File No: LTD/1986

September 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

2-Propenoic acid, 2-methyl-, 2,2,3,3,4,4,5,5-octafluoropentyl ester (INCI Name: Octafluoropentyl Methacrylate)

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

This Public Report is 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

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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
LTD/1986	Dermalogica Pty Ltd	2-Propenoic acid, 2-methyl-, 2,2,3,3,4,4,5,5-octafluoropentyl ester (INCI Name: Octafluoropentyl Methacrylate)	Yes	≤ 1 tonne/s per annum	Additive for hair care products

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Flammable Liquids (Category 4)	H227 – Combustible liquid

The environmental hazard classification according to the *Globally Harmonised System of 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 2	H401: Toxic to aquatic life

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

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

Environmental risk assessment
On the basis of the assessed use pattern, the notified chemical itself is not considered to directly pose an unreasonable risk to the environment. However, the notified chemical contains fluorinated carbon groups that have the potential to degrade to the exceptionally persistent short-chain polyfluorinated carboxylic acid, pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro-. The assessed use pattern of the notified chemical does not control the release of breakdown products into the environment during use and after disposal and the long-term environmental risk profile of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- is currently unknown. Consequently, the long-term risk profile for the notified chemical and its degradation products is unknown.

The persistence of chemicals similar to pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- in the environment is of concern because they have potential to be globally distributed. Based on the currently available environmental hazard information, pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- is considered to have lower overall ecotoxicity concerns than homologous long-chain perfluorocarboxylic acids, which contain seven or more perfluorinated carbon atoms, such as perfluorooctanoic acid (PFOA).

The environmental degradation of the notified chemical is expected to contribute to the cumulative emissions of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- to the environment. Based on the currently available evidence, the concentrations of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- and other short chain per- and polyfluorinated carboxylic acids are not considered to pose a concern for the environment. However, if additional hazard information becomes available to indicate that short-chain per- and polyfluorinated carboxylic acids have hazard characteristics of high concern for the environment (such as PBT), then the risks posed by industrial uses of precursors to these environmental degradants may need to be re-assessed.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Flammable Liquids (Category 4): H227 – Combustible liquid

The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present and the intended use/exposure scenario.

- Due to the flammable properties of the notified chemical, the notifier should consider their obligations under the Australian Dangerous Goods Code.

CONTROL MEASURES

Occupational Health and Safety

- As no skin irritation study was available and the notified chemical may be a slight skin irritant, 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 chemical as introduced:
  - Gloves

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of 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

- If additional hazard information becomes available to indicate that short-chain per- and polyfluorinated carboxylic acids have hazard characteristics of high concern for the environment (such as PBT), then the risks posed by industrial uses of precursors to these environmental degradants may need to be re-assessed.

Disposal

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

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

- Spills or accidental release of the notified chemical 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 chemical 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 one tonne per annum notified chemical;
- additional information has become available to the person as to an adverse effect of the polyfluoroalkyl degradation products of the notified chemical;
- additional information has become available to the person as to the environmental fate of the notified chemical or its polyfluoroalkyl degradation products in relation to degradation or partitioning behaviour, including during water treatment processes;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from ingredient in hair care products or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

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

Safety Data Sheet
The SDS of the notified chemical (and products containing the notified chemical) provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

This notification has been conducted under the cooperative arrangement with Canada. The health and environmental hazard assessment components of the Canadian report were provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS and the Department of the Environment.

APPLICANT(S)
Dermalogica Pty Ltd (ABN: 46 067 065 105)
111 Chandos Street
CROWS NEST NSW 2065

NOTIFICATION CATEGORY
Limited-small volume (Approved Foreign Scheme): Chemical other than polymer (1 tonne or less per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: other names, analytical data, degree of purity, impurities, and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: adsorption/desorption.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
Canada (2016)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Living Proof No Frizz Shampoo
Living Proof No Frizz Conditioner
Living Proof No Frizz Leave-in Conditioner
Living Proof No Frizz Weightless Styling Spray
Living Proof No Frizz Nourishing Styling Cream
Living Proof No Frizz Humidity Shield
Living Proof No Frizz Nourishing Oil
Living Proof Full Shampoo
Living Proof Full Conditioner
Living Proof Full Root Lift
Living Proof Full Thickening Cream
Living Proof Full Thickening Mousse
Living Proof Full Dry Volume Blast
Living Proof Restore Shampoo
Living Proof Restore Conditioner
Living Proof Restore Mask Treatment
Living Proof Restore Repair Leave-In
Living Proof Restore Instant Protection Hairspray
Living Proof Restore Perfecting Spray
Living Proof Perfect Hair Day (PhD) Shampoo
Living Proof Perfect Hair Day (PhD) Conditioner
Living Proof Perfect Hair Day (PhD) Dry Shampoo
Living Proof Perfect Hair Day (PhD) Night Cap Overnight Perfector
Living Proof Perfect Hair Day (PhD) 5-in-1 Styling Treatment
Living Proof Perfect Hair Day (PhD) Fresh Cut Split End Mender
Living Proof Curl Conditioning Wash

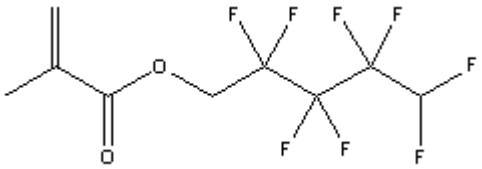
Living Proof Curl Detangling Rinse
Living Proof Curl Leave-in Conditioner
Living Proof Curl Enhancing Styling Mousse
Living Proof Curl Defining Styling Cream
Living Proof Style|Lab Control Hairspray
Living Proof Style|Lab Blowout
Living Proof Timeless Shampoo
Living Proof Timeless Conditioner
Living Proof Timeless Plumping Mousse
Living Proof Timeless Pre-Shampoo Treatment
Living Proof Style|Lab Amp^2 Instant Texture Volumizer
Living Proof Style|Lab Straight Hairspray
Living Proof Style|Lab Prime Style Extender
Living Proof Style|Lab Flex Shaping Hairspray
Living Proof Style|Lab Instant Texture Mist

CAS NUMBER
355-93-1

CHEMICAL NAME
2-Propenoic acid, 2-methyl-, 2,2,3,3,4,4,5,5-octafluoropentyl ester

MOLECULAR FORMULA
$C_9H_8F_8O_2$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
300.15 g/mol

ANALYTICAL DATA
Reference NMR spectra was provided.

3. COMPOSITION

DEGREE OF PURITY
> 99%

DEGRADATION PRODUCTS
The notified chemical may potentially degrade to 1-pentanol, 2,2,3,3,4,4,5,5-octafluoro- (CAS No. 355-80-6) or pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- (CAS No. 376-72-7) that may be persistent in the environment.

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa:

Property	Value	Data Source/Justification
Freezing Point	< -80 °C	Measured
Boiling Point	180.5 °C at 101.3 kPa	Measured
Density	1,425 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.24 kPa at 25.5 °C	Measured
Water Solubility	0.03 g/L at 20 °C	Measured

Hydrolysis as a Function of pH	t½ = 4.7, 5.5 and 0.5 days at pH 4, 7 and 9, respectively, at 25 °C	Measured
Partition Coefficient (n-octanol/water)	log Pow = 3.03 ± 0.27	Measured
Adsorption/Desorption	Not determined	May have low absorption based on the presence of perfluorinated functionalities that are known to be surface active.
Dissociation Constant	Not determined	No dissociable functionality.
Flash Point	75 °C	Measured
Flammability	Not determined	Expected to be a flammable liquid based on measured flash point.
Autoignition Temperature	408 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties.

DISCUSSION OF PROPERTIES

For full details of tests on physical and chemical properties that were not assessed by Canada, refer to Appendix A.

Reactivity

The notified chemical is stable under normal conditions of storage. It contains a reactive acrylic functional group that may undergo polymerization.

Physical hazard classification

Based on the submitted physico-chemical data depicted in the above table, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	***Hazard statement***
Flammable Liquids (Category 4)	H227 – Combustible liquid

5. INTRODUCTION AND USE INFORMATION

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

The notified chemical will not be manufactured in Australia. It will be imported as a component of finished hair care products at concentrations ≤ 5%. The neat form of the notified chemical will not be imported and reformulated in Australia.

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

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

PORT OF ENTRY

Sydney.

