/kg bw/day based on excessive body weight gain during lactation. There were no biologically significant adverse effects on pups (DuPont, 2007c).
8. In a developmental toxicity study with NaPFHx in rats, there was evidence of maternal (reduced body weight and body weight gain) and foetal toxicity (reduced neonatal bodyweight) at 500 mg/kg bw/day (DuPont, 2007d). In a second developmental toxicity study in mice with ammonium PFHx, foetal toxicity (increased incidence of still births, perinatal death, and microphthalmia and corneal opacity) was noted at 175 mg/kg bw/day in the absence of maternal toxicity. There was no toxicity in pups post-weaning. The NOAEL was 35 mg/kg bw/day (Daikin Industries, 2011).
9. No evidence of genotoxicity was observed in an *in vitro* mutagenicity assay in bacteria (DuPont, 2006i) or in a test for chromosome aberrations in human peripheral blood lymphocytes (DuPont 2006j).

The toxicology of PFOA has been characterised previously (Environment Canada, 2012; Chemical Safety Report, 2009). Comparative analysis of the toxicokinetics of PFHxA and PFOA indicated the following:

- Bioavailability of PFHxA and PFOA after oral administration was high.

- In repeat oral exposure studies, PFHxA showed no evidence of bioaccumulation, whereas PFOA showed some evidence of bioaccumulation.
- Excretion of PFHxA via the urine was rapid and virtually complete over 24 hours, whereas excretion of PFOA was slower, with only 20% excreted over 24 hours.
- Half-lives of excretion of PFHxA after oral exposure were 2–3 hours, whereas the excretion half-life of PFOA was 4.8 days.

Comparative analysis of the toxicity of PFHxA and PFOA indicated the following:

- The acute toxicities of PFHxA and PFOA were low.
- No data were available to compare eye and skin irritation or sensitisation.
- In 90-day repeat dose studies in rats, the LOAEL for PFHxA (100 mg/kg bw/day) occurred at higher doses than for PFOA (0.64 mg/kg bw/day).
- In chronic toxicity studies in rats, the LOAEL for PFHxA (100/200 mg/kg bw/day [m/f]) was higher than for PFOA (14.2/16.1 mg/kg bw/day [m/f]).
- Reproduction studies with PFHxA produced no effect on reproductive parameters with a NOAEL of 500 mg/kg bw/day, whereas PFOA produced increased mortality, decreased bodyweight and delayed sexual maturity in the F1 generation with a NOAEL of 10 mg/kg bw/day in females.
- The LOAEL was 175 mg/kg bw/day for developmental effects in a rat study with ammonium PFHx. The NOEL for developmental effects for PFOA was 150 mg/kg bw/day in a rat study.
- There was no evidence of genotoxicity for PFHxA or PFOA.
- A carcinogenicity study in rats with PFHxA produced no evidence of a treatment-related increase in tumours, whereas a study in rats with PFOA produced an increased tumour incidence in males (Klaunig *et al.*, 2014). The US EPA considers PFOA is “likely to be carcinogenic to humans” (US EPA, 2012).

BIBLIOGRAPHY

AGC Chemicals (2010) A 24-month Oral (Gavage) Combined Chronic Toxicity/Carcinogenicity Study of Perfluorohexanoic Acid (PFHxA) in Rats (Study no. WIL-534009). Ahiba, Japan. AGC Chemicals, Asahi Glass Company (Unpublished report submitted by the notifier).

Ahrens L, Felizeter S, Sturm R, Xie Z and Ebinghaus R (2009). Polyfluorinated compounds in wastewater treatment plant effluents and surface waters along the River Elbe, Germany. Mar Pollut Bull, 58(9):1326-1333.

Arp H, Niederer C and Goss K (2006) Predicting the Partitioning Behaviour of Various Highly Fluorinated Compounds. *Environmental Science and Technology*, 40(23) pp 7298-7304.

Chemical Safety Report (2009) Risk Assessment of Perfluorooctanoic Acid (PFOA) as Part of a Strategic Partnership Between German Authorities and Industry (Unpublished report provided by the notifier).

Chengelis CP, Kirkpatrick JB, Myers NR, Shinohara M, Stetson PL and Sved, DW (2009a) Comparison of the Toxicokinetic Behaviour of Perfluorohexanoic Acid (PFHxA) and Nonafluorobutane-1-sulfonic acid (PFBS) in Cynomolgus Monkeys and Rats. Reproductive Toxicology, 27(3-4):342-51.

Chengelis CP, Kirkpatrick JB, Radovsk Ann and Shinohara, M (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(3-4):400-6.

