File No.: STD/1717

May 2020

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1,3-Propanediol, 2,2-dimethyl-, 1,3-diacetate

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 Agriculture, Water and the Environment.

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:

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

Director
NICNAS

TABLE OF CONTENTS

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
STD/1717	BASF Australia Ltd	1,3-Propanediol, 2,2-dimethyl-, 1,3-diacetate	No	< 10 tonnes per annum	Fragrance ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

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.

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 3)	H402 – Harmful 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 PEC/PNEC ratio, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

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 chemical during reformulation:
  - Enclosed, automated processes, where possible
  - Local exhaust ventilation and/or appropriate extraction systems, 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 chemical during reformulation:
  - Avoid inhalation of aerosols or mists

- 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 during reformulation:
  - Respiratory protection if aerosols or mists may occur

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.

Emergency procedures

- Spills or accidental release of the notified chemical should be collected using an inert absorbent material and appropriately sealed in labelled drums.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

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 final use concentration of the notified chemical exceeds 0.2% in cosmetic and household products;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a fragrance ingredient, 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.

Safety Data Sheet
The SDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
BASF Australia Ltd (ABN: 62 008 437 867)
Level 28, Freshwater Place
SOUTHBANK VIC 3006

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year)

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include: analytical data, degree of purity, impurities, additives/adjuvants, use details, import volume and identity of manufacturer.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for dissociation constant, flammability, explosive properties and oxidising properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2018), Switzerland (2018)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Velberry

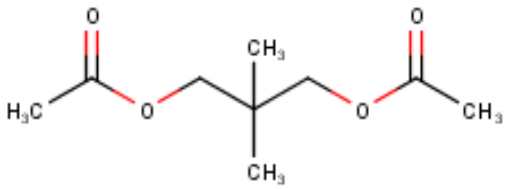
CAS NUMBER
13431-57-7

CHEMICAL NAME
1,3-Propanediol, 2,2-dimethyl-, 1,3-diacetate

OTHER NAME(S)
Neopentyl glycol diacetate
NPG diacetate
EC 826-122-1

MOLECULAR FORMULA
$C_9H_{16}O_4$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
188.22 g/mol

ANALYTICAL DATA
Reference NMR, IR, GC-FID, GC-MS, UV-Vis spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 95%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: colourless liquid

Property	*Value*	*Data Source/Justification*
Melting Point	-10 °C	Measured
Boiling Point	219.3 °C at 101.3 kPa	Measured
Density	1,012.7 kg/m^3 at 20 °C	Measured
Viscosity	3.80 mPa·s at 20 °C 2.28 mPa·s at 40 °C	Measured
Vapour Pressure	6 x 10^{-3} kPa at 20 °C 9 x 10^{-3} kPa at 25 °C 7.5 x 10^{-2} kPa at 50 °C	Measured
Water Solubility	14.3 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	281.8 hr at pH 9 and 20 °C 149.9 hr at pH 9 and 25 °C Hydrolytically stable at pH 4 and 7	Measured
Partition Coefficient (n-octanol/water)	log Pow = 1.9 at 20 °C	Measured
Adsorption/Desorption	log K_{oc} = 2.82 – 3.30	Measured
Dissociation Constant	Not determined	Contains no dissociable functional groups
Flash Point	99 °C at 101.3 kPa	Measured
Flammability	Not determined	Not expected to be highly flammable based on flash point
Autoignition Temperature	415 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties

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

Reactivity
The notified chemical 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 chemical is not 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 notified chemical has a flash point of 99 ºC which is greater than 93 °C. Based on *Australian Standard AS1940* definitions for combustible liquid, the notified chemical may be considered as a Class C2 combustible liquid if the chemical has a fire point below the boiling point.

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 into Australia either as a component of fragrance formulations at > 95% concentration for reformulation or in finished consumer products at ≤ 0.2% concentration.

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

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

PORT OF ENTRY
Melbourne, Sydney, Brisbane, Adelaide and Perth

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of fragrance formulations at > 95% concentration in steel drums or as a component of various finished cosmetic and household products in suitable packaging for retail sale. The products containing the notified chemical will be transported primarily by road to various warehouses and stores.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products at final use concentrations of ≤ 0.2% concentration.