TRANSPORTATION AND PACKAGING

The notified chemical will be imported as a component of finished hair care products in containers up to 1 L in capacity that are suitable for retail sale including bottles, tubes and jars. The majority of the containers are expected to have a volume of 236 ml (8 oz). The finished hair care products will be distributed throughout Australia by road to beauty salons and retail shops.

USE
The notified chemical is an additive in leave-on and rinse-off hair care products. The notified chemical will be present in the finished products at concentrations of ≤ 5%. In the aerosol hair spray products, the concentration of the notified chemical will be ≤ 1%.

OPERATION DESCRIPTION
The finished hair care products containing the notified chemical at ≤ 5% concentration will be used by consumers and professionals such as hairdressers and beauty salon workers. The finished products may be applied to the hair in a number of ways mainly using applicators, by spray or by hand.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Hairdressers/Beauty Salon Workers	8	300

EXPOSURE DETAILS
Transport and storage workers may come into contact with the notified chemical at concentrations up to 5%, only in the event of accidental rupture of packaging.

Dermal, ocular and inhalation exposure to up to 5% concentration of the notified chemical in the finished hair care products may occur in professionals (e.g. hair dressers or beauty salon workers) where the services provided involve the application of the products to clients. Such professionals may use limited personal protective equipment (PPE), such as gloves, to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers to the notified chemical is expected to be of a similar or lesser extent than the exposure experienced by consumers using the finished products at home.

6.1.2. Public Exposure
The public will be exposed to the notified chemical (at ≤ 5% concentration) through the use of the rinse-off/leave-on hair care products. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if the products are applied by spray.

Data on typical use patterns of hair care product categories in which the notified chemical may be present are shown in the following tables (SCCS, 2012; Cadby *et al.*, 2002; SDA, 2005). For the purposes of the exposure assessment via the dermal route, Australian use patterns for various product categories are assumed to be similar to those in Europe. For the inhalation exposure assessment (European Commission, 2003; SDA, 2005), an adult inhalation rate of 20 m^3/day (enHealth, 2004) was used and the bioavailability of the notified chemical was assumed as 100%. An adult average bodyweight of 64 kg was used in the calculations.

Dermal exposure

Product type	**Amount** (mg/day)	**C** (%)	**RF**	**Daily dermal exposure** (mg/kg bw/day)
Shampoo	10,460	5	0.01	0.082
Conditioner	3,920	5	0.01	0.031
Hair styling	4,000	5	0.1	0.31
Total				**0.42**

C = concentration of the notified chemical; RF = retention factor.
Daily dermal exposure = Amount × C × RF / body weight

Inhalation exposure

Product type	Amount (g/use)	C (%)	Inhalation rate (m^3/day)	Exposure duration (Zone 1) (mins)	Exposure duration (Zone 2) (mins)	Fraction inhaled (%)	Volume (Zone 1) (m^3)	Volume (Zone 2) (m^3)	Daily inhalation exposure (mg/kg bw/day)
Aerosol Hairspray	9.89	1	20	1	20	50	1	10	**0.032**

C = concentration of the notified chemical
Daily inhalation exposure = Daily systemic exposure in Zone 1 [(amount × C × inhalation rate × exposure duration (zone 1) × fraction inhaled)/(volume (zone 1) × body weight)] + Daily systemic exposure in Zone 2 [(amount × C × inhalation rate × exposure duration (zone 2) × fraction inhaled)/(volume (zone 2) × body weight)]

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a dermal exposure dose of 0.42 mg/kg bw/day and an inhalation exposure dose of 0.032 mg/kg bw/day. It is acknowledged that inhalation exposure to the notified chemical from use of other non-aerosolised hair spray products (e.g pump spray) may also occur. However, it is considered that the assumed aerosol spray inhalation exposure assessment parameters are sufficiently protective to cover the additional inhalation exposure caused by the use of pump spray hair care products which possess lower inhalation exposure factors due to the nature of the spray pumps.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical were previously assessed by Canada and are described in the table below. For full details of tests on physical and chemical properties that were not assessed by Canada, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, eye irritation	Slightly-irritating
Mouse, skin sensitisation – Local lymph node assay	No evidence of sensitisation
Human, skin sensitisation – RIPT (2%)	No evidence of sensitisation
Rat, repeat dose oral toxicity – 7 day range finding	NOAEL = 300 mg/kg bw/day
Rat, repeat dose dermal toxicity – 28 days	NOAEL > 1,300 mg/kg bw/day
Rat, repeat dose inhalation toxicity – 5 days	NOAEC > 168 ppm
Mutagenicity – bacterial reverse mutation	Non mutagenic
Mutagenicity – bacterial reverse mutation	Non mutagenic
Genotoxicity – *in vitro* mammalian cell micronucleus test	Non genotoxic
Rat, developmental toxicity – dermal	NOEL > 1,300 mg/kg bw/day; slight skin irritation
Rabbit, developmental toxicity – dermal	NOAEL > 1,300 mg/kg bw/day
Skin Absorption: *in vitro* method	Dermal delivery rates: 1.53% under occlusive conditions 0.49% under unocclusive conditions
Basal Cytotoxicity – Neutral Red Uptake (NRU) Assay	NRU_{50} > 2,500 µg/mL

Toxicokinetics, metabolism and distribution
No studies were provided on the metabolism and distribution for the notified chemical.

Since the chemical is proposed to be used in cosmetic hair products applied by hands or spray, the main absorption route is expected to be dermal and to a lesser extent via inhalation. In an *in vitro* percutaneous absorption test conducted using ^{14}C radiolabelled notified chemical at a concentration of 2%, under unocclusive conditions that represent the intended consumer use, the dermal delivery rate (percent of applied dose) of the notified chemical was determined as 0.49% (equivalent to a dermal delivery of 2.32 µg/cm^2) with an absorbed dose (percent of applied dose) of 0.18% (equivalent to an absorbed dose of 0.87 µg/cm^2).

Acute toxicity
Based on an *in vitro* neutral red uptake (NRU) study on the notified chemical using mouse fibroblasts, the rodent oral LD50 was estimated to be > 3,183 mg/kg bw. A rat oral acute toxicity study on the notified chemical determined the LD50 to be > 2,000 mg/kg bw, indicative of low toxicity via the oral route.

Irritation and sensitisation
The notified chemical was considered to be slightly irritating in an eye irritation study conducted in rabbits.

No skin irritation study report was provided for the notified chemical. However, in a repeat dose dermal toxicity study in rats (WIL 2008a) and a dermal developmental toxicity study in rats (WIL 2008b), the notified chemical applied neat to the skin of the test animals did not produce significant skin irritation. In a dermal developmental toxicity in rabbits (WIL 2008c), the notified chemical showed slight skin irritating properties in 4/20 of the test animals.

A mouse local lymph node assay on the notified chemical up to 45% concentration did not show evidence of skin sensitisation for the chemical. Human repeated insult patch tests (RIPTs) were conducted using 4 different cosmetic products containing 2% of the notified chemical and results did not reveal evidence of skin sensitisation.

Repeated dose toxicity
In a 7-day range-finding oral toxicity study in rats, the notified chemical at a dose level of 1,000 mg/kg bw/day caused impaired muscle coordination and/or impaired equilibrium in rats. Hypoactivity, decreased respiration rate and prostration were also noted in female rats at this dose level. No significant clinical observations were noted at dose levels of 100 and 300 mg/kg bw/day and hence the NOAEL was 300 mg/kg bw/day.

In a rat 28-day repeated dose dermal toxicity study conducted on the notified chemical, evidence of systemic effects that may be attributable to the notified chemical were limited to lower total protein and lower globulin levels. No adverse effects were noted at the dose level of > 1,300 mg/kg bw/day in the study.

In a rat repeated dose inhalation toxicity study, the test animals were exposed to the notified chemical at concentrations up to 168 ppm, for 6 hours per day over 5 consecutive days. No adverse effects were noted in the study and the No Observed Adverse Effect Concentration (NOAEC) was considered to be > 168 ppm, based on the highest concentration tested.

Mutagenicity/Genotoxicity
The notified chemical was not mutagenic in two bacterial reverse mutation studies and was not clastogenic in an in vitro mammalian cell micronucleus test with human peripheral blood lymphocytes.

