File No: EX/190 (LTD/1498)

September 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Polyfluorinated Polymer ELN101570-2 in Capstone® ST-100/ST-110/ST-100HS/FS-82

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.

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:

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Director
NICNAS

TABLE OF CONTENTS

This assessment report is for an extension of original assessment certificate for Polyfluorinated Polymer ELN101570-2 in Capstone® ST-100/ST-110/ST-100HS/FS-82. 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/190 (LTD/1498)	Laticrete Pty Ltd	Polyfluorinated Polymer ELN101570-2 in Capstone® ST-100/ST-110/ST-100HS/FS-82	Yes	≤ 15 tonnes per annum	Component of stone and tile sealants

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	H332 – Harmful if inhaled

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:

R20: Harmful by inhalation

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 for perfluorohexanoic acid (PFHxA) in the environment, and PFHxA 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.

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): H332 – Harmful if inhaled*

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

- Aerosol or spray products containing the notified polymer should carry the following safety directions on the label:
  - Avoid breathing of vapours, mists and sprays
  - May be harmful if inhaled
  - Use in well-ventilated areas, where possible
  - In case of insufficient ventilation, wear suitable respiratory equipment

(Material) Safety Data Sheet

- The (M)SDS for products containing the notified polymer should include the following:
  - Avoid breathing of vapours, mists and sprays
  - May be harmful if inhaled
  - Use in well-ventilated areas, where possible
  - In case of insufficient ventilation, wear suitable respiratory equipment

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:
  - Enclosed, automated processes, where possible
  - Airless spray or low pressure spray equipment should be utilised during spray operations, 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 as introduced or in formulated products:
  - Avoid breathing of vapours, mists and sprays
  - Avoid prolonged spraying

- 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 as introduced or in formulated products:
  - Respiratory protection when conducting spray operations in areas with insufficient ventilation
  - Gloves
  - Coveralls

  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 perfluoroalkyl 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 perfluoroalkyl 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 fifteen tonnes per annum notified chemical;
- the polymer has a number-average molecular weight of less than 1000;
- the use changes from a component of stone and tile sealants;
- the notified polymer is intended for use in spray products at > 3% concentration for consumer or professional use;
- further information on the repeated inhalation toxicity of the notified polymer becomes available;
- additional information has become available to the person as to an adverse effect of the poly- or perfluoroalkylated degradation products of the notified polymer (such as perfluorohexanoic acid);
- additional information has become available to the person as to the environmental fate of the polymer or its poly- or perfluoroalkylated degradation products (such as perfluorohexanoic acid) 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 polymer has changed from a component of stone and tile sealants, or is likely to change significantly;
- the amount of polymer 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 Entry

- 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:
The applicant for the extension application (Laticrete Pty Ltd) has provided an MSDS for a product containing the notified polymer. The accuracy of the information on the MSDS remains the responsibility of the extension 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 and recommendations on the safe use of the notified chemical were carried out by NICNAS and the Department of the Environment.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Holder of Original Assessment Certificate (LTD/1498):
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

Anderson Dry-Treat Trust & Salmon Dry-Treat Trust (ABN 28 702 168 959)
65 Nicholson Street
ST LEONARDS NSW 2065

Applicant for an Extension of the Original Assessment Certificate:
Laticrete Pty LTD (ABN: 57 069 067 992)
29 Telford Street,
VIRGINIA QLD 4014

NOTIFICATION CATEGORY
Limited: Synthetic polymer with Mn ≥1000 Da.

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: melting point/freezing point, boiling point, density, vapour pressure, hydrolysis as a function of pH, partition coefficient (n-octanol/water), adsorption/desorption, dissociation constant, flash point, flammability, autoignition temperature, explosive properties, and oxidising properties

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA, Canada

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
ELN101570-2 (notified polymer)
Capstone® P-620, Capstone® ST-100, Capstone® ST-110, Capstone® P-623, Capstone® FS-82 (up to 30% notified polymer)

MOLECULAR WEIGHT
> 10,000 Da

ANALYTICAL DATA

A reference IR spectrum was provided.

3. COMPOSITION

The notified polymer contains a polyfluoroalkyl carbon side chain with six perfluorinated carbons.

DEGREE OF PURITY > 90%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
Below classification cut-offs.

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

DEGRADATION PRODUCTS
The notified polymer is a potential precursor for PFHxA in the environment (PFHxA - perfluorohexanoic acid - 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 °C AND 101.3 kPa: Light yellow liquid*

Property	Value	Data Source/Justification
Boiling Point	Not determined	Expected to decompose prior to boiling.
Density	1104 kg/m^3	(M)SDS*
Vapour Pressure	Not determined	Based on the high molecular weight of the polymer, the vapour pressure is expected to be low.
Water Solubility	< 0.006 g/L at 20 °C < 0.59 mg/g (water extractable fraction)	Measured. Expected to be low based on the high molecular weight and hydro/lipophobicity of the polymer. Based on structural considerations and product formulation, the notified polymer has the potential to disperse in water.
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionality. However, hydrolysis is expected to occur very slowly under environmental conditions.
Partition Coefficient (n-octanol/water)	Not determined	On the basis of its hydro/lipophobic tendencies, the notified polymer is expected to partition between the octanol and water phases.
Adsorption/Desorption	Not determined	Generally, polymers similar to the notified polymer are expected to adsorb to soil, sediments and sludge. However, the notified polymer may have low absorption based on the presence of perfluoroalkyl functionalities which have both hydrophobic and lipophobic tendencies.
Dissociation Constant	Not determined	May have the potential to dissociate under environmental conditions (pH 4-9).
Particle Size	Sample 1: 227.4 nm Sample 2: 158.4 nm Sample 3: 248 nm	Measured for dispersion of the notified polymer*
Flash Point	> 200 °C	Data sheet

Flammability	Not determined	Not expected to be flammable based on the partial fluorination.
Autoignition Temperature	Not determined	Expected to autoignite at very high temperatures.
Explosive Properties	Not expected	Contains no explosophores.
Oxidising Properties	Not expected	Estimated based on structure.

*Aqueous product containing the notified polymer at up to 30%

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties that were not assessed by US EPA, 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 OVER NEXT 5 YEARS
The notified polymer will not be manufactured within Australia. The notified polymer will be imported into Australia as an aqueous dispersion at concentrations of up to 30 wt% in various formulated products.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 5	< 10	< 15	< 15	< 15

PORT OF ENTRY
Sydney, Melbourne and Brisbane.

TRANSPORTATION AND PACKAGING
The products containing the notified polymer (up to 30 wt% concentration) will be imported by sea in 40 kg or 900 kg polyethylene drums, and transported within Australia by road.

USE
The notified polymer 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 polymer). The use categories of the notified polymer are identical to those of the existing polymer it replaces, as outlined below.

Stone and tile sealants
The notified polymer will be used in stone and tile sealants by professionals and consumers (up to 3 wt% concentration).

OPERATION DESCRIPTION
The notified chemical will not be manufactured in Australia. The notified polymer will be imported at up to 30 wt% concentration.

Reformulation
The notified polymer (up to 30 wt% concentration) will be reformulated into finished stone and tile sealants (up to 3 wt% concentration). The notified polymer (up to 30 wt% concentration) will either be weighed manually or pumped into the mixing vessel. The final products (up to 3 wt% concentration) will then be dispensed and packaged into suitable containers.