OPERATION DESCRIPTION

Reformulation
Reformulation of the notified chemical into finished consumer goods may vary depending on the type of product and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

End-use products containing the notified chemical at ≤ 0.2% concentration will be used by consumers and professionals such as hairdressers, beauticians or cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

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)*
Mixer	none	incidental
Drum handling	4	10 – 20
Drum cleaning/washing	4	10 – 20
Maintenance	4	10 – 20
Quality control	4	10 – 20
Professional end users	0.5	10 – 20
Mixer	8	240

EXPOSURE DETAILS
Transport and Storage
Transport and storage workers are not expected to be exposed to the notified chemical except in the unlikely event of accidental rupture of containers.

Reformulation
During reformulation, dermal, ocular and perhaps inhalation exposure (if aerosols or mists are generated) of workers to the notified chemical (at > 95% concentration) may occur during weighing and transfer stages, blending, quality control analysis, and cleaning and maintenance of equipment. Inhalation exposure to vapours of the notified chemical is not expected given the low vapour pressure of the notified chemical (6×10^{-3} kPa at 20 °C). Exposure is expected to be minimised through the use of local exhaust ventilation, automated and enclosed systems and personal protective equipment (PPE) such as impervious gloves, googles, protective clothing and respiration protection (if aerosols or mists may occur), as anticipated by the notifier.

End use
Exposure to the notified chemical in end-use products at ≤ 0.2% concentration may occur in professions where the services provided involve the application of cosmetics to clients (e.g. hair dressers and workers in beauty salons), or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical at ≤ 0.2% concentration through the use of a wide range of cosmetic and household products. The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible, particularly if the products are applied by spray.

Data on typical use patterns of product categories in which the notified chemical may be used are shown in the following tables and these are based on information provided in various literatures (SCCS, 2012; Cadby *et al*., 2002; ACI, 2010; Loretz *et al*., 2006). For the purposes of exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A dermal absorption (DA) rate of 100% was assumed for the notified chemical for calculation purposes. For the inhalation exposure assessment, a 2-zone approach was used (Steiling *et al*., 2014; Rothe *et al*., 2011; Earnest, Jr., 2009). An adult inhalation rate of 20 m^3/day (enHealth, 2012) was used and it was conservatively assumed that the fraction of the notified chemical inhaled is 50%. A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

Cosmetic products (dermal exposure)

Product type	**Amount** (mg/day)	**C** (%)	**RF** (unitless)	**Daily systemic exposure** (mg/kg bw/day)
Body lotion	7820	0.2	1	0.2444
Face cream	1540	0.2	1	0.0481
Hand cream	2160	0.2	1	0.0675
Fine fragrances	750	0.2	1	0.0234
Deodorant	1500	0.2	1	0.0469
Shampoo	10460	0.2	0.01	0.0033
Conditioner	3920	0.2	0.01	0.0012
Shower gel	18670	0.2	0.01	0.0058
Hand soap	20000	0.2	0.01	0.0063
Hair styling products	4000	0.2	0.1	0.0125
Total				**0.4594**

C = maximum intended concentration of notified chemical; RF = retention factor
Daily systemic exposure = (Amount × C × RF × DA)/BW

Household products (Indirect dermal exposure – from wearing clothes)

Product type	**Amount** (g/use)	**C** (%)	**Product Retained (PR)** (%)	**Percent Transfer (PT)** (%)	**Daily systemic exposure** (mg/kg bw/day)
Laundry liquid	230	0.2	0.25	10	0.0068
Fabric softener	90	0.2	0.25	10	0.0027
Total					**0.0095**

C = maximum intended concentration of notified chemical
Daily systemic exposure = (Amount × C × PR × PT × DA)/BW

Household products (Direct dermal exposure)