Conder JM, Hoke RA, De Wolf W, Russell MH and Buck RC (2008) Are PFCAs Bioaccumulative? A Critical Review and Comparison with Regulatory Criteria and Persistent Lipophilic Compounds. Environmental Science and Technology, 42(4):995-1003.

Daikin Industries (2011). Oral (gavage) Combined Developmental and Perinatal/Postnatal Reproduction Toxicity Study of PFH Ammonium Salt in Mice (study no. UZS00010). Osaka, Japan (Unpublished report submitted by the notifier).

Danish EPA (2008) Survey and environmental/health assessment of fluorinated substances in impregnated consumer products and impregnating agents, http://www2.mst.dk/common/Udgivramme/Frame.asp?http://www2.mst.dk/udgiv/Publications/2005/87-7614-668-5/html/default_eng.htm accessed 20 May 2013.

DuPont (Unspecified date) Octanol/Water Partition Coefficient of [notified polymer] using HPLC OECD TG 117 (Study number not specified, date not specified). Location and test facility not specified (Unpublished report submitted by the notifier)

DuPont (2002a) Analogue 1: Subchronic Toxicity 90-Day Gavage Study in Rats with One-Generation Reproduction Evaluations (Study No. DuPont-5990, 18 January, 2002). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2003). Hexanoic acid, undecafluro-: (Biopersistence) Screening-10-Dose Oral Gavage Study in Rats (Study No. 11560, April 2003). Delaware, USA. E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2006a) Sodium Perfluorohexanoate: Bacterial Reverse Mutation Test (Study No. 20947, October 2006). Delaware, USA. E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2006b) Sodium Perfluorohexanoate: in vitro Mammalian Chromosome Aberration Test in Human Peripheral Blood Lymphocytes (Study No. 20880, November 2006). Delaware, USA. E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2006c) Sodium Perfluorohexanoate: Repeated-Dose Oral Toxicity-two Weeks Gavage Study in Rats and Mice (Study No. 18510, June 2006). Delaware, USA. E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2007a) Sodium Perfluorohexanoate: 90-Day Gavage Study in Rats with One-generation Reproduction Evaluation (Study No. 19715, July 2007). Delaware, USA. E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2007b) Sodium Perfluorohexanoate: Developmental Toxicity in Rats (Study No. 20639, April 2007). Delaware, USA. E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010a) Notified polymer – variation 3: Acute Oral Toxicity Study in Rats – Up-And Down Procedure (Study No. DuPont-19142-834, July, 2010). Newark, Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010b) Notified polymer – variation 3: Acute Dermal Toxicity Study in Rats (Study No. DuPont-19142-673, August, 2010). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010c) Notified polymer – variation 1: Inhalation Approximate Lethal Concentration (ALC) in Male Rats (Study No. DuPont-18828-700, April, 2010). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010d) Notified polymer – variation 1: Local Lymph Node Assay (LLNA) in Mice (Study No. DuPont-18828-1234, March, 2010). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010e) Notified polymer – variation 3: Local Lymph Node Assay (LLNA) in Mice (Study No. DuPont-19142-1234, July, 2010). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010f) Notified polymer – variation 1: Bacterial reverse Mutation Test (Study No. DuPont-18828-500, March, 2010). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010g) Analogue 1: One-Generation Reproduction Study in Rats (Study No. DuPont-13784, 25 February, 2010). Delaware, USA, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010h) Notified polymer – variation 1: Static, Acute, 96-hour Toxicity Test with Rainbow Trout, *Oncorhynchus mykiss* (Study No. 18828-228, March, 2010). Wilmington, Delaware, United States, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010i) Notified polymer – variation 1: Static, Acute, 48-hour Toxicity Test with the Cladoceran, *Daphnia magna* (Study No. 18828-241, March, 2010). Wilmington, Delaware, United States, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2010j) Notified polymer – variation 1: Static, 72-hour Growth Inhibition Toxicity Test with the Green Alga, *Pseudokirchneriella subcapitata* (Study No. 18828-280, March, 2010). Wilmington, Delaware, United States, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2011) Notified polymer – variation 3: Static, Acute, 96-hour Toxicity Test with Rainbow Trout, *Oncorhynchus mykiss* (Study No. 19142-228, July, 2011). Wilmington, Delaware, United States, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

DuPont (2012) Solubility Limit and Stability of [variation of the notified polymer] in Haskwell Well Water (Study No. 18828-298 AN, September, 2012). Wilmington, Delaware, United States, E.I. du Pont de Nemours and Company (Unpublished report submitted by the notifier).

Environment Canada (2012) Screening Assessment Report – Perfluorooctanoic Acid, its Salts, and its Precursors. Government of Canada, August, 2012, <www.ec.gc.ca/ese-ees/default.asp?lang=En&n=370AB133-1>.