Toxicity for development
Study reports on developmental toxicity via the dermal route for the notified chemical were provided. The notified chemical was tested in rats and rabbits at a dose level of 1,300 mg/kg bw. In the rat study, no significant clinical effects of the notified chemical on dams were noted and no developmental toxicity effects of the chemical on foetus were recorded. In the rabbit study, some slight skin irritation effects of the notified chemical were noted in the dams treated with the notified chemical. There were no foetal malformation or developmental variations attributed to the notified chemical noted in the study.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified chemical will not be reformulated in Australia. It will be imported as a component in finished hair care products at concentrations up to 5%.

Beauty care professionals may use the products containing the notified chemical at ≤ 5% concentrations in salons and beauty shops. The beauty care professionals may use limited PPE, such as gloves, during work, to minimise exposure. In addition, local exhaust ventilation is expected to be a standard engineering control in

beauty salons. If PPE is used, the risk to workers is expected to be of a similar or lesser extent than that experienced by consumers using the same products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health

Members of the public may experience repeated dermal and inhalation exposure to the notified chemical (at ≤ 5% concentration) through the use of the finished hair care products. Based on repeated–dose dermal and inhalation toxicity studies, and given the proposed end use concentrations of the notified chemical in finished hair care products, the risk of systemic toxicity is not considered to be unreasonable.

Irritation

The notified chemical may be slightly irritating to the skin and eye. However, irritation effects are not expected from use of the notified chemical at the proposed use concentrations in the finished hair care products.

Based on the information available, the risk to the public associated with the use of the finished hair care products containing the notified chemical at ≤ 5% in concentrations is not considered to be unreasonable.

Risk from exposure to degradants

The public may potentially be exposed indirectly to the ultimate degradants of the notified polymer, such as 1-pentanol, 2,2,3,3,4,4,5,5-octafluoro- (CAS No. 355-80-6) or pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- (CAS No. 376-72-7). However, the long term significance and magnitude of such exposure remain unknown. The dispersive use pattern of the notified chemical and its limited introduction volume, coupled with the fact that the ultimate degradants are less bioaccumulative in the environment, are expected to mitigate long-term impacts.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported as a component of finished hair care products. As the notified chemical will not be manufactured or reformulated in Australia, no environmental releases will occur from these activities. Environmental release may occur as a result of spills and leaks during transport. In the rare event of an accidental spill or leak during transport, the products containing the notified chemical are expected to be collected with inert material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical is expected to be released to sewers in domestic situations across Australia as a result of its use in cosmetic products, which are washed off the hair of consumers.

RELEASE OF CHEMICAL FROM DISPOSAL

Wastes and residues of the notified chemical in empty containers are likely to either share the fate of the container and be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in hair care products in Australia, the majority of the notified chemical is expected to enter the sewer system, before potential release to surface waters nationwide. Based on the result of two biodegradability studies, the notified chemical is not considered to be readily biodegradable (27% and 22% in 28 days). For details of the environmental fate studies, please refer to Appendix C. The notified chemical is not likely to be mobile in the environment, due to its limited solubility in water and potential to adsorb to soil and sediment, based on its expected surfactant properties. Therefore, a significant portion of the notified chemical is expected to partition to sludge during wastewater treatment processes in sewage treatment plants (STPs). Thus, very little of the notified chemical is expected to partition to the supernatant water which is released to surface waters.

The notified chemical will eventually degrade in landfill and has the potential to release polyfluoroalkyl degradation products, including pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro-, which is expected to be analogous to the short-chain perfluorinated carboxylic acid perfluoropentanoic acid (PFPeA).

PFPeA is a globally distributed pollutant and is expected to be recalcitrant in the environment, potentially expected to 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 under environmental conditions (NICNAS, 2016a, b).

PFPeA is expected to be less bioaccumulative than perfluorooctanoic acid (PFOA) and other long-chain perfluoroalkyl acids, supported by the available laboratory (Higgins et al., 2007; Martin et al., 2003a, b; Woodcroft et al., 2010) and field (Falandysz et al., 2006; Falandysz et al., 2007, Furdui et al., 2007) evidence. In general, bioaccumulation potential decreases when the length of the perfluorinated carbon chain is decreased (Ng and Hungerbühler, 2014, Giesy et al., 2010). The short-chain perfluorocarboxylic acids, including PFPeA, have been assessed to have low bioaccumulation potential based on the currently available information (NICNAS, 2016a, b).

7.1.3. Predicted Environmental Concentration (PEC)

PEC for the notified chemical

The following predicted environmental concentrations (PEC) have been calculated assuming that all of the imported quantity of notified chemical will be released to sewer, nationwide, over 365 days. It has been assumed for the worst case that there is no removal of the notified chemical during sewage treatment processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.56	µg/L
PEC - Ocean:	0.06	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 0.56 µg/L may potentially result in a soil concentration of approximately 3.74 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 19 µg/kg and 37 µg/kg, respectively.

PEC for PFPeA and other perfluorocarboxylic acids

The notified chemical has the potential to degrade and ultimately form the persistent degradant, pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro-, which is expected to be analogous to PFPeA. However, the yield and rate of conversion of the notified chemical to pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- has not been established.

Environmental monitoring data shows that PFPeA and PFOA are widely found in the environment, particularly in fresh water close to industrial sources (NICNAS, 2016a).

Monitoring of European River Rhine upstream of significant industrial sources has found PFPeA at mean concentrations of 3.65 ng/L. Concentrations of PFPeA were below 60 ng/L in river waters (Möller, et al., 2010). Similar results were obtained from water samples taken in the Upper Mississippi River Basin in the USA. Median concentrations of 0.71 ng/L were determined for PFPeA. In Spain, mean concentrations of 0.40 ng/L for PFPeA was obtained from samples taken from the Llobregat River system (Campo, et al., 2015). Analyses of drinking water samples from Europe, Canada, the USA, Japan, India and China have also detected PFPeA and other perfluorocarboxylic acids (Eschauzier, et al., 2013; Llorca, et al., 2012; Mak, et al., 2009). Limited Australian monitoring data are available for PFPeA.

The lifetimes of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- or PFPeA in the aquatic environment is unknown, but is expected to be comparable to the very long lifetimes established for homologous perfluorinated acids such as PFOA and PFOS (NICNAS, 2016 c, d).

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 > 11 mg/L	The notified chemical is not harmful up to the limit of solubility for invertebrates (acute)
Daphnia Toxicity	21 d NOEC = 1.8 mg/L	The notified chemical is not harmful up to the limit of solubility for invertebrates (chronic)
Daphnia Toxicity	21 d NOEC = 73 mg/L	The expected degradant (octafluoro-1-pentanol) of the notified chemical is not harmful to invertebrates (chronic)
Algal Toxicity	72 h EC50 = 4.4 mg/L	The notified chemical is toxic to algae (acute)

Based on the available measured endpoints the notified chemical is considered to be toxic to algae. Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is formally classified as 'Acute Category 2: Toxic to aquatic life'. Based on the low chronic toxicity of the notified chemical, it is not formally classified under the GHS for chronic toxicity. The endpoints supplied for the octafluoro-1-pentanol degradant of the notified chemical indicate that it is not harmful to aquatic organisms on a chronic basis.

Effects of PFPeA and other perfluorocarboxylic acids

The current available data, summarised in the *NICNAS IMAP Environment Tier II Assessment for Short-Chain Perfluorocarboxylic Acids and their Direct Precursors*, indicate that PFPeA and other short-chain perfluorinated acids (i.e. those with five or fewer perfluorinated carbon atoms) have low toxicity to aquatic life (NICNAS, 2016a,b) compared to PFOA and perfluorooctanesulfonic acid (PFOS) (NICNAS, 2016c,d). However, no long-term intergenerational studies were identified for pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- or PFPeA and other short chain short-chain PFCAs. Emerging evidence suggest that the most significant aquatic toxicity effects of PFOA and PFOS may manifest in offspring when the parent generation is exposed to PFOA or PFOS (NICNAS, 2016c, d).

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) for the notified chemical was calculated from the endpoint of the most sensitive species (algae). The acute and chronic endpoint for algae was used to represent the worst case scenario. A conservative assessment factor of 100 is appropriate in this case as endpoints for two acute trophic levels and one chronic trophic level were available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Algae, 48 h)	4.4	mg/L
Assessment Factor	100	
Mitigation Factor	1	
PNEC:	44	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the predicted PEC and PNEC.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.56	44	0.013
Q - Ocean	0.05	44	0.001

The risk quotient for discharge of effluents containing the notified chemical indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in aquatic environments based on its annual import quantity. The notified chemical is not likely to bioaccumulate in aquatic organisms. Therefore, on the

basis of the PEC/PNEC ratio, maximum annual import volume and assessed use pattern in cosmetics, the notified chemical is not expected to pose an unreasonable risk to the environment.