Product type	**Frequency** (use/day)	**C** (%)	**Contact area** (cm^2)	**Product use C** (g/cm^3)	**Film thickness** (cm)	**Time scale factor**	**Daily systemic exposure** (mg/kg bw/day)
Laundry liquid	1.43	0.2	1980	0.01	0.01	0.007	0.0001
Dishwashing liquid	3	0.2	1980	0.009	0.01	0.03	0.0005
All-purpose cleaner	1	0.2	1980	1	0.01	0.007	0.0043
Total							**0.0049**

C = maximum intended concentration of notified chemical
Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor × DA)/BW

Hair spray (inhalation exposure)

Product type	Amount	C	Inhalation Rate	Exposure Duration (Zone 1)	Exposure Duration (Zone 2)	Fraction Inhaled	Volume (Zone 1)	Volume (Zone 2)	Daily systemic exposure
	(g/day)	(%)	(m^3/day)	(min)	(min)	(%)	(m^3)	(m^3)	(mg/kg bw/day)
Hairspray	9.89	0.2	20	1	20	50	1	10	**0.0064**

C = maximum intended concentration of notified chemical
Total daily systemic 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 at the maximum intended concentrations specified by the notifier in various product types. This would result in a combined internal dose of 0.4802 mg/kg bw/day for the notified chemical. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic and household products (in addition to hair spray) may occur. However it is considered that the combination of the conservative hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% dermal absorption rate, is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic and household products with lower exposure factors (e.g. air fresheners).

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Acute oral toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Acute dermal toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Skin corrosion – *in vitro* EpiDerm reconstructed human epidermis test	non-corrosive
Skin irritation – *in vitro* EpiDerm reconstructed human epidermis test	non-irritating
Eye irritation – *in vitro* EpiOcular reconstructed human cornea-like epithelium test	non-irritating
Skin sensitisation – *in chemico* direct peptide reactivity assay (DPRA)	negative
Skin sensitisation – *in vitro* ARE-Nrf2 luciferase test	negative
Combined repeated dose oral toxicity study with the reproduction/developmental toxicity screening test – rat, up to 51 days	Systemic toxicity NOAEL = 300 mg/kg bw/day (males) and 1,000 mg/kg bw/day (females)* Reproductive/developmental NOAEL = 1,000 mg/kg bw/day*
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian cell gene mutation test	non clastogenic
Genotoxicity – *in vitro* mammalian cell micronucleus test	non clastogenic

* Established by the study authors

Toxicokinetics

No information on the toxicokinetics of the notified chemical was provided. For dermal absorption, molecular weights below 100 g/mol are favourable for absorption and molecular weights above 500 g/mol do not favour absorption (ECHA, 2017). Substances with water solubilities below 1 mg/L are likely to have low dermal uptake while absorption is considered low to moderate if water solubility is between 1-100 mg/L (ECHA, 2017). Dermal absorption is also expected to be more rapid for those substances with log P values between 1 and 4, while for substances with log P values above 4 the rate of penetration may be limited by the rate of transfer between the stratum corneum and the epidermis (ECHA, 2017). Given the low molecular weight of the notified chemical

(188.22 g/mol), water solubility (14.3 g/L at 20 °C) and partition coefficient of 1.9, there is potential for the chemical to cross biological membranes.

Acute Toxicity
The notified chemical is of low acute oral and dermal toxicity based on studies conducted in rats.

Irritation
In two *in vitro* studies using the EpiDerm™ reconstructed human epidermis test model, the notified chemical was determined not to require classification for skin corrosion or irritation under the GHS.

In an *in vitro* eye irritation test using the EpiOcular™ test method, the notified chemical was determined not to require classification for eye irritation under the GHS.

Sensitisation
One *in chemico* and one *in vitro* cell based assay were conducted to evaluate the skin sensitisation potential of the notified chemical. The tests are part of Integrated Approach to Testing and Assessment (IATA) which address specific events of the Adverse Outcome Pathway (AOP) leading to development of skin sensitisation (OECD, 2016). The tests are thus considered relevant for assessment of the skin sensitisation potential of the notified chemical, along with other supporting information.