Stone and tile use
Professionals will apply stone and tile sealants containing the notified polymer (up to 3 wt% concentration) in industrial and commercial settings by brush, roller or low-pressure spray. Consumers will apply products

containing the notified polymer (up to 3 wt% concentration) by brush, roller or spray (mainly using pump packs, trigger packs or squeeze bottles, with the possibility of some aerosol use).

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

The notified polymer may undergo slow degradation in the environment. 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 low concentration of polyfluoroalkyl impurities in the notified polymer, in the imported products or in end-use products.

The notified polymer is a potential precursor for PFHxA in the environment. This 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 30 wt% concentration) in the unlikely event of an accident.

Reformulation processes
Dermal and ocular exposure may occur when workers manually weigh and pour products containing the notified chemical (up to 30 wt% concentration) into mixing equipment, or when connecting and disconnecting hoses, and during cleaning and maintenance operations. Inhalation exposures are not expected based on the expected 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.

Stone and tile sealant application
Dermal and ocular exposures to the notified polymer (up to 3 wt% concentration) may occur when workers are applying stone and tile sealants by brush, roller or sponge, with some potential for inhalation exposure when applying by low-pressure spray. PPE is expected to be worn, including gloves, safety glasses and respiratory protection when aerosols may be present. Professionals may be exposed on a repeated basis.

6.1.2. Public Exposure
Public exposure to the notified polymer (up to 3 wt% concentration) may occur when stone and tile products are applied. Dermal, ocular and inhalation exposure may occur. Consumer exposure is expected to be acute in nature because repeated daily uses are considered unlikely and exposure is expected to be infrequent and short-term (ie. duration of up to 15 minutes). Products may be applied using aerosol cans and the highest exposures will occur when products are sprayed in enclosed settings such as bathrooms. Aerosols of the notified polymer are expected to generate relatively large droplet sizes, given that the target is intended to be well-coated.

Inhalation exposure is considered for the purposes of exposure assessment, with a concentration for a single exposure calculated using ConsExpo (ConsExpo, 2006). For a 15 minute exposure, the average exposure concentration of the notified polymer is estimated to be up to 5 mg/m^3, based on scenarios to estimate bathroom sprays (RIVM, 2006).

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified polymer (up to 30 wt% concentration) are summarised in the following table. Details of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 1,000 mg notified polymer/kg bw; low toxicity

Rat, acute inhalation toxicity	1,200 < LC50 < 1,700 mg notified polymer/m^3/4 hours); harmful by inhalation
Rabbit, skin irritation	non-irritating*
Rabbit, eye irritation	slightly irritating*
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation*
Rat, repeat dose oral toxicity – 14 days	NOAEL > 1000 mg/kg bw/day
Rat, repeat dose oral toxicity – 90 days	LOAEL = 100 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* Mammalian Chromosome Aberration Test	non clastogenic
Developmental toxicity, rat	NOAEL (maternal) = 500 mg/kg bw/day NOAEL (foetal) > 1,000 mg/kg bw/day
Rat, one-generation reproductive toxicity	NOAEL (systemic, males) = 20 mg/kg bw/day NOAEL (systemic, females) = 100 mg/kg bw/day NOAEL (reproductive) > 1,000 mg/kg bw/day

* Tested using an aqueous solution containing the notified polymer at approximately 19 wt%.

Toxicokinetics, metabolism and distribution
The notified polymer is not expected to cross biological membranes (skin or gastrointestinal tract) based on its high molecular weight (> 10,000 Da), the low proportion (< 1%) of low molecular weight species (< 500 Da), and its expected low water solubility. This is supported by the lack of observed systemic toxicity in the acute oral toxicity study with the notified polymer. In addition, inhalation of the notified polymer itself is not expected to result in significant absorption from the respiratory tract. Some accumulation in the respiratory tract may occur from respirable particles (< 10 µm). Alternatively, larger inhalable particles (< 100 µm) are likely to deposit in the nasopharyngeal region and will be removed by mucociliary mechanisms or swallowed. Ingestion after swallowing dust is not expected to lead to significant absorption from the GI tract due to the high molecular weight of the notified polymer and its stability to hydrolysis.

Acute toxicity
An aqueous solution containing the notified polymer at approximately 19 wt% concentration was of low acute oral toxicity in rats (LD50 > 5,000 mg/kg bw, equivalent to LD50 > 1,000 mg notified polymer/kg bw).

Inhalation toxicity
Concerns exist that high molecular weight (> 10,000 Da) water insoluble polymers may cause overloading effects in the lungs (US EPA, 2013). Additionally, perfluorinated polymers with surfactant properties have been known to cause lung injury, which is characterised by respiratory problems ranging from mild to severe effects associated with acute or repeated exposures.

The notified polymer was harmful via inhalation in rats, with 8/10 mortalities in the group exposed to 1,700 mg/m^3/4 hours, with no mortalities observed at 1,200 mg/m^3/4 hours, thus the LC50 is between these concentrations. Laboured breathing was observed in the rats exposed to 1,700 mg/m^3/4 hours. Microscopic examination of the respiratory tract of rats exposed to 1,700 mg/m^3/4 hours that died within the course of the study revealed mild to moderate acute haemorrhage into the alveolar spaces and minimal perivascular inflammation in the lungs and haemorrhage in the nasal cavity. Interstitial inflammation and acute and chronic haemorrhage were observed in the lungs of one of the two surviving rats exposed to 1,700 mg/m^3/4 hours. The respiratory tract of rats exposed to 1,200 mg/m^3/4 hours were not examined microscopically, therefore, a no effect level for histopathological effects in the lungs was not determined.

No repeated dose inhalation studies with the notified polymer have been submitted and significant uncertainties remain surrounding possible chronic respiratory tract effects following repeated exposures to the notified polymer. A safe level for repeated inhalation exposures therefore cannot be determined.

Irritation and Sensitisation
The notified polymer (at approximately 19 wt% concentration) was not a skin irritant in rabbits but was a slight eye irritant in rabbits. The notified polymer (at approximately 19 wt% concentration) was not a skin sensitiser in an LLNA assay in mice.

Repeated-dose toxicity
In a preliminary 14 day oral toxicity study in rats there were no treatment related effects when the notified

polymer (in an aqueous solution at approximately 20 wt% concentration) was administered at doses up to 1000 mg/kg bw/day.

In a 90 day repeated oral toxicity study in rats, the lowest observed adverse effect level (LOAEL) was determined to be 100 mg notified polymer /kg bw/day, on the basis of the nasal lesions that were observed at all dose levels. These lesions did not completely resolve following one or three month recovery periods. The study authors considered the lesions likely to be secondary to regurgative rhinitis caused by gavage administration of the test substance.

A one-generation reproductive toxicity study in rats was also conducted. Investigations of the non-reproductive parameters in this study also revealed minimal to moderate regurgitation rhinitis (an inflammatory response to regurgitation of the test substance) in males treated with doses of 100 mg notified polymer /kg bw/day and above, and females treated with the two highest doses (500 and 1000 mg notified polymer /kg bw/day). This suggests that the notified polymer was irritating to the nasal and bronchial epithelium and resulted in upper respiratory tract injury secondary to gavage induced regurgitation. Based on these findings in the nose the NOAEL was determined to be 20 mg/kg bw/day for males and 100 mg/kg bw/day for females.