However, the notified chemical has the potential to eventually degrade to form pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro-, which is expected to be analogous to the very persistent chemical PFPeA. PFPeA is currently understood to have low potential for bioaccumulation (NICNAS, 2016a). The currently available data also indicate that PFPeA and other short-chain perfluorocarboxylic acids and their direct precursors have low toxicity to aquatic life (NICNAS, 2016a, b).

The main environmental risks associated with polyfluoroalkyl chemicals relate to the release of per- and polyfluorinated degradation products such as pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro-. It is not possible to quantify the release of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- to the environment from the use of the notified chemical at present. However, as use of chemicals/polymers that degrade to form pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- increases, levels of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- may build up in the environment. Hence, there could be potential for environmentally significant concentrations to eventually be reached following its accumulation in the environment.

Conclusions
On the basis of the assessed use pattern, the notified chemical itself is not considered to directly pose an unreasonable risk to the environment. However, the notified chemical contains fluorinated carbon groups that have the potential to degrade to the exceptionally persistent short-chain polyfluorinated carboxylic acid, pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro-.

The environmental degradation of the notified chemical is expected to contribute to the cumulative emissions of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- to the environment. Based on the currently available evidence, the concentrations of pentanoic acid, 2,2,3,3,4,4,5,5-octafluoro- and other short-chain per- and polyfluorinated carboxylic acids are not considered to pose a concern for the health of the environment. However, if additional hazard information becomes available to indicate that short-chain per- and polyfluorinated carboxylic acids have hazard characteristics of high concern for the environment (such as PBT), then the risks posed by industrial uses of precursors to these environmental degradants may need to be re-assessed.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Freezing Point -80 °C

Method EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature.
Remarks The notified chemical was a very thick viscous fluid at -78 °C becoming a soft solid at -80 °C.
Test Facility DEKRA (2015a)

Boiling Point 180.5 °C at 101.3 kPa

Method Five millilitres (5 mL) of the notified chemical was placed in a round bottom flask equipped with a magnetic stirring bar, condenser and thermocouple. The test substance was heated to boiling on an oil bath and the temperature was then recorded.
Remarks The boiling point measuring was a part of the operation to obtain vapour pressure of the notified chemical.
Test Facility Impact (2014)

Density 1425 kg/m^3 at 20 °C

Method EC Council Regulation No 440/2008 A.3 Relative Density.
Remarks Glass pycnometer method.
Test Facility DEKRA (2015a)

Vapour Pressure 1.24 kPa (0.18 psia) at 25.5 °C

Method Similar to OECD TG 104 Vapour Pressure (Static Method).
Remarks A vapour-liquid equilibrium (VLE) apparatus was used to collect pressure data as a function of temperature.
Test Facility Impact (2014)

Water Solubility 0.03 g/L at 20 °C

Method Internal SOP
Remarks Shake Flask Method
Test Facility Chilworth (2014)

Hydrolysis as a Function of pH $t_{½}$ = 4.7, 5.5, and 0.5 days at 25 °C and pH 4, 7, and 9, respectively

Method OECD TG 111 Hydrolysis as a Function of pH

pH	*T (°C)*	$t_{½}$
4	25	4.7 days
7	25	5.5 days
9	25	0.5 day

Remarks The test was conducted at 50 °C for 5 days, and in buffers at pH 4, 7, and 9, respectively. Significant decrease in the test concentration was determined at pH 7 and 9. In the case of pH 9, no detectable notified chemical was present in the test solutions.
Test Facility Living Proof, Inc (2014a)

Partition Coefficient (n-octanol/water) log Pow = 3.03

Method OECD TG 117 Partition Coefficient (n-octanol/water)
Remarks HPLC Method. The column temperature was 35 °C. The estimated log P_{OW} using ACD/Labs was reported as 3.81, which is comparable to the measured value.
Test Facility Living Proof, Inc (2014b)

Flash Point 75 °C

Method	ASTM D 93
Remarks	Pensky-Martens Closed Cup
Test Facility	DEKRA (2015b)

Autoignition Temperature 408 °C

Method	ASTM E659 - Standard Test Method for Autoignition Temperature of Liquid Chemicals
Remarks	No test details were provided.
Test Facility	Intertek (2014a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: NOTIFIED CHEMICAL (PURITY > 99%)

METHOD: OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure.
- Species/Strain: Rat/Wistar albino (females)
- Vehicle: Test substance administered as supplied
- Remarks - Method: No significant protocol deviation was noted.

RESULTS

Number and Sex of Animals	*Dose (mg/kg bw)*	*Mortality*
5 females	2,000	0/5

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity: One animal lost weight during the second week of observation.

  Instance of wetness of the anogenital area, ataxia, prostration, flaccid muscle tone and coma were noted on the day of dosing. All animals appeared normal from the second day on in the study.
- Effects in Organs: No abnormalities were noted.
- Remarks - Results: All animals survived the test.

CONCLUSION: The notified chemical is of low toxicity via the oral route.

TEST FACILITY: MB Research Laboratories (2008)

B.2. Irritation – eye

TEST SUBSTANCE: Notified chemical (98% in purity)

METHOD: US EPA Health Effects Test Guidelines, OPPTS 870.2400, *Acute Eye Irritation*, August 1998
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 females
- Observation Period: 72 hours
- Remarks - Method: The test was conducted as a non-GLP study. 0.1 mL of undiluted test substance was administered to the test animals. No significant protocol deviation was recorded.

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	0	0	0	0	-	0
Conjunctiva: chemosis	0	0	0	0	-	0
Conjunctiva: discharge	0	0	0	1	< 24 h	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

- Remarks - Results: Slight, clear fluid was discharged on the fur below the eye of two animals at the 1-hour time point. The animals were recovered from the signs of discharge at the 24-hour time point.

CONCLUSION: The notified chemical is slightly-irritating to the eye.

TEST FACILITY IITRI (2007)

B.3. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE Notified chemical (98% in purity)

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/CBA/J females
Vehicle Acetone: olive oil (4:1)
Remarks - Method The test was conducted as a non-GLP study. Highest concentration tested was 45% which was considered as the solubility limit in an acetone:olive oil 4:1 mixture.

Positive controls:
1-Chloro-2,4-dinitrobenzene (DNCB)
Hexyl cinnamic aldehyde (HCA)

RESULTS

Concentration	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	671.72	1.00
11.3%	1111.72	1.66
22.5%	1115.66	1.66
33.8%	878.79	1.31
45%	980.03	1.46
Positive Control		
2.5 µg/mL of DNCB	13024.53	19.39
42.5% of HCA	4260.59	6.34

Remarks - Results There were no mortalities and no signs of systemic toxicity or irritation noted for the test and control animals.

Evidence of induction of T-cell proliferation was not observed with the test substance, as the stimulation index was less than three at each of the test concentrations.

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

TEST FACILITY IITRI (2008a)

B.4. Skin sensitisation – human volunteers

TEST SUBSTANCE Cosmetic spray product 1 containing 2% notified chemical
Cosmetic cream product 1 containing 2% notified chemical

METHOD Repeated insult patch test with challenge
Study Design Induction Procedure: The induction phase consisted of 9 consecutive applications of the test substance in a period of 3 weeks. For each application, the test substance was left on the skin site for 24 hours.

Rest Period: 10 – 15 days

Challenge Procedure: Identical patches were applied to the skin sites previously unexposed to the test substance. The patches were removed after 24 hours and the skin sites were graded after 48 and 72 hours.
Study Group 49 F, 9 M; age range 18 to over 65 years; 7 females and 1 male did not complete the test.
Vehicle None, cosmetic products were directly applied to the test skin sites.