The *in chemico* direct peptide reactivity assay (DPRA) aims to address the first key event (molecular initiation) of the AOP by measuring the interaction of the notified chemical with cysteine and lysine, small synthetic peptides representing the nucleophilic centres in skin proteins. The ARE-Nrf2 Luciferase Assay aims to address the second key event (keratinocyte activation) of the AOP by measuring the expression of a report luciferase gene under the control of a promoter from the antioxidant response element (ARE), a responding gene known to be upregulated by contact sensitisers.

The notified chemical showed negative responses in the two tests (DPRA assay and ARE-Nrf2 Luciferase assay), suggesting no potential for skin sensitisation. However, according to the OECD test guidelines (TG 442c, 442d and 442e), the suite of tests based on the AOP may not detect pre-haptens (chemicals that become sensitisers following auto-oxidation) and pro-haptens (chemicals requiring enzymatic activation to become sensitisers). Therefore, the negative result in the ARE-Nrf2 Luciferase assay may not reflect the actual skin sensitisation potential of the test substance. The study authors of the ARE-Nrf2 Luciferase assay stated that no metabolites of the notified chemical were identified via the skin metabolism simulator of the OECD Toolbox. There are no structural alerts indicative of sensitisation potential. Based on the available information, the notified chemical is not expected to be a skin sensitiser.

Repeated Dose Toxicity
In a combined repeated dose oral toxicity study with the reproduction/developmental toxicity screening test in rats with the notified chemical, the No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day for systemic toxicity for females (based on the absence of test substance-related adverse effects up to the highest dose tested) and 300 mg/kg bw/day for males (based on significantly reduced prothrombin time combined with significantly increased cholesterol levels observed in males treated at 1,000 mg/kg bw/day at the end of administration period). There were no test substance-related reproductive/developmental effects up to the highest dose tested therefore the NOAEL for reproductive/developmental toxicity was established as 1,000 mg/kg bw/day.

Mutagenicity/Genotoxicity
The notified chemical was found to be negative in a bacterial reverse mutation assay, an *in vitro* gene mutation test using Chinese hamster ovary (CHO) cells and in an *in vitro* mammalian cell micronucleus test using human lymphocytes.

Health Hazard Classification
Based on the available information, the notified chemical is not classified as hazardous 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

Based on the available toxicological information, the notified chemical is a non-hazardous substance with low toxicity.

Reformulation

Exposure of workers to the notified chemical (at > 95% concentration) may occur during reformulation. No hazards are identified for the notified chemical, however, mild skin and eye irritation from exposure to high concentrations of the notified chemical cannot be ruled out. No inhalation toxicity data were provided, but due to the low vapour pressure of the notified chemical inhalation exposure to vapours of the notified chemical is not expected. The use of local exhaust ventilation, enclosed/automated processes and PPE (i.e. protective clothing, impervious gloves, goggles and respiratory protection if areoles and mists may be generated), as anticipated by the notifier, are expected to minimise the potential for exposure.

Therefore, under the conditions of the occupational settings described, the risk to workers from use of the notified chemical is not considered to be unreasonable.

End-use

Cleaners and beauty care professionals will handle the notified chemical at ≤ 0.2% concentration, similar to public use. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. Therefore the risk to workers who use products containing the notified chemical is expected to be of a similar or lesser extent than consumers who use such products on a regular basis. 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 exposure to the notified chemical through the use of cosmetic and household products containing the notified chemical at ≤ 0.2% concentration.

Repeat dose toxicity

The repeat dose toxicity potential was estimated by calculation of the margin of exposure (MoE) of the notified chemical using the worst case exposure scenario from use of multiple products by an individual with total exposure of 0.4802 mg/kg bw/day (see Section 6.1.2). Using a NOAEL for the notified chemical of 300 mg/kg bw/day, derived from a combined repeated dose oral toxicity study with the reproduction/developmental toxicity screening test on the notified chemical, the margin of exposure (MOE) was estimated to be 624.7. A MOE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences, and to account for long-term exposure. Therefore the estimated MOE is acceptable, indicating no unreasonable risks to consumers.