Eurofins (2010a) Notified polymer – variation 2: Acute Oral Toxicity – Up-And Down Procedure in Rats (Study No. 29230, April, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010b) Notified polymer – variation 1: Acute Oral Toxicity – Up-And Down Procedure in Rats (Study No. 28768, March, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010c) Notified polymer – variation 1: Acute Dermal Toxicity in Rats (Study No. 28769, March, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010d) Notified polymer – variation 3: Primary Skin Irritation in Rabbits (Study No. 29940, June, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010e) Notified polymer – variation 1: Primary Skin Irritation in Rabbits (Study No. 28771, March, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010f) Notified polymer – variation 2: Primary Skin Irritation in Rabbits (Study No. 29121, April, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010g) Notified polymer – variation 1: Primary Eye Irritation in Rabbits (Study No. 28770, March, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Eurofins (2010h) Notified polymer – variation 2: Primary Eye Irritation in Rabbits (Study No. 29120, April, 2010). New Jersey, USA, Eurofins PSL (Unpublished report submitted by the notifier).

Falandysz J, Taniyasu S, Gulkowska A, Yamashita N and Schulte-Oehlmann U (2006) Is Fish A Major Source of Fluorinated Surfactants and Repellents in Humans Living on the Baltic Coast? Environ Sci Technol, 40(3):748-751.

Falandysz J, Taniyasu S, Yamashita N, Rostkowski P, Zalewski K and Kannan K (2007) Perfluorinated compounds in some terrestrial and aquatic wildlife species from Poland. J Environ Sci Health, Part A: Environ Sci Eng. 42(6):715-719.

Fischer M, Koch W., Windt H and Dasenbrock C (2012) A Pilot Study on the Refinement of Acute Inhalation Toxicity Studies: the Isolated Perfused Rat Lung as a Screening Tool for Surface-active Substances. ATLA, 40:199-209.

Furdui V, Stock N, Ellis D, Butt C, Whittle D, Crozier P, Reiner E, Muir D and Mabury S (2007) Spatial Distribution of Perfluoroalkyl Contaminants in Lake Trout from the Great Lakes. Environ Sci Technol, 41(5):1554-1559.

Gannon SA, Johnson T, Nabb DL, Serex TL, Buck RC and Loveless SE (2011) Absorption, Distribution, Metabolism and Excretion of [1-14C]-Perfluorohexanoate ([14C]-PFHx) in rats and mice. Toxicology 238(1):55-62.

Giesy JP, Nail JE, Khim JS, Jones PD and Newsted JL (2010) Aquatic Toxicology of Perfluorinated Chemicals. Reviews of Environmental Contamination and Toxicology, 202:1-52.

Higgins C, McLeod P, Macmanus-Spencer L and Luthy R (2007) Bioaccumulation of Perfluorochemicals in Sediments by the Aquatic Oligochaete Lumbriculus variegatus. Environ Sci Technol, 41(13):4600-4606.

Huset C A, Barlaz M A, Barofsky D F and Field J A (2011). Quantitative determination of fluorochemicals in municipal landfill leachates, Chemosphere, Volume 82, Issue 10, 1380-1386.

Klaunig J, Shinohara M, Iwai H, Chengelis C, Kirkpatrick J, Wang Z and Bruner R (2014) Evaluation of the Chronic Toxicity and Carcinogenicity of Perfluorohexanoic Acid (PFHxA) in Sprague-Dawley Rats. Toxicologic Pathology, 43(2):209-220 (http:\\dx.doi.org\10.1177/0192623314530532).

Kumar K, Zushi Y, Masunaga S, Gilligan M, Pride C and Sajwan K (2009) Perfluorinated Organic Contaminants in Sediment and Aquatic Wildlife, Including Sharks, From Georgia, USA. Baseline/Mar Pollut Bull, 58:601-634.

Latala A, Nedzi M & Stepnowski P (2009) Acute Toxicity Assessment of Perfluorinated Carboxylic Acids Towards the Baltic Microalgae. Environ Toxicol Pharmacol, 28:167-171.

Loveless SE, Slezaka B, Serex T, Lewisa J, Mukerji P, O'Connor JC, Donnera EM, Frame SR, Korzeniowski SH and Buck RC (2009) Toxicological Evaluation of Sodium Perfluorohexanoate. Toxicology, 264(1-2):32-44.

Martin J, Mabury S, Solomon K and Muir D (2003a) Bioconcentration and Tissue Distribution of Perfluorinated Acids in Rainbow Trout (*Oncorhynchus mykiss*). Environ Sci Technol, 22(1):196:204.