Remarks - Method	Occluded. For the spray and the cream products respectively, 0.2 mL and 0.2 g of the cosmetic products were spread on 2 cm × 2 cm patches and applied to the infrascapular area of the back either to the right or left of the midline, or to the upper arm.
RESULTS	There were no adverse events reported.
Remarks - Results	Among 58 test subjects, 50 of them completed the study, 6 lost to follow-up and 2 discontinued due to exclusionary medications.
CONCLUSION	There was no evidence of sensitisation to the test substances under the conditions of the test.
TEST FACILITY	TKL Research (2008a)

B.5. Skin sensitisation – human volunteers (2)

TEST SUBSTANCE	Cosmetic spray product 2 containing 2% notified chemical Cosmetic cream product 2 containing 2% notified chemical
METHOD	Repeated insult patch test with challenge
Study Design	Induction Procedure: The induction phase consisted of 9 consecutive applications of the test substance in a period of 3 weeks. For each application, the test substance was left on the skin site for 24 hours. Rest Period: 10 – 15 days Challenge Procedure: Identical patches were applied to the skin sites previously unexposed to the test substance. The patches were removed after 24 hours and the skin sites were graded after 48 and 72 hours.
Study Group	41 F, 17 M; age range 18 to over 65 years; 7 females and 1 male did not complete the test.
Vehicle	None, cosmetic products were directly applied to the test skin sites.
Remarks - Method	Occluded. For the spray and the cream products respectively, 0.2 mL and 0.2 g of the cosmetic products were spread on 2 cm × 2 cm patches and applied to the infrascapular area of the back either to the right or left of the midline, or to the upper arm.
RESULTS	There were 3 non-serious adverse events reported: 1. Bug bites symptom; unlikely related to the study; discontinued 2. Pregnancy; unrelated to the study, discontinued 3. Rash; unlikely to be related to the study; discontinued
Remarks - Results	Among 58 subjects, 50 of them completed the study, 3 lost to follow-up, 2 voluntarily withdrew and 3 discontinued due to adverse events unrelated or unlikely to be related to the study.
CONCLUSION	There was no evidence of sensitisation to the test substances under the conditions of the test.
TEST FACILITY	TKL Research (2008b)

B.6. Repeat dose dermal toxicity

TEST SUBSTANCE	Notified chemical (99% in purity)
METHOD	In-house protocol similar to OECD TG 410 Repeated Dose Dermal Toxicity: 21/28-day Study
Species/Strain	Rat/Crl:CD(SD)
Route of Administration	Dermal – occluded
Exposure Information	Total exposure days: 28 days

	Dose regimen: 7 days/week Duration of exposure (dermal): 6 hours/day Post-exposure observation period: None
Vehicle	The test substance was administered undiluted. Deionised water was used as vehicle (negative) control.
Remarks - Method	The test was conducted as non-GLP study. The test substance at the level of 0.91 mL/kg bw (equivalent to 1,300 mg/kg bw based on the density of 1.432 g/mL) was dosed to individual animals via dermal application to clipped dorsum under occlusive conditions once daily for a minimum of 6 hours per day for 28 consecutive days. All animals were observed twice daily for mortality and moribundity. Clinical examinations were performed. Pathology evaluations were performed on all animals on the day of scheduled necropsy (Day 28 of the study). Complete necropsies were conducted on all animals.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Negative control	20 (10 M, 10 F)	1,300	0/20
Test group	20 (10 M, 10 F)	1,300	1/20

Mortality and Time to Death

One male in test group was found dead on Day 13 of the study. The cause of the death was undetermined. Due to lack of significant indication of toxicity in the treated animals, this death was considered by the study authors to be likely not test substance related.

Clinical Observations

There were no test substance related effects noted on clinical findings, including dermal observations, body weights and food consumption.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

There were no test substance related effects noted in haematology, coagulation or urinalysis parameters. Lower total protein (-5%) and globulin (-9%) levels were recorded as treatment related alterations in serum chemistry parameters in the test substance treated males. The values for the total protein and globulin were within historical control ranges for the laboratory and hence study authors considered the alterations as non-adverse.

Effects in Organs

There were no test substance related effects noted in selected organs and microscopic tissue samples. No test substance related microscopic findings were noted on treated skin tissues. Minimal to mild acute inflammation of the urinary bladder was observed in 2 of 10 test substance treated females and was considered by the study authors to be related to the administration of the test substance and to be non-adverse.

Remarks – Results

Evidence of systemic effects that may be attributable to the test substance were limited to lower total protein and lower globulin.

CONCLUSION

There were no adverse effects noted at the dose level of 1,300 mg/kg bw/day via dermal route in this study.

TEST FACILITY WIL (2008a)

B.7. Repeat dose oral toxicity – rat, 7-day range-finding

TEST SUBSTANCE Notified chemical (99.0% in purity)

METHOD	In-house protocol
Species/Strain	Rat/Crl:CD(SD)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 7 days Dose regimen: 7 days per week
Vehicle	Corn oil

Remarks - Method

The test was conducted as non-GLP study.

The notified chemical in the vehicle, corn oil, was administered orally by gavage once daily for 7 consecutive days to 3 groups of test animals at the dose levels of 100, 300 and 1,000 mg/kg bw/day. A concurrent control group received vehicle only on a comparable regimen. The dose volume was 5 mL/kg bw for all groups. Following 7 days of dose administration, all test animals were euthanized for gross necropsies.

During the study, all test animals were observed twice daily for mortality and moribundity. Clinical examinations were performed daily at the time of dosing and approximately 1 and 4 hours post-dosing and detailed physical examinations were performed weekly. Individual body weight and food consumption were recorded on study Days 0 and 7.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	10 (5 F/5 M)	0	0/10
Low dose	10 (5 F/5 M)	100	0/10
Mid dose	10 (5 F/5 M)	300	0/10
High dose	10 (5 F/5 M)	1,000	0/10

Mortality and Time to Death

All test animals survived to the scheduled necropsy.

Clinical Observations

Test substance related clinical observations noted in the 1,000 mg/kg bw/day group as early as study Day 0 and throughout 7-day dosing period included impaired muscle coordination and/or impaired equilibrium in both sexes of the test animals with higher frequency in females. Hypoactivity, decreased respiration rate and prostration were noted in females on study Day 0. These effects did not persist to the 4-hour post-dosing observation on study Days 0 to 6 for males and study Days 4 to 6 for females. These effects were considered by the study authors as adverse since they persisted throughout the 7-day dosing period at approximately 1 hour post-dosing. No significant clinical observations were recorded in the 100 and 300 mg/kg bw/day groups.

A test substance related effect on body weight was noted in test substance treated animals, showing a trend towards slightly lower body weight gains. However, this effect was not considered by the study authors as adverse.

There were no test substance related effects on food consumption and no significant macroscopic findings noted in the study.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Laboratory examinations were not performed in this study.

Effects in Organs

No organs were selected for examination in this study.

Remarks – Results

Adverse effects were observed in the test animals at the dose level of 1,000 mg/kg bw/day for 7 days in this study. No adverse effects were noted in the test animals treated with the test substance at dose levels of 100 and 300 mg/kg bw/day for 7 days.

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) was established as 300 mg/kg bw/day in this study, based on adverse effects seen at the higher dose.

TEST FACILITY WIL (2009)

B.8. Repeat dose inhalation toxicity – rat, 5 day study

TEST SUBSTANCE Notified chemical (99.7% in purity)

METHOD In-house protocol
Species/Strain Rat/Crl:CD(SD)
Route of Administration Inhalation – Nose-only exposure
Exposure Information Total exposure days: 5 consecutive days
Duration of exposure (inhalation): 6 hours/day
Vehicle Nitrogen gas mixed with filtered air
Physical Form Vapour (vaporised aerosols generated using nebulisers)
Remarks - Method The test substance was administered to test animals via nose-only inhalation for 6 hours per day for 5 consecutive days at targeted dose levels of 42, 84 and 168 ppm. A concurrent control group was exposed to filtered air on a comparable regimen. On the day following the fifth exposure, all test animals were euthanized and subjected to necropsy.

The test animals were observed twice daily for mortality and moribundity. Clinical examinations were performed 3 times daily and detailed physical examinations were performed during the exposure phase on study Days 0 and 4. Individual body weights and food consumption were recorded weekly during the pre-test phase and on study Days 0 and 4. Complete necropsies were conducted on all test animals, and liver, lungs and kidneys were weighed. Selected organs and tissues were examined microscopically in the negative control and the 168 ppm test groups. Gross lesions were examined microscopically for all test animals when possible.

RESULTS

Group	*Number and Sex of Animals*	*Concentration (ppm)*			*Mortality*
		Nominal	*Targeted*	*Actual*	
Control	10 (5 F/5 M)	0	0	0	0/10
Low dose	10 (5 F/5 M)	81	42	40	0/10
Mid dose	10 (5 F/5 M)	169	84	89	0/10
High dose	10 (5 F/5 M)	219	168	168	0/10

Mortality and Time to Death
No unscheduled animal death was noted.