The study authors suggest that the microscopic findings in the nose of the animals were secondary to regurgitation of the notified polymer associated with gavage administration, rather than being a direct effect on the nose. In addition, it is unlikely that such effects are of relevance to humans.

Mutagenicity.
The notified polymer (up to 30 wt% concentration) was not mutagenic in a bacterial reverse mutation assay and was not clastogenic in an *in vitro* chromosome aberration test.

Developmental and reproductive toxicity
In a developmental study, pregnant female rats (22 rats per dose) were administered the notified polymer (in an aqueous solution at approximately 20 wt% concentration) by gavage at 0, 100, 500 or 1,000 mg/kg bw/day during gestation days 6 to 20. The maternal NOAEL was established as 500 mg/kg bw/day based a statistically significant decreased body weight gain in the females treated at 1,000 mg/kg bw/day. The foetal NOAEL was > 1,000 mg/kg bw/day, based on the lack of foetal toxicity.

In a one-generation reproductive toxicity study in rats, the NOAEL for reproductive toxicity was >1000 mg/kg bw/day, based on the lack of effects on reproductive parameters.

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	H332 – Harmful if inhaled

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:

R20 Harmful by inhalation

Toxicology of breakdown products
The notified polymer contains perfluoroalkyl side-chains that are potential precursors of PFHxA in the environment (PFHxA; CAS No. 307-24-4). PFHxA is a perfluorocarboxylic acid consisting of 5 perfluorinated carbons (a short chain perfluorinated chemical). The polymer that is proposed for replacement by the notified polymer is expected to breakdown 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 breakdown products are generally less favourable compared to the short chain breakdown 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 breakdown product of the notified polymer (PFHxA) are likely to be similar or less than the human health hazards associated with the expected breakdown 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 by inhalation, with all other toxicology studies indicative of low hazard. The notified polymer as imported (up to 30 wt% concentration) is harmful by the inhalation route, however, inhalation toxicity is not of concern during reformulation as aerosols will not be generated. Slight eye irritation may occur during reformulation but automated processes are expected to be in place and PPE (clothing, gloves and goggles) will be worn during reformulation, which will further minimise exposure. The risk to reformulation workers handling the notified polymer is therefore not considered to be unreasonable.

Repeated dermal exposure of workers to the notified polymer may occur during stone and tile treatment. The repeated dermal toxicity of the notified polymer has not been investigated, however, only minimal signs of toxicity were observed in the repeated oral toxicity studies, the developmental study and the reproductive toxicity study in rats, which indicates that the notified polymer is of low hazard by repeated exposures. Additionally, systemic exposure to the notified polymer is expected to be low based on the high molecular weight (> 10,000 Da) of the notified polymer and the low proportion (< 1%) of low molecular weight species < 1000 Da. Systemic exposure of workers to breakdown products (e.g., PFHxA) is not expected based on the stability of the notified polymer. Worker exposure to impurities of the notified polymer is not expected to be significant. In addition, the use of engineering controls and PPE are expected to further lower exposure to the notified polymer, its breakdown products and impurities. Overall, the risk of repeat dose toxicity to workers resulting from repeated dermal exposure is not considered to be unreasonable.

Repeated inhalation exposure to the notified polymer may occur during spray operations. 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. Based on the uncertainties surrounding repeated inhalation exposure to the notified polymer, measures should be taken to minimise exposure. The risk of inhalation toxicity resulting from repeated exposure to the notified polymer is not considered to be unreasonable provided that users minimise inhalation of the notified polymer.

The risk to professionals of acute inhalation toxicity from the notified polymer is not considered to be unreasonable, as the controls used to minimise exposure to prevent repeated toxicity from inhalation are expected to also be protective of acute inhalation toxicity.

Workers may also be exposed to perfluoroalkyl impurities of the notified polymer at relatively low concentrations (< 1 wt%). 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 will apply stone and tile sealant products containing the notified polymer (up to 3 wt% concentration) by brush, roller, sponge or spray and may experience dermal, ocular or inhalation exposure. Exposure is expected to be short-term and infrequent (certainly less frequent than that experienced by professional users).

Slight eye irritation resulting from ocular exposure to the notified chemical is not expected based on the low concentration in end-use products (up to 3 wt% concentration). Dermal exposure to the notified polymer (up to 3 wt% concentration) is not expected to result in adverse effects, based on the low toxicity of the notified polymer. Additionally, the risk to public health from exposures to perfluoroalkyl impurities during use of products containing the notified polymer (up to 3 wt% concentration) is not considered to be unreasonable based on their low concentration (< 0.1 wt%) in end-use products.

A worst case scenario for acute inhalation exposure of members of the public is estimated to be the inhalation of up to a 5 mg/m^3 concentration of the notified chemical for 15 minutes for a typical spray application in an

enclosed bathroom (see Section 6.1.2). This is not expected to result in adverse health effects when compared to the nonlethal exposure determined from an acute inhalation toxicity study in rats (1,200 mg/m^3/4hr). The lack of repeated dose inhalation data for the notified polymer is of less concern for public exposure based on the expected infrequent use of the products. The risk to public health from use of the notified polymer in sprays (up to 3 wt% concentration) is not considered to be unreasonable, based on the infrequent and short-term exposure.

Therefore, the risk to public health from exposures to the notified polymer and perfluoroalkyl impurities during application of stone and tile products is not considered to be unreasonable.

The public may be exposed to the notified polymer and relatively low levels of perfluoroalkyl impurities through dermal contact with treated stone and tile surfaces. This exposure may be on a long term repeated basis. Repeated dose toxicity studies generally indicated low repeated dose toxicity for the notified polymer, additionally the high molecular weight (> 10,000 Da) of the notified polymer is expected to prevent any significant dermal absorption. The risk to public health from repeated dermal contact with the notified polymer is not considered to be unreasonable. Additionally, the risk to public health from exposures to perfluoroalkyl impurities resulting from dermal contact with treated surfaces is not considered to be unreasonable based on their low concentration (< 0.1 wt%) in end-use products.

The public may be exposed indirectly to PFHxA, formed by degradation of the notified polymer in 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 perfluoroalkyl substances that are the ultimate breakdown products of the majority of perfluoroalkyl polymers currently in Australian commerce (such as PFOA). In particular, it is noted that the polymer being replaced contains perfluoroalkyl carbon chain lengths > 6. It is concluded that the risks to human health from indirect exposure to breakdown products of perfluoroalkyl 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 perfluoroalkyl polymer.

It should also be noted that the notified polymer has been approved for the same uses in the US 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 enter wastewater streams during stone and tile treatment reformulation. Up to 0.2 kg of notified polymer in each container is estimated to be released as a result of rinsing empty import containers and up to 2.4 kg per day is expected to be released during transfer and equipment cleaning activities. It is expected that 50 batches over 50 days will be used in Australia per year. Therefore, up to 130 kg (0.7% of the total import volume) of the notified polymer is estimated to be released in wastewater streams due to stone and tile treatment reformulation activities. Wastewaters may be disposed of to sewer via waste treatment plants.