Martin J, Mabury S, Solomon K and Muir D (2003b) Dietary Accumulation of Perfluorinated Acids in Juvenile Rainbow Trout (Oncorhynchus mykiss). Environ Toxicol Chem, 22(1):189-195.

McLachlan M, Holmstrom K, Reth M and Berger U (2007) Riverine Discharge of Perfluorinated Carboxylates from the European Continent. Environ Sci Technol, 41(21):7260-7265.

Nakayama S, Strynar M, Helfant L, Egeghy P, Ye X and Lindstrom A (2007) Perfluorinated Compounds in the Cape Fear Drainage Basin in North Carolina. Environ Sci Technol, 41(15):5271-5276.

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia

Russell M, Berti W, Szostek B and Buck R (2008) Investigation of the biodegradation potential of a fluoroacrylate polymer product in aerobic soils. Environmental Science and Technology, **42**(3):800-807.

Russell M, Berti W, Szostek B, Wang N and Buck R (2010) Evaluation of PFO formation from the biodegradation of a fluorotelomer-based urethane polymer product in aerobic soils. Polymer Degradation and Stability, **95**:79-85.

Russell M, Nilsson H and Buck R (2013) Elimination kinetics of perfluorohexanoic acid in humans and comparison with mouse, rat and monkey. Chemosphere, 93(10):2419-2425 (http://dx.doi.org/10.1016/j.chemosphere.2013.08.060)

Skutlarek D, Exner M & Färber H (2006) Perfluorinated Surfactants in Surface and Drinking Waters. Environ Sci Pollut Res, 13(5):299-307.

So M, Miyake Y, Yeung W, Ho Y, Taniyasu S, Rostkowski P, Yamashita N, Zhou B, Shi X, Wang J, Giesy J, Yu H and Lam P (2007) Perfluorinated compounds in the Pearl River and Yangtze River of China. Chemosphere, 68(11):2085-2095.

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >.

US EPA (2002) Revised Draft Hazard Assessment of Perfluorooctanoic Acid and its Salts. US Environment Protection Agency, Office of Pollution Prevention and Toxics Risk Assessment Division, 4 November 2002.

US EPA (2012) Perfluorooctanoic Acid (PFOA) and Fluorinated Telomers – Risk Assessment. <http://www.epa.gov/opptintr/pfoa/pubs/pfoarisk.html>.

US FDA (2009) Environmental Assessment. US Food and Drug Administration, 22 April, 2009. Available at: http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM176786.pdf.

Wildlife International, Ltd. (2010) Notified polymer – variation 2: Biodegradability by the carbon dioxide evolution test method (Study No. 112E-118, May, 2010). Easton, Maryland, United States, Wildlife International, Ltd. (Unpublished report submitted by the notifier).

Washington J, Ellington J, Jenkins T, Evans J, Yoo H and Hafner S (2009) Degradability of an acrylate-linked, fluorotelomer polymer in soil. Environmental Science and Technology, **43**(17):6617-6623.

Wang Y, Yeung L, Taniyasu S, Yamashita N, Lam J and Lam P (2008) Perfluorooctane Sulfonate and Other Fluorochemicals in Waterbird Eggs from South China. Environ Sci Technol, 42(21):8146-8151.

Woodcroft M, Ellis D, Rafferty S, Burns D, March R, Stock N, Trumpour K, Yee J and Munro K (2010) Experimental Characterization of the Mechanism of Perfluorocarboxylic Acids' Liver Protein Bioaccumulation: The Key Role of the Neutral Species. Environ Toxicol Chem, Early View. DOI: 10.1002/etc.199.

Ye X, Strynar M, Nakayama S, Varns J, Helfant L, Lazorchak J and Lindstrom A (2008a) Perfluorinated compounds in whole fish homogenates from the Ohio, Missouri and Upper Mississippe Rivers, USA. Environ Pollut, 156(3):1227-1232.

Ye X, Schoenfuss H, Jahns N, Delinsky A, Strynar M, Varns J, Nakayama S, Helfant L and Lindstrom A (2008b) Perfluorinated compounds in common carp (*Cyprinus carpio*) fillets from the Mississippi River. Environmental International, 34(7):832-938.

Zhao L, Folsom, PW, Wolstenholme BW, Sun H, Wang N, Buck R (2013) 6:2 Fluorotelomer alcohol biotransformation in an aerobic river sediment system, Chemosphere, 90: 203-209.

Extension Application (EX/213)

Unpublished report, (2017). A 28-day Study of [Notified Chemical] by Oral Gavage in Mice with a 28-day Recovery Period. 24 January 2017 (unpublished report provided by the notifier).