Clinical Observations
No test substance related effects were noted in clinical observations including daily examinations, body weights and food consumption.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Laboratory examinations were not conducted in this study.

Effects in Organs
No test substance related effects were noted in livers, lungs and kidneys of the test animals as examined in organ weights, macroscopic findings and microscopic findings.

Remarks – Results
All macroscopic and microscopic findings observed in the study were considered by the study authors as normal background lesions and not related to the test substance. The mean bodyweight of male and female rats combined in the high dose group was 213 g over the period in which the test substance was administered.

CONCLUSION
The No Observed Adverse Effect Concentration (NOAEC) was considered to be > 168 ppm in this study, based on the absence of adverse treatment related effects at the highest concentration tested.

TEST FACILITY WIL (2010)

B.9. Skin Absorption – *in vitro* method

TEST SUBSTANCE
Notified chemical (99.8% purity at 2% in a leave-on hair styling cream)
and
Octafluoropentyl methacrylate [methacrylic acid-^{14}C]
Radiochemical purity: 93.6%
Specific activity: 5 mCi/mmol

METHOD
OECD TG 428 Skin Absorption: *In Vitro* Method
The OECD TG 428 method was used in accordance with OECD Guidance Document No. 28 *Guidance Document For The Conduct Of Skin Absorption Studies.*

STUDY DESIGN AND OBJECTIVE
Percutaneous absorption of 2% of the test substance in a leave on cream formulation was investigated in human skin preparations, which were continuously rinsed with physiological receptor fluid at 32 °C. The cream formulation was applied at a rate of 20 mg/cm^2 to 24 human split thickness skin membranes mounted into flow through diffusion cells. Immediately after dosing 12 of the membranes were covers with a occlusive trap, with the remaining 12 left uncovered. Integrity of skin preparations was determined by examining penetration characteristics with tritiated water, with the threshold for an acceptability being 0.6% penetration. The receptor fluid was collected at hourly intervals from 0 to 8 h and then every 2 hours until 24 hours post application. At 24 h post application exposure was terminated by washing the cells with water and sodium dodecyl sulfate solution. The stratum corneum was removed from the skin using tape strips and the epidermis separated from the dermis. Liquid scintillation counting was used to determine the amount of the test substance in the receptor fluid or skin.

RESULTS
Of the occluded samples 9 had a mass balance with the acceptable limits for the study (100 ± 15%) and 3 were > 115 % and were not used in calculating the mean value. All of the 12 unoccluded samples had mass balances < 10%, which was considered by the study authors to be a result of the test substances volatility. The concentration of the notified chemical in the cream formulation was determined to be 2.11 % (w/v) based on the radioactivity.

The mean values for the occluded and unoccluded samples are as follows:

Amount of test substance in:	µg equivalent/cm^2		% Applied dose	
	Occluded	Unoccluded	Occluded	Unoccluded
Non-volatile components	21.80	23.53	4.65	5.02
Volatile components	415.29	-	88.61	-
Dislodgeable dose	437.10	23.53	93.25	5.02
Stratum corneum	5.33	3.17	1.14	0.68
Unabsorbed dose	442.85	26.78	94.48	5.71
Epidermis	0.87	0.56	0.19	0.12
Dermis	0.79	0.89	0.17	0.19
Absorbed dose	5.52	0.87	1.18	0.18
Dermal delivery	7.18	2.32	1.53	0.49
Mass balance	450.03	29.10	96.01	6.21

Remarks - Results
The results under unocclusive conditions were considered by the study authors to represent the intended consumer use scenario of the hair styling product.

CONCLUSION
Under the conditions tested, the absorbed dose and dermal delivery rates of the notified chemical were determined as 1.18% and 1.53% for occluded skin and 0.18% and 0.49% for unoccluded skin.

TEST FACILITY
Charles River (2010)

B.10. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical (98% in purity)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	Aroclor 1254 induced rat liver fraction (S9)
Concentration Range in Main Test	a) With metabolic activation: 0.01 to 5 µL/plate b) Without metabolic activation: 0.01 to 5 µL/plate
Vehicle	Ethanol
Remarks - Method	The test was conducted as a non-GLP study. Positive controls (strain specific): Positive controls: with metabolic activation – 2-Aminoanthracene (TA-98, TA100, TA1535, TA1537), 2-Aminofluorene (TA98, TA100), Danthron (TA102); without metabolic activation – Daunomycin (TA98), Methyl methanesulfonate (TA100), Cumene hydroperoxide (TA102), Sodium azide (TA1535), ICR-191 (TA1537).

RESULTS

Metabolic Activation	*Test Substance Concentration (µL/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 1	-	≥ 1	Negative
Test 2	-	≥ 1	≥ 1	Equivocal
Present				
Test 1	≥ 1	-	≥ 1	Equivocal
Test 2	-	≥ 1	≥ 1	Negative

Remarks - Results	Statistically significant ($p < 0.05$) increases in revertants were observed in initial assay for strain TA102 with metabolic activation at dose level of 0.50 µL/plate and in confirmatory assay for strains TA102 and TA1535 without metabolic activation at dose level of 1.0 µL/plate. However, no clear dose-dependent response was noted in the study and the observed increases in revertants did not exceed 2-fold of the vehicle controls (or 3 fold for strains TA1535 and TA1537). The results were considered negative by the study authors. The mutagenicity data derived from top two dose levels (i.e. 2.5 and 5 µL/plate) were not reported due to excessive cytotoxicity and/or visible precipitation of the test substance.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	IITRI (2008b)

B.11. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Initial test: Plate incorporation procedure. Confirmatory test: Pre incubation procedure.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2*uvr*A
Metabolic Activation System	Aroclor 1254-induced rat liver fraction (S9)

Concentration Range in Test 1	a) With metabolic activation: 1.5 to 5000 µg/plate b) Without metabolic activation: 1.5 to 5000 µg/plate
Concentration Range in Test 2	a) With metabolic activation: 15 to 5000 µg/plate b) Without metabolic activation: 15 to 5000 µg/plate
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks - Method	GLP compliant. No deviations from the protocol. Positive controls: with metabolic activation – 2-Aminoanthracene; without metabolic activation – 2-Nitrofluorene (TA98), Sodium azide (TA100, TA1535), 9-Aminoacridine (TA1537), Methyl methanesulfonate (WP2 *uvr*A).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	> 5,000	non-mutagenic
Test 2	> 5,000	> 5,000	
Present			
Test 1	> 5,000	> 5,000	non-mutagenic
Test 2	> 5,000	> 5,000	

Remarks - Results	Precipitation was not observed in either test 1 or 2. Cytotoxicity was not observed in the absence or presence of metabolic activation in tests 1 and 2. No positive mutagenic responses were observed in the presence or absence of metabolic activation in any of the tested strains in either test 1 or 2.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	BioReliance (2016)

B.12. Genotoxicity – *in vitro*

TEST SUBSTANCE	Notified chemical (99% in purity)
METHOD	OECD TG 487 *In Vitro* Mammalian Cell Micronucleus Test
Species/Strain	Human blood cells
Cell Type/Cell Line	Peripheral Blood Lymphocyte
Metabolic Activation System	Aroclor™ 1254 induced rat liver post-mitochondrial fraction (S9) coupled with NADP and isocitric acid
Vehicle	Dimethylsulfoxide (DMSO)
Remarks - Method	Mitomycin (MMC) and cyclophosphamide (CP) were used as positive controls. Cytochalasin B was used to block the cytoplasmic cell division after the treatment in order to observe the nuclear status of the test cells. Slight protocol deviations were recorded which were not considered to have an impact on the integrity of the study.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period (hour)*	*Harvest Time (hour)*
Absent			
Test 1	0, 250, 500, 1000	3	24
Test 2	0, 125, 250, 500, 1000	24	24
Test 3	0, 250, 400, 500, 750, 1000	3	24
Test 4	0, 62.5, 125, 175, 250, 300, 400, 500, 750, 1000	24	24

Test 5	0*, 300, 400, 500, 525, 550, 575, 600, 625, 650*, 700*, 750, 800*	3	24
Test 6	0*, 150, 175, 200, 213*, 225*, 250*, 275, 300, 400	24	24
Present			
Test 1	0, 250, 500, 1000	3	24
Test 2	0*, 400, 500*, 750*, 1000*	3	24

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 1000	-	≥ 500	Not analysed
Test 2	≥ 500	-	≥ 500	Not analysed
Test 3	-	≥ 750	> 1000	Not analysed
Test 4	-	≥ 250	≥ 1000	Not analysed
Test 5	-	> 800	> 800	Negative
Test 6	-	≥ 275	> 400	Negative
Present				
Test 1	> 1000	-	≥ 500	Not analysed
Test 2	-	> 1000	≥ 1000	Negative

Remarks - Results

Due to a lack of appropriate toxicity, the assays without metabolic activation were repeated.