Overall, based on the information available, the risk to the public associated with use of the notified chemical at ≤ 0.2% in cosmetic and household products, is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical is not manufactured in Australia, therefore no release is expected from this activity. The notifier estimates that up to 1% of the import volume may be lost from accidental spills during transport and a further 1% of the import volume may be lost from accidental spills during reformulation. Any accidental spills are to be collected and disposed of in accordance with local government regulations. Wash waters from equipment cleaning, containing the notified chemical are expected to be disposed of to sewer as trade waste.

RELEASE OF CHEMICAL FROM USE

A majority of the notified chemical is expected to be washed into sewer waters as a part of its use in various cosmetic and household products where it will be treated in sewage treatment plants nationwide before being released into surface waters.

RELEASE OF CHEMICAL FROM DISPOSAL

A small proportion of the notified chemical is expected to remain as residues in empty product containers. These containers are expected to be either recycled or disposed of to domestic landfill. Collected wastes of the notified chemical are to be disposed of by licensed waste contractors to eventually be disposed of to landfill or released into the sewer system.

7.1.2. Environmental Fate

Following its use in cosmetic products and household cleaning products, the notified chemical is expected to be primarily released into the sewer system and treated at sewage treatment plants before release to surface waters nationwide.

The notified chemical is readily biodegradable (84% biodegradation using 301B method, 77.4% degradation using 301F method). For details of the biodegradation studies, refer to Appendix C. The notified chemical is not expected to bioaccumulate due to its low log Pow (log Pow = 1.9). Some of the notified chemical may remain in the end use and bulk containers, which are either recycled or disposed of to landfill. In surface waters and landfill, the notified chemical is expected to degrade into water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The use pattern will result in most of the notified chemical being washed into the sewer. The predicted environmental concentration (PEC) has been calculated assuming the realistic worst-case scenario with 100% release of the notified chemical into sewer systems nationwide over 365 days per annum. The extent to which the notified chemical is removed from the effluent in STP processes based on the properties of the notified chemical has not been considered for this scenario and therefore no removal of the notified chemical during sewage treatment processes is assumed. The PEC in sewage effluent on a nationwide basis is estimated as follows:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	10,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	10,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	27.4	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	
Daily effluent production:	4,877	ML
Dilution Factor – River	1	
Dilution Factor – Ocean	10	
PEC - River:	5.62	µg/L
PEC - Ocean:	0.56	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 5.618 µg/L may potentially result in a soil concentration of approximately 3.745 E^{-2} mg/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 1.873 E^{-1} mg/kg and 3.745 E^{-1} mg/kg, respectively.

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*
Fish Toxicity	LC50 (96 h) = 40.4 mg/L	Harmful to fish
Daphnia Toxicity	EC50 (48 h) = 116 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity	NOEC > 143 mg/L	Not harmful to algal growth
Inhibition of Bacterial Respiration	IC50 > 1,000 mg/L	Not inhibitory to bacterial respiration

Based on the above ecotoxicological endpoints for the notified chemical, it is expected to be harmful to fish. Therefore, the notified chemical is classified as 'Acute (Category 3): H402 – Harmful to aquatic life' according to

the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009). The notified chemical is readily biodegradable and is not expected to bioaccumulate. Therefore, the notified chemical is not formally classified under the GHS for its long-term hazard.

7.2.1. Predicted No-Effect Concentration

A Predicted No-Effect Concentration (PNEC) was calculated based on the acute endpoint for fish (EC50 = 40.4 mg/L) using an assessment factor of 100.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Fish).	40.4	mg/L
Assessment Factor	100	
Mitigation Factor	1	
PNEC:	404	µg/L

7.3. Environmental Risk Assessment

A Predicted No-Effect Concentration (PNEC) was calculated based on the most sensitive acute endpoint for fish (EC50 = 40.4 mg/L) using an assessment factor of 100 as three acute trophic endpoints are available.

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	5.62	404	0.01
Q - Ocean:	0.56	404	< 0.01

The risk quotient (Q = PEC/PNEC) has been calculated based on the worst-case assumption of complete release into