Residues in import containers may enter the wastewater streams following plastic container recycling. Alternatively, empty containers with residues of the notified polymer may be disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

When used in 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 default estimate for release to wastewater of a chemical (with solubility in excess of 100 mg/L) is 5% for both industrial and private

use in the paints, lacquers and varnishes industry (European Commission, 2003, pp. 241-242). Therefore, assuming a worst-case scenario whereby the notified polymer is at least dispersible, and where the entire import volume remains and is used in Australia up to 0.75 tonne of the notified polymer is estimated to be released in wastewater to sewers around Australia following its use in stone and tile treatments.

It is expected that stone and tile use 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. 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 treated stone and tile surfaces 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 stone and tile is expected to share the fate of articles. The majority of articles are expected to ultimately be disposed of to landfill.

The notified polymer applied to surfaces may also degrade as a result of weathering upon being exposed to environmental conditions. Degradation may result in the widespread release of PFHxA to surface waters, landfill and landfill leachates, soils, and other regions where release is not foreseen.

7.1.2. Environmental Fate

No environmental fate data were submitted.

The majority of the introduced notified polymer is expected to be reformulated into stone and tile treatment products. The majority of the introduced notified polymer is expected to adhere to stone and tile articles following application of the product containing the notified polymer. 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, cationic polymers have the potential to be removed from influent in sewage treatment plants (STP) via sorption to sludge. However, predictions of the environmental partitioning behaviour of polyfluoroalkyl polymers 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 perfluoroalkyl functionality as they assume lipophilicity for hydrophobic functionality, whereas the perfluoroalkyl functionality is both hydrophobic and lipophobic. The assumption that cationicity 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 the potential for the notified polymer to disperse in water, the notified polymer, and any associated degradation products and/or impurities/residual monomers of poly- or perfluoroalkyl compounds, may remain in the aqueous phase following wastewater treatment. As such, the notified polymer, its degradation products and the poly- or 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.

If the notified polymer is released it has the potential to disperse in water but it is not expected to hydrolyse under environmental conditions (pH 4 to 9, 25 C) based on structural considerations. Investigations of the biodegradation potential of fluoroacrylate polymer and fluorotelomer-based urethane polymer in aerobic soils (Russell *et al*., 2008; Russell *et al*., 2010; Washington *et al*., 2009) indicate very limited degradation of the fluorinated polymers. Biodegradation of the backbone of the notified polymer is expected to occur slowly under environmental conditions due to its high molecular weight. Thus, the notified polymer is considered to be persistent in the soil and water compartments.

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 polyfluoroalkyl functionality. The expected initial polyfluoroalkyl degradation products are assumed to undergo further degradation to form, among other compounds, the very persistent perfluorocarboxylic acid, 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 is expected to contain relatively low levels of

impurities that may degrade to form PFOA and other long-chain perfluorocarboxylic 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. 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.

Due to its high molecular weight which limits the ability to cross biological membrane, the notified polymer is not expected 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 perfluoroalkylated compounds, which short-chain six-fluorinated carbon fluorotelomer chemistry, that may degrade to form PFHxA, is replacing (although PFHxA and PFOA are not considered bioaccumulative in aquatic ecosystems). However, both are bioavailable and have been detected in wildlife as demonstrated by monitoring studies (Kumar *et al*., 2009; Ye *et al*., 2008ab; Wang *et al*., 2008). In general, the available evidence indicates that the bioaccumulation potential of perfluoroalkyl compounds is correlated with increasing carbon chain length (Giesy *et al*., 2010). Therefore, PFHxA has a lower bioaccumulation potential than PFOA and other long chain perfluoroalkyl substances.

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 and 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 stone and tile treatments is calculated assuming a worst-case release from reformulation to an STP with a daily effluent flow rate of 456 ML in a single major city. For this scenario, up to 1% of the total import volume of the notified polymer released during reformulation over 50 working days per year is used, and it is assumed there is no onsite treatment of waste water.

Predicted Environmental Concentration (PEC) for release to the aquatic compartment during reformulation		
Total Annual Import Volume	15,000	kg/year
Proportion expected to be released to sewer	1%	
Annual quantity of chemical released to sewer	150	kg/year
Days per year where release occurs	50	days/year
Daily chemical release:	3	kg/day
Individual Sewage Treatment Plant Average Daily Flow:	456	ML/day
Removal within STP	0%	
Effluent concentration	6.58	µg/L

The PEC due to releases from use in stone and tile treatments is calculated assuming nationwide release over a conservative 260 working days per year. Under a worst-case scenario, it is estimated that 5% of the notified polymer used in stone and tile treatments will be released to sewer during use. The resulting concentration in sewage effluent on a nationwide basis is estimated as follows:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	15,000	kg/year
Proportion expected to be released to sewer	5%	
Annual quantity of chemical released to sewer	750	kg/year
Days per year where release occurs	260	days/year
Daily chemical release:	2.88	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	0.63	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 7.21 µg/L. Therefore, the PEC for the aquatic compartments are calculated as follows:

Predicted Environmental Concentration (PEC) for release to the aquatic compartment duri□g use		
Combined effluent concentration	7.21	µg/L
Dilution Factor – River	1	
Dilution Factor – Ocean	10	
PEC – River	7.21	µg/L
PEC – Ocean	0.72	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 7.21 µg/L may potentially result in a soil concentration of approximately 48.0 µg/kg. Assuming accumulation of the notified chemical 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 240 µg/kg and 480 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. 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 ≥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 PHFxA 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 substances, 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 polyfluoroalkyl polymers in aerobic soil have been found to be indeterminate, with calculated half-lives ranging from decades to millennia (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 based on the information provided by the notifier. 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. A study report for acute toxicity to daphnia was submitted by the notifier. Details of this study can be found in Appendix C. The toxicity to fish and algae on an acute basis, and the toxicity to aquatic organisms on a chronic basis were calculated using the US EPA Interpretive Assistance Structure-Activity Relationship (SAR) for polymers containing cationic components (US EPA 2010). A worst-case approach was taken in calculation of the ecotoxicity.

Endpoint	*Result*	*Assessment Conclusion*
Measured data for the notified polymer		
Acute Toxicity		
Daphnia Toxicity (48 hour)	EC50 > 120 mg/L (product) EC50 > 24 mg/L* (notified polymer)	Potentially harmful to aquatic invertebrates
US EPA Interpretive Assistant SAR for the notified polymer		
Acute Toxicity		
Fish Toxicity (96 hour)	LC50 = 59.2 mg/L	Harmful
Daphnia Toxicity (48 hour)	EC50 = 203 mg/L	Not harmful
Algal Toxicity (96 hour)	EC50 = 23.6 mg/L	Harmful
Chronic Toxicity		
Fish Toxicity	ChV = 3.29 mg/L	Not harmful
Daphnia Toxicity	ChV = 14.5 mg/L	Not harmful
Algae Toxicity	ChV = 6.54 mg/L	Not harmful

*Calculated assuming the product contains ~20% of the notified polymer.

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is considered to be harmful to aquatic invertebrates and is formally classified as 'Acute Category 3: Harmful to aquatic life'.