No toxicologically significant increases in the number of cells with aberrations were noted, with or without metabolic activation.

The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.

CONCLUSION

The notified chemical was not clastogenic to human peripheral blood lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY

Covance (2009)

B.13. Developmental toxicity – rat, dermal

TEST SUBSTANCE

Notified chemical (99.0% in purity)

METHOD

In-house protocol

Species/Strain: Rat/Crl:CD(SD), time-mated females

Route of Administration: Dermal – occluded

Exposure Information: Exposure days: 11 days from gestation Days 6 to 17
Duration of exposure: 6 hours/day
Post-exposure observation period: 3 days until gestation Day 20.

Vehicle: The test substance was administered undiluted. Deionised water was used as vehicle (negative) control.

Remarks - Method: The test was conducted as non-GLP study. The test substance at the level of 1,300 mg/kg bw was dosed to individual test animals via dermal application to clipped dorsum under occlusive conditions, once daily for a minimum of 6 hours per day for 11 consecutive days from gestation Days 6 to 17. All animals were observed twice daily for mortality and moribundity. On gestation Day 20 a laparohysterectomy was performed on each female to examine embryo/foetal development effects.

RESULTS

Group	*Number of Animals*	*Dose (mg/kg bw/day)*	*Mortality*

Negative control	25	1,300	0/25
Test group	25	1,300	0/25

Mortality and Time to Death

No unscheduled deaths were observed in the test animals.

Effects on Dams

No test substance related clinical findings or dermal observations were noted. Mean body weights, body weight gains, net body weights, net body weight gains, gravid uterine weight and food consumption were unaffected by the treatment. No test substance related macroscopic findings were noted at the necropsy.

Effects on Foetus

There were no effects on intrauterine growth and survival. No foetal malformations or developmental variations were attributed to the test substance administration.

Remarks – Results

Enlarged mandibular lymph nodes and dark red placental material were observed in single animals treated with the test substance. Malformations were observed in 6 foetuses (2 litters) in the treatment group and in 1 foetus (1 litter) in the negative control group. These malformations were considered by the study authors as spontaneous in origin.

CONCLUSION

The No Observed Effect Level (NOEL) was established as > 1,300 mg/kg bw/day in this study, based on the absence of adverse treatment related effects.

TEST FACILITY WIL (2008b)

B.14. Developmental toxicity – rabbit, dermal

TEST SUBSTANCE Notified chemical (99% in purity)

METHOD In-house protocol

Species/Strain	Rabbit/New Zealand White, time-mated females
Route of Administration	Dermal – occluded.
Exposure Information	Exposure days: 13 days from gestation Days 7 to 20 Duration of exposure: 6 hours/day Post-exposure observation period: 9 days until gestation Day 29.
Vehicle	
Remarks – Method	The test was conducted as non-GLP study. The test substance at the level of 1,300 mg/kg bw was dosed to individual test animals via dermal application to clipped dorsum under occlusive conditions, once daily for a minimum of 6 hours per day for 13 consecutive days from gestation Days 7 to 20. All animals were observed daily for mortality and moribundity. On gestation Day 29 a laparohysterectomy was performed on each test animal to examine embryo/foetal developmental effects.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Negative control	22	1,300	1/22
Test group	22	1,300	1/22

Mortality and Time to Death

One animal treated with the test substance was found dead on gestation Day 16. A single clinical observation (red material in cage pan) was noted prior to the death. Due to lack of indications of maternal toxicity, the death of the animal was not considered by the study authors to be test substance related.

One animal in the negative control group was euthanized in extremis on gestation Day 14. Clinical signs noted prior to the euthanasia included hypoactivity, brown material around anogenital area and decreased defecation.

Effects on Dams

One animal in the negative control group aborted on gestation Day 28. There were no test substance related clinical

findings noted in the test animals. Slight erythema was noted on the treatment skin sites in 4 of 22 animals treated with the test substance during gestation Days 12 to 14. This was considered by the study authors as dermal irritation caused by the test substance and but was not considered to be adverse due to its transient and mild nature. Desquamation was also noted in 2 and 7 animals in the negative control group and the treatment group respectively. Mean body weights, body weight gains, net body weights, net body weight changes, gravid uterine weights and food consumption in the treatment group were unaffected by the treatment.

Effects on Foetus

There were no effects on intrauterine growth and survival. Malformations were observed in 4 foetuses (in 4 litters) in the treatment group and were considered by the study authors to be spontaneous in origin. No foetal malformations or developmental variations were attributed to the test substance administration.

Remarks – Results

Three animals in the treatment group were found to be not pregnant at the scheduled necropsy.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as > 1,300 mg/kg bw/day in this study, based on the absence of adverse treatment related effects.

TEST FACILITY WIL (2008c)

B.15. Basal Cytotoxicity – neutral red uptake (NRU) assay

TEST SUBSTANCE	Notified chemical
METHOD	Neutral Red Uptake (NRU) Bioassay (non-GLP) based on the methods described by Borenfreund and Puerner (1984) and Babich et al (1989).
Species/Strain	Mouse/Balb/c
Cell Type/Cell Line	Fibroblasts/3T3
Vehicle	Ethanol
Concentration Range in Tests	Range finding: from 0.00025 to 2,500 µg/mL Main test: from 40.8 to 2,500 µg/mL
Exposure period	≥ 46 hours
Remarks - Method	Cell suspension at a density of 3.0×10^4 cells/mL were prepared and distributed into 96-well plates at 100 µL/well. The plates were incubated for 24 hours to form approximately 20% confluent monolayer prior to the tests. The cells were then washed with fresh medium and treated with the test substance. The cells were then rinsed with Dulbecco's phosphate buffered saline (D-PBS) to remove the test substance and 250 µL of medium containing neutral red (NR) at 25 µg/mL was added to each well, followed by a 3-hour incubation. Unincorporated NR was removed by rinses and the uptake of NR by the cells were determined by resolving the cells in 100 µL of NR Desorb (Solvent) and measuring absorption at 550 nm with a plate reader (Molecular Devices V*max*). Test concentration causing a reduction of 50% in cell NRU was considered to be NRU50. Based on NRU50 determined, rodent oral LD50 was estimated following the equation shown below: Estimated log LD50 (mmol/kg bw) = 0.435 × log NRU50 (mM) + 0.625 Positive control: Sodium lauryl sulphate
RESULTS	None of the doses of the test substance resulted in less than 50% NRU, the mean NRU50 value was considered as > 2,500 µg/mL, the highest concentration tested.

Dose range finding assay

Test Conc. (µg/mL)	0.0003	0.003	0.025	0.25	2.5	25	250	2500
NR uptake (%)	98.1±3.4	96.9±2.7	95.2±2.3	95.8±2.1	94.2±4.9	89.7±3.3	93.3±1.9	83.8±6.2

Test 1

Test Conc. (µg/mL)	40.8	73.5	132	238	429	772	1389	2500
NR uptake (%)	96.7±7.8	91.5±4.2	93.3±2.3	98.7±4.7	100.2±15.4	90.8±6.5	95.5±3.0	99.4±3.2

Test 2

Test Conc. (µg/mL)	40.8	73.5	132	238	429	772	1389	2500
NR uptake (%)	97.3±5.3	98.7±3.6	88.5±4.9	94.6±3.6	87.7±8.6	97.8±11.3	98.4±6.7	91.9±4.8

Remarks - Results

The positive control results fell within 2 standard deviations of the historical mean value and negative vehicle control results did not differ by more than 15% from the mean value, indicative of a valid assay.

CONCLUSION

NRU50 > 2,500 µg/mL (highest concentration tested)

Based on the *in vitro* test results, an estimate of rodent oral LD50 was determined to be > 3,183 mg/kg bw.

TEST FACILITY

Institute for In Vitro Sciences (2008)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 310 Ready Biodegradability - CO_2 in sealed vessels (Headspace Test)
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	TOC-V-CSH Carbon Analyzer for analysis of CO_2 produced
Remarks - Method	Conducted in accordance with the test guidelines above, and in compliance with GLP standards and principles.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
6	15	2	61
14	23	14	99
21	22	21	81
28	27	28	81

Remarks - Results	All validity criteria for the test were satisfied. The reference compound, sodium benzoate, reached the 60% pass level by day 3 indicating the suitability of the inoculum. The toxicity control exceeded 25% biodegradation within 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after 28 days was 27%. The test substance cannot be classified as readily biodegradable according to the OECD (310) guideline.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Harlan (2010a)

C.1.2. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 310: Ready Biodegradability - CO_2 in sealed vessels (Headspace Test)
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Inorganic carbon analysis for CO_2 production
Remarks - Method	Conducted in accordance with the test guidelines above, and in compliance with GLP standards and principles.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
3	0	3	63
9	12	9	62
14	18	14	72
21	19	21	72

28	22	28	65

Remarks - Results	All validity criteria for the test were satisfied. The reference compound, sodium benzoate, reached the 60% pass level by day 3 indicating the suitability of the inoculum. The toxicity control attained 50% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after 28 days was 22%. The test substance cannot be classified as readily biodegradable according to the OECD (310) guideline.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Envigo (2016)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – Static Test
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	Test concentrations were analysed using gas chromatography (GC) at 0 hour and 48 hours.
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Cumulative % Immobilised*	
Nominal	*Geometric mean*		*24 h*	*48 h*
Control	Control	20	0	0
1.7	0.96	20	0	0
3.1	1.9	20	0	0
5.4	3.3	20	0	0
9.5	5.8	20	0	0
17	11	20	0	0

EC50	> 11 mg/L at 48 hours
NOEC	11 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. Decline in the test concentrations was observed over the 48 hours test period. This was considered due to the volatile nature of the notified chemical. The endpoints were expressed on the basis of geometric mean concentrations. Given the EC50 is above the saturated concentration, the notified chemical is considered not to be harmful to aquatic invertebrates.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates
TEST FACILITY	Harlan (2010b)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 1.0, 3.2, 10, 32, and 100 mg/L (loading rate, dilution of filter saturated solution) Measured: 0.051, 0.17, 0.61, 2.2, and 7.6 mg/L (at 0 hr)
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	Test concentrations were analysed using gas chromatography (GC) at 0 hour and 72 hours
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported. Following a range-finding test, the definitive test was conducted in Water Accommodated Fractions (WAFs) of the test chemical at the loading rates of 100 mg/L. WAF was prepared by stirring 100 mg/L of test item in culture medium using a propeller stirrer for 24 hours. Then, the mixture was filtered through a filter of 0.2 µm. The filtrate was used as treatment solutions with appropriate dilutions.

RESULTS

Biomass (72 h) (geometric mean values)		*Growth (72 h) (geometric mean values)*	
E_yC50 (mg/L)	*NOE_yC (mg/L)*	*E_rC50 (mg/L)*	*NOE_rC (mg/L)*
2.1	0.53	4.4	0.53

Remarks - Results	All validity criteria for the test were satisfied. An increase in pH values of the test solutions was observed (from 7.7 at 0 hour to 9.2 – 9.4 at 72 hours). The study author considered this was due to the amount of CO_2 required by the large number of algal cells in growth). This was not considered to influence the test outcome given the increase in the cell number in the control cultures exceeded the validation criterion. The endpoints were expressed on the basis of geometric mean concentrations. Based on the determined ErC50 of 4.4 mg/L, the notified chemical is considered to be toxic to algae.
CONCLUSION	The notified chemical is toxic to algae
TEST FACILITY	Harlan (2010c)

C.2.3. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical (octafluoropentyl methacrylate)
METHOD	OECD TG 211 *Daphnia magna* Reproduction Test – Semi Static
Species	*Daphnia magna*
Exposure Period	21 d
Auxiliary Solvent	None
Water Hardness	120 mg/L as $CaCO_3$
Analytical Monitoring	Gas chromatography mass spectrometry
Remarks - Method	Conducted in accordance with the test guidelines above, and

in compliance with GLP standards and principles. Daphnids were exposed to a geometric series of five test concentrations and a negative (dilution water) control. Ten replicate test chambers containing one daphnid and twenty replicate test chambers containing one daphnid each were tested for each of the test substance treatment concentration and control groups, respectively.
A calculated amount of test substance was rinsed into a glass aspirator bottle, equipped with draining spigot at the bottom of the bottle, to achieve a final stock concentration of 100 mg/L. The mixture was stirred overnight. At the end of the stirring, the solution was filtered through a 0.2 micron membrane filter, the first 500 mL of the filtrate was discarded. The remaining filtrate was used as a primary stock solution.

Day 21			
Mean measured target concentration (mg/L)	*Percent Adult Survival*	*Mean Number of Living Offspring Produced per female*	*Mean Total Body Length in mm*
Negative Control	95	95.3	4.6
0.22	80	124.5	4.7
0.7	70	153.3	4.7
1.8	70	153.7	4.6
4.8	80	156.8	4.5
16	100	0.70	3.6

NOEC 1.8 mg/L at 21 days

Remarks - Results

Growth, measured as dry weight, was the most sensitive biological endpoint measured in this study. Daphnids exposed to the notified chemical at concentrations ≥ 4.8 mg/L had statistically significant reductions in dry weight in comparison to the negative control. Consequently, the NOEC, based on growth, was 1.8 mg/L, the LOEC was 4.8 mg/L.

All validity criteria of the test guideline were satisfied. The measured concentrations of the test substance among replicate test chambers over each renewal period varied more than 20%, due to degradation of octafluoropentyl methacrylate to octafluoro-1-pentanol. However, the initial measured concentrations at each renewal did not vary more than 20% establishing the consistency of initial exposures at each exposure level and the combined total concentration octafluoropentyl methacrylate and octafluoro-1-pentanol averaged >80% of the target concentration. It was reported that there was a statistically significant decrease in mean neonate production per surviving adult in the 16 mg/L treatment group in comparison to the negative control ($p \leq 0.05$). Furthermore, the mean length and mean dry weight of surviving adults in the 16 mg/L treatment group also showed a decrease at 3.6 mm and 0.52 mm, respectively. This could be due to degradation of octafluoropentyl methacrylate to octafluoro-1-pentanol and methacrylic acid.

CONCLUSION The notified chemical is not harmful to aquatic invertebrates with long lasting effects.

TEST FACILITY EAG (2016a)

C.2.4. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Expected degradant octafluoro-1-pentanol
METHOD	OECD TG 211 *Daphnia magna* Reproduction Test – Semi Static
Species	*Daphnia magna*
Exposure Period	21 d
Auxiliary Solvent	None
Water Hardness	143 mg/L as $CaCO_3$
Analytical Monitoring	Gas chromatography mass spectrometry
Remarks - Method	Conducted in accordance with the test guidelines above, and in compliance with GLP standards and principles. Daphnids were exposed to a geometric series of five test concentrations and a negative (dilution water) control. Ten replicate test chambers containing one daphnid and twenty replicate test chambers containing one daphnid each were tested for each of the test substance treatment concentration and control groups, respectively. A calculated amount of test substance was rinsed into a glass aspirator bottle, equipped with draining spigot at the bottom of the bottle, to achieve a final stock concentration of 100 mg/L. The bottle was covered with Parafilm™ and the solution was stirred overnight. At the end of the stirring, the solution was filtered through a 0.2 micron membrane filter, the first 500 mL of the filtrate was discarded. The remaining filtrate was used as the highest test solution.

Day 21			
Mean measured target concentration (mg/L)	*Percent Adult Survival*	*Mean Number of Living Offspring Produced per female*	*Mean Total Body Length in mm*
Negative Control	91	276	5.0
3.7	77	245	5.0
8.5	83	274	5.0
17	100	260	4.9
31	83	288	5.0
73	100	249	4.7

NOEC	73 mg/L at 21 days
Remarks - Results	All validity criteria of the test guideline were satisfied. However, the measured concentrations of the test substance among replicate test chambers over each renewal period varied more than 20%. Thus, the time-weighted mean measured concentration during renewal periods was calculated and reported. However, the initial measured concentrations at each renewal did not vary more than 20% establishing the consistency of initial exposures at each exposure level.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates with long lasting effects
TEST FACILITY	EAG (2016b)

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