Based on worst-case SAR, the notified polymer is potentially harmful to aquatic organisms in environmental waters with typical levels of total organic carbon. The notified polymer, it is also 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 calculated chronic value (ChV) for fish. This endpoint was used to calculate the predicted no-effect concentration (PNEC). An assessment factor of 50 was used as a worst-case calculated chronic endpoint was used for determination of the PNEC.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
ChV (Fish)	3.29	mg/L
Assessment Factor	50	
PNEC:	65.8	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	*Q*
Q - River:	7.21	65.8	0.11
Q - Ocean:	0.72	65.8	0.011

Based on a worst-case scenario where 5% of the total import volume of the notified polymer is released to sewer from use and 1% of the total import volume of the notified polymer is released to sewer from reformulation, 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 potentially harmful to aquatic life. As a polymer with high molecular weight, it is assumed to persist in the environment but it is not expected to bioaccumulate. However, the notified polymer is assumed to eventually 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 and longer chain perfluorocarboxylic acids. 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 and longer chain perfluorocarboxylic acids, 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 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 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) perfluoroalkyl acids that PFHxA is expected to replace. 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.

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.

RISK ASSESSMENT FOR EXTENSION APPLICATION

There are no changes under the proposed extension to the introduction volume, the use, or the occupational, public and environmental exposure. 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

Water Solubility < 0.006 g/L at 20 °C
< 0.59 mg/g (water extractable fraction)

Method	OECD TG 120 Solution/extraction behaviour of polymers in water.
Remarks	Test conducted on the product containing the notified polymer using the flask method. The concentration in the water phase was extrapolated by fluorine detection. The detected levels of fluorine present in the solutions were below the limit of detection. The level of notified polymer in the water extract was therefore less than 6 mg/L and the mean water extractable fraction of the notified polymer was less than 0.59 mg/g.
Test Facility	DuPont (Undated)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified polymer (approximately 19 wt% aqueous solution)
METHOD	OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure
Species/Strain	Rat/Crl:CD(SD)
Vehicle	None – administered as supplied
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose of test substance mg/kg bw*	*Mortality*
1	1F	175	0/1
2	1F	550	0/1
3	1F	1,750	0/1
4	1F	5,000	0/1
5	1F	5,000	0/1
6	1F	5,000	0/1

LD50	>5,000 mg test substance/kg bw (> 1,000 mg notified polymer/kg bw)
Signs of Toxicity	None
Effects in Organs	None
CONCLUSION	The test substance containing the notified polymer at approximately 19 wt% concentration is of low toxicity via the oral route.
TEST FACILITY	DuPont (2008a)

B.2. Acute toxicity – inhalation

TEST SUBSTANCE	Notified polymer (approximately at 20 % concentration)
METHOD	Similar to OECD TG 403 Acute Inhalation Toxicity
Species/Strain	Rat/Crl:CD(SD)
Vehicle	None – administered as supplied
Method of Exposure	Nose-only exposure
Exposure Period	4 hours
Physical Form	Liquid aerosol
Particle Size	MMAD±GSD = 4.0±3.2 and 3.8±3.9 µm for groups 2 and 3, respectively.
Remarks - Method	A control group was exposed to air. Two control animals were sacrificed 1 day post-exposure with the remaining two sacrificed 14 days post-exposure. The dosed groups were maintained until death or until 14 days post-exposure. All surviving rats were sacrificed on day 14 by carbon dioxide asphyxiation. Microscopic examination of the lungs was conducted on the control and Group 3 animals.

RESULTS

Group	*Number and Sex of Animals*	*Concentration mg/m³*		*Mortality*
		Total aerosol	*Dry aerosol[1]*	
1	4 M	0	0	0/4
2	5 M	2,200*	1,200	0/5
3	10 M	4,700**	1,700	8/10

*MMAD±GSD: 4.0 ± 3.2µm (78% particles by mass < 10 µm)

**MMAD±GSD: 3.8 ± 3.9μm (77% particles by mass < 10 μm)
[1]corresponding to the concentration of notified polymer

LC50	1200 < LC50 < 1700 mg notified polymer/m^3/4 hours
Signs of Toxicity	In Group 3, eight rats died within two days of being exposed, with seven of the animals dying on the first day. Weight loss (~30 g) was observed in the survivors, with weight gain after day 2. Clinical signs in rats from Group 3 included laboured breathing, discharge from the mouth, nose or eyes, stained fur, fast breathing, decreased muscle tone with no grasping reflex and a wound on the chin of one animal. In Group 2, one rat lost 2 g of weight by the first day. All animals in the group gained weight normally after day 2. Nasal discharge was observed in one animal. There were no adverse clinical signs observed in the control group.
Effects in Organs	Red staining of the skin around the nose/mouth or stained fur on head/face/chin was observed in most animals that died during the study. Discolouration of the lungs was also observed in one surviving animal from Group 3 that survived to the scheduled sacrifice. Microscopic examination of the lungs of the mortalities revealed lung lesions characterised by mild to moderate acute haemorrhage into the alveolar spaces. Minimal perivascular inflammation, minimal to mild infiltration of inflammatory cells within alveoli spaces, and haemorrhage in the nasal cavity was also present in many animals. In one of the survivors from Group 3, microscopic findings included interstitial inflammation characterised by multifocal thickening of alveolar septa by mononuclear cell infiltrates and fibrous tissue, and chronic haemorrhage in the lungs characterised by erythrophagocytosis and accumulation of pigmented macrophages within alveolar spaces. Effects were limited to minimal perivascular inflammation in the other surviving rat.
Remarks - Results	Necroscopy was not conducted on the rats from Group 2, thus it was not possible to determine a NOAEL for histopathological effects. The study authors suggest that the likely cause of death was acute pulmonary haemorrhage.
CONCLUSION	The notified polymer is harmful via inhalation.
TEST FACILITY	DuPont (2013)

B.3. Irritation – skin

TEST SUBSTANCE	Notified polymer (approximately 19 wt% aqueous solution)
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 Males
Vehicle	None – administered as supplied
Observation Period	72 Hours
Type of Dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations.

RESULTS

Remarks - Results	Scores of zero were observed at all observation points for both erythema and oedema formation.

CONCLUSION The test substance (notified polymer at approximately 19 wt% concentration) is non-irritating to the skin.

TEST FACILITY DuPont (2008b)

B.4. Irritation – eye

TEST SUBSTANCE Notified polymer (approximately 19 wt% aqueous solution)

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 Males
Vehicle None – administered as supplied
Observation Period 72 Hours
Remarks - Method No significant protocol deviations.

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	0.3	2	< 72 hours	0
Conjunctiva: chemosis	1	0	0	2	< 72 hours	0
Conjunctiva: discharge	0	0	0	2	< 24 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	1	< 24 hours	0

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

Remarks - Results Iridial inflammation was observed in two animals at one hour and slight to moderate conjunctival irritation (redness and chemosis) was observed in all animals, mostly at one and 24 hours. Moderate conjunctival discharge was observed in one animal at one hour. All animals were free of irritation at 72 hours.

CONCLUSION The test substance (notified polymer at approximately 19 wt%) is slightly irritating to the eye.

TEST FACILITY DuPont (2008c)

B.5. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE Notified polymer (approximately 19 wt% aqueous solution)

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/CBA/JHsd
Vehicle Propylene glycol
Remarks - Method No significant protocol deviations.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	364	-
5	302	0.83
25	325	0.89
50	238	0.65
100	188	0.52
Positive Control (HCA)		
25	2,237	6.15

HCA, hexylcinnamaldehyde.

Remarks - Results	There were no treatment related clinical signs of toxicity or statistically significant changes in body weights. The stimulation index was similar in treated and control groups and was below the threshold for a positive response (<3).
CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the test substance (notified polymer at approximately 19 wt%).
TEST FACILITY	DuPont (2008d)

B.6. Repeat dose toxicity – 14-day range finding study

TEST SUBSTANCE	Notified polymer (aqueous solution at approximately 20% concentration)
METHOD	Similar to OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Crl:CD(SD)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 14 days Dose regimen: 7 days per week
Vehicle	0.5% methylcellulose
Remarks - Method	No significant protocol deviations. Sample preparation was adjusted for purity.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M, 5F	0	0
low dose	5M, 5F	100	0
mid dose	5M, 5F	500	0
high dose	5M, 5F	1,000	0

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Glucose levels were decreased in males and females (69 and 70%, respectively) treated at 1,000 mg/kg bw/day. Whilst the changes were only minimal, the possibility that they were treatment related cannot be ruled out.

There were no significant changes in plasma fluoride levels in any animals dosed with the test substance. However, statistically significant and treatment related increases were observed in the urine fluoride levels of males and females, mainly at the two highest dose levels (500 and 1000 mg/kg bw/day). These increases were considered to be the result of exposure to the fluorine-containing test substance.

Effects in Organs

Males treated with 1,000 mg/kg bw/day displayed a statistically significant increase in kidney weight (116% of control) relative to body weight. Absolute kidney weight and kidney weight relative to brain weight were also increased in the same group of males, though the changes were not statistically significant.

Minimal to moderate increased accumulation of hyaline droplets in renal cortical tubules was observed in all males treated with 500 and 1,000 mg/kg bw/day. A minimal increase in hyaline droplet accumulation was observed in one male treated with 100 mg/kg bw/day. These changes are considered to be test-substance related. However, the study authors did not consider this to be an adverse effect, given that increased hyaline droplet accumulation is commonly observed in control male rats and the effects were not associated with other findings suggestive of renal cytotoxicity.

Two females treated with 1,000 mg/kg bw/day were found to have a minimal increase in mineralisation of renal tubules. The study authors considered that this was not a treatment related effect, given that the changes were similar to that of control animals.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as > 1,000 mg/kg bw/day in this study, based on the absence of adverse effects at all dose levels tested in this study.

TEST FACILITY DuPont (2011a)

B.7. Repeat dose toxicity – 90-day study

TEST SUBSTANCE Notified polymer (aqueous solution at approximately 20% concentration)

METHOD OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents.

Species/Strain	Rat/Crl:CD(SD)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: approximately 92 days Dose regimen: 7 days per week Post-exposure observation period: up to 3 months
Vehicle	0.5% methylcellulose
Remarks - Method	No significant protocol deviations. Samples of the test substance were adjusted for purity.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10M, 10F	0	0
low dose	10M, 10F	100	1
mid dose	10M, 10F	500	1
high dose	10M, 10F	1,000	1
control recovery (1 month)	10M, 10F	0	0
high dose recovery (1 month)	10M, 10F	1,000	1
control recovery (3 months)	5M, 5F	0	0
low dose recovery (3 months)	5M, 5F	100	1
mid dose recovery (3 months)	5M, 5F	500	0
high dose recovery (3 months)	5M, 5F	1,000	0

Mortality and Time to Death
The mortalities that occurred during the study period were not considered to be related to test substance treatment. The animals were either found dead or were euthanised in extremis.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Absolute neutrophil count was statistically significantly increased in males treated with 500 and 1000 mg/kg bw/day at test day 40 and 97. Similar increases were also seen in females (though not all were statistically significant). Mean total white blood cell count and absolute lymphocyte (not statistically significant) and monocyte counts were increased in female rats treated with 1000 mg/kg bw/day at test day 98. After one month recovery, absolute neutrophil count remained elevated relative to controls (though not statistically significant) in males and females dosed with 1000 mg/kg bw/day. The study authors suggest that these changes in white blood cell parameters are the result of inflammation caused by regurgitation of the test substance.

Specific gravity and urine total protein concentration were decreased in males dosed with 500 and 1000 mg/kg bw/day on day 97. The study authors indicate that this is likely due to the increased urine volume in these groups, which were not statistically significant changes.

Increased incidences of granular casts in the urine were observed in all male dose groups at test day 40. The incidence was lower by test day 97 and the effect was no longer observed after one month recovery. This effect was considered to be adverse and treatment related at dose levels of 500 and 1000 mg/kg bw/day as they correlated with findings of hyaline droplet nephropathy, chronic progressive nephropathy, and tubular casts (discussed below).

There were no significant changes in plasma fluoride levels in any animals dosed with the test substance either during the dosing period or after the recovery periods. However, statistically significant and treatment related increases were observed in the urine fluoride levels of males and females at the two highest dose levels (500 and 1000 mg/kg bw/day). After the one month recovery, levels in males and females remained increased in the 1000 mg/kg bw/day group, which was the only dose group tested (though only statistically significant in females). After the three month recovery, these levels were no longer statistically significantly different from controls, though in males they remained slightly elevated. These increases were considered to be the result of exposure to the fluorine-containing test substance.

Effects in Organs

Kidneys

The mean absolute and relative (relative to body weight and brain weight) kidney weights of males treated with 500 and 1000 mg/kg bw/day were statistically significantly increased relative to controls during the dosing period. Such effects were not observed after the one or three month recovery periods.

Enlarged kidneys were observed in 2/10 and 4/10 males treated with 500 and 1000 mg/kg bw/day, respectively. Discoloured kidneys were observed in 1/10 animals in each of the male groups treated with 500 and 1000 mg/kg bw/day.

Increased hyaline droplets were observed in the kidneys of all males treated with 500 and 1000 mg/kg bw/day of the test substance during the dosing period. The severity of this effect was dose related. Small amounts of hyaline droplets are a common finding in the kidneys of male rats. Increased levels of hyaline droplets are known to be caused by several xenobiotics.

Granular tubular casts were observed in males treated with 500 mg/kg bw/day (3/10 animals, all of minimal severity) and 1000 mg/kg bw/day (1/10 animals, of mild severity). Following the one month recovery period, several males treated with 1000 mg/kg bw/day still displayed this effect, though it had resolved by the three month recovery period. All animals with tubular casts also had increased hyaline droplets.

The incidence and severity of chronic progressive nephropathy was increased in males treated with 500 and 1000 mg/kg bw/day of the test substance during the dosing period. Following the one month recovery period, the majority of males treated with 1000 mg/kg bw/day still displayed chronic progressive nephropathy, though it had resolved by the three month recovery period. The study authors suggest that the increase in chronic progressive nephropathy is related to the increase in tubular hyaline droplets, rather than being a direct effect of the test substance.

Adrenal glands

Mean absolute adrenal weights and adrenal weights relative to body and brain weights were statistically significantly increased relative to controls in males treated with 1000 mg/kg bw/day during the dosing period.

Liver

The mean relative liver weight compared to body weight of males treated with 1000 mg/kg bw/day was statistically significantly increased during the dosing period.

Nose

Microscopic changes were observed in the noses of male and females from all groups, including some from the control groups. A summary of the incidences and average severity of some of the findings is shown below:

Sex:	Males				Females			
Dose (mg/kg bw/day)	0	100	500	1000	0	100	500	1000
Rats/group	10	10	10	10	10	10	10	10
Inflammation, subacute/chronic	0	1(2)	10(2.7)	10(2.9)	0	1(1)	10(2.9)	8(2.6)
Foreign material	0	1(2)	10(2.6)	10(2.9)	0	1(1)	10(2.8)	9(2.4)
Inflammation, subacute/chronic, maxillary	0	0	9(1.2)	10(1.8)	0	0	8(1.4)	5(2)

sinus								
Foreign material, maxillary sinus	0	0	9(1.7)	10(1.5)	0	0	9(2)	7(1.4)
Degeneration/regeneration, olfactory epithelium	1(1)	7(1.3)	10(2.5)	10(2.4)	5(1)	7(1.4)	10(2.5)	8(2)
Degeneration/regeneration, respiratory mucosa	0	0	7(1)	5(1.2)	0	0	5(1.2)	4(1.5)
Respiratory metaplasia, olfactory epithelium	0	0	10(2.2)	10(1.9)	1(1)	1(1)	9(2)	5(1.6)
Fibrosis/adhesions, turbinates	0	0	5(2.2)	10(2.2)	0	0	10(1.8)	7(2.4)

( ), Average severity of affected animals: 1=minimal, 2=mild, 3=moderate, 4=severe

Following the one month recovery period effects in the nose were not resolved in males and females and were of a similar type to those observed at the end of the dosing period. The lesions were of minimal to moderate severity in the high dose recovery animals (note that there were no low or mid dose one month recovery animals examined).

Following the three month recovery period effects in the nose were not fully resolved in males or females, particularly in the mid and high dose animals. The incidence and severity of the lesions were similar to those observed at the end of the dosing period.

Remarks – Results

Administration of the test substance at doses of ≥ 500 mg/kg bw/day resulted in adverse effects in the kidneys of male rats. Such effects included hyaline droplet accumulation, urinary and microscopic granular casts, chronic progressive nephropathy, increased kidney weights and some enlarged and discoloured kidneys. Given that such changes are known to be species and sex specific findings, they are not considered to be predictive of effects in other species.

Nasal lesions may be the result of regurgitation of the test substance into the nose, rather than being directly related to the test substance. The study authors cite several reasons why this is considered to be the case:

(a) In the animals most severely affected, lesions associated with foreign material were observed in the nasal cavity.
(b) The distribution of test substance mainly in the posterior nasal cavity is as expected.
(c) The lower amount of test substance in the nose of most animals dosed with 100 mg/kg bw/day is consistent with the lower viscosity of the dosing suspension in comparison to higher doses.

The underlying cause of the regurgitation could not be determined. It is unlikely that such effects would be relevant to humans.

CONCLUSION

The Lowest Observed Adverse Effect Level (LOAEL) was established as 100 mg/kg bw/day in this study, based on the presence of nasal lesions in all groups treated with the test substance.

TEST FACILITY DuPont (2011b)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE	Notified polymer (approximately 20% concentration)
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	Rat S9 fraction from Aroclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 333 – 5,000 µg/plate b) Without metabolic activation: 333 – 5,000 µg/plate
Vehicle	Water
Remarks - Method	No significant protocol deviations. Sample preparation of the test substance was not adjusted for purity. A range-finding study was conducted in all strains at up to 5000 µg/plate. Vehicle and positive controls were conducted concurrently.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000	-	≥ 3,333	negative
Test 2	-	>5000	≥ 3,333	negative
Present				
Test 1	> 5,000	-	≥ 3,333	negative
Test 2	-	> 5,000	≥ 3,333	negative

CONCLUSION The test substance (an aqueous solution containing the notified polymer at approximately 20%) was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY DuPont (2008e)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE Notified polymer (at approximately 20% concentration)

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test
Cell Type/Cell Line Human peripheral blood lymphocytes
Metabolic Activation System Rat S9 fraction from Aroclor 1254 induced rat liver
Vehicle Water
Remarks - Method No significant protocol deviations.

Sample preparation of the test substance was not adjusted for purity.

A dose-finding study was conducted in the presence and absence of metabolic activation at concentrations of up to 5,000 µg/mL.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 250, 500, 1,000*, 2,500*, 5,000*, MMC*	4	22
Test 2	0*, 250, 500, 1,000*, 2,500*, 5,000*, MMC*	22	22
Present			
Test 1	0*, 250, 500, 1,000*, 2,500*, 5,000*, CP*	4	22

*Cultures selected for metaphase analysis.
MMC, Mitomycin C. CP, Cyclophosphamide.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000	> 5,000	> 5,000	negative
Test 2	> 5,000	> 5,000	> 5,000	negative
Present				
Test 1	> 5,000	> 5,000	> 5,000	negative

Remarks - Results The positive and vehicle controls gave satisfactory responses, confirming the validity of the test system. A precipitate was observed at ≥ 3,000 µg/mL at the end of the dose finding test, however no precipitate was observed in the main test.

The mitotic index was decreased in the absence of metabolic activation at the highest dose, however, the decrease was < 50% so it did not qualify as cytotoxic. In all three tests a portion of the cells were not able to be scored due to changes in the chromosome morphology and were excluded from the data set.

In the two tests with a 4 hour exposure, with and without metabolic activation period, the test material did not induce any statistically significant increases in the percentage of cells with numerical or structural aberrations.

In Test 2, with an exposure period of 22 hours in the absence of metabolic activation, there was a statistically significant increase in the number of structural aberrations at the maximum concentration of 5,000 µg/mL. The number of cells with structural aberrations at a concentration of 5,000 µg/mL was 5.0% compared to the control value of 1.5%. The historical control data provided indicates that the range for the number of cells with structural aberrations in the solvent control is 0 – 5% in the absence of metabolic activation. The value seen at a concentration of 5,000 µg/mL in the absence of metabolic activation and with an exposure period of 22 hours are within the historical control values and are therefore not considered to be indicative of clastogenic activity.

CONCLUSION The test substance (an aqueous solution of the notified polymer at approximately 20% concentration) was not clastogenic to human peripheral lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY DuPont (2008f)

B.10. Developmental toxicity

TEST SUBSTANCE Notified polymer (aqueous solution at approximately 20% concentration)

METHOD
- Species/Strain: Rat/Crl:CD(SD)
- Route of Administration: Oral – gavage
- Exposure Information: Exposure days: gestation days 6-20; Post-exposure observation period: none
- Vehicle: 0.5% Methylcellulose in water
- Remarks - Method: No significant protocol deviations.

Sample preparation was adjusted for purity of the notified polymer.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	22	0	0/22
2	22	100	0/22
3	22	500	0/22
4	22	1,000	1/22

Mortality and Time to Death

One female in the 1,000 mg/kg bw/day group died prior to initiation of dosing on gestation day 6, thus this mortality is not considered to be treatment related.

Effects on Dams

A statistically significant lower bodyweight gain over gestation days 6-8 was observed in females treated at 1,000 mg/kg bw/day. This decrease in bodyweight corresponded to a decrease in food consumption in these animals during this period. There were no other adverse effects noted in the dams.

Effects on Foetus

Multiple malformations were observed in one foetus from the control group, including cleft lip and palate, microglossia (small tongue) and micrognathia (small jaw). In the 100 mg/kg/day group, one foetus had a cleft palate. In the 1,000 mg/kg bw/day dose group, one foetus had an umbilical hernia. The effects seen in the foetuses were not considered to be test substance related due to the low incidence and lack of any dose response relationship.

Remarks - Results

Resorptions and live foetuses were comparable across all dose groups and the control group, as were the mean foetal weight, litter sex ratio, and foetal malformations.

CONCLUSION

The maternal NOAEL was established as 500 mg/kg bw/day in this study, based on significantly lower bodyweight gain over gestation days 6-8. The foetal NOAEL was established as > 1,000 mg/kg bw/day based on the absence of adverse treatment related effects at any dose level.

TEST FACILITY DuPont (2009)

B.11. Toxicity to reproduction – one generation study

TEST SUBSTANCE Notified chemical (aqueous solution at approximately 20% concentration)

METHOD OECD TG 415 One-Generation Reproduction Toxicity Study

Species/Strain	Rat/Crl:CD(SD)
Route of Administration	Oral – gavage
Exposure Information	Exposure period - males: at least approx. 84 days Exposure period - females: up to 128 days in total
Vehicle	0.5% aqueous methylcellulose
Remarks – Method	No significant protocol deviations. Sample preparation of the test substance was adjusted for purity of the notified polymer.. Additional evaluations beyond those specified in the protocol included: the evaluation of estrous and sperm in parental animals; and the examination of developmental landmarks for males and females of the F1 generation (and scheduled sacrifice on postnatal day 60).

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	25M, 25F	0	0
2	25M, 25F	20	0
3	25M, 25F	100	0
4	25M, 25F	500	1
5	25M, 25F	1,000	0

Mortality and Time to Death

The small number of deaths (one male on day 108 and one F1 female) observed during the study were not considered to be related to test substance treatment.

Effects on Parental (P) animals:

There were statistically significant reductions compared to controls in mean body weights and body weight gains in males treated with 1,000 mg/kg bw/day during various time periods of the study. There were also statistically significant reductions compared to controls in mean food consumption and food efficiency in males treated with 1,000 mg/kg bw/day during various time periods of the study.

There were statistically significant increases in kidney weight parameters (mean absolute, mean relative to brain

weights, and mean relative to body weights) in males treated with 1,000 mg/kg bw/day and 500 mg/kg bw/day. This corresponded with the presence of hyaline droplet accumulation in the proximal renal tubules of all males at these treatment levels (minimal or mild severity in 500 mg/kg bw/day males, and the majority were of mild severity in 1,000 mg/kg bw/day males, ie. a dose related increase in severity was evident). Four of these animals also had granular casts in the medulla. Three males treated with 500 mg/kg bw/day and six males treated with 1,000 mg/kg bw/day showed pale discoloration of the kidneys, whilst none of the control or animals treated with lower doses showed this effect. This finding was considered to be the result of the hyaline droplet accumulation in renal tubules. Hyaline droplet accumulation is known to be unique to male rats and thus not of significance to other species.

There was a slight increase in the mean absolute kidney weight of females treated with 1,000 mg/kg bw/day, and also statistically significant increases in the mean kidney weights relative to body weight and brain weight of the same group. There were no corresponding morphological changes in the kidneys of female animals.

Hepatocellular hypertrophy was observed in the livers of many males treated with 500 mg/kg bw/day and 1,000 mg/kg bw/day with dose related increases in incidence and severity. This was considered to be the result of the induction of hepatocellular enzymes and non-adverse.

Most males and females treated with 500 and 1,000 mg/kg bw/day showed minimal to moderate regurgitation rhinitis (inflammation and degenerative and regenerative changes in olfactory and respiratory mucosa associated with regurgitated test substance), with a slight dose-related trend in incidence and severity. This effect was also observed in several males treated with 100 mg/kg bw/day (minimal to mild severity). This indicates that the test substance increased the frequency of regurgitation and was irritating to the nasal and bronchial epithelium.

There were also statistically significant increases in male adrenal gland weight parameters in animals treated with 1,000 mg/kg bw/day. There were no corresponding changes to adrenal pathology and thus the study authors suggest that this observation was caused by increased adrenal endocrine activity resulting from the regurgitation rhinitis in these males.

In three male rats (one at 500 mg/kg bw/day and two at 1,000 mg/kg bw/day) the test substance was observed in the lung airways together with peribronchial inflammation associated with aspirated material. These animals also displayed regurgitation rhinitis.

Effects on 1st Filial Generation (F1)

There were no significant test substance related findings noted in any animals of the F1 generation.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) for systemic toxicity was determined to be 20 and 100 mg/kg bw/day for males and females, respectively, based on the presence of nasal lesions. The NOAEL for reproductive toxicity was determined to be 1000 mg/kg bw/day, as there were no changes observed in the reproductive parameters.

TEST FACILITY DuPont (2011c)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Ecotoxicological Investigations

C.1.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified polymer (~20% in water)
METHOD	Method comparable to OECD TG 202 *Daphnia* sp. Acute Immobilisation Test - Static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	100 - 140 mg $CaCO_3$/L
Analytical Monitoring	Not reported
Remarks - Method	The test was conducted according to good laboratory practice (GLP). The 120 mg/L test solution was cloudy with undissolved test material present during the test.

RESULTS

Concentration mg/L Nominal	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
0	10	0	0
0.12	10	0	0
1.2	10	0	0
12	10	0	0
120	10	0	1

EC50	> 120 mg test substance/L at 48 hours
Remarks - Results	All relevant test validity criteria were met. The immobilisation observed at 120 mg/L may be influenced by undissolved solids which may affect daphnia mobility. As the test was conducted on a product containing approximately 20% of the notified polymer, the EC50 needs to be corrected to > 24 mg/L to reflect the concentration of the notified polymer.
CONCLUSION	The notified polymer is, at worst, harmful to aquatic invertebrates.
TEST FACILITY	DuPont (2008g)

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, 2006c; DuPont, 2007a, 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, 2007a).
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, 2007b). 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, 2006a) or in a test for chromosome aberrations in human peripheral blood lymphocytes (DuPont 2006b).

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, for PFOA, effects were observed at 0.64 mg/kg bw/day (LOAEL), while for PFHxA, no effects were observed at 10 mg/kg bw/day with a LOAEL of 100 mg/kg bw/day.
- In chronic toxicity studies in rats, for PFOA, effects were observed at 14.2/16.1 (m/f) mg/kg bw/day (LOAEL), while for PFHxA, no effects were observed at 15/30 (m/f) mg/kg bw/day with a LOAEL of 100/200 (m/f) mg/kg bw/day.
- 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 to be “likely to be carcinogenic to humans” (US EPA, 2012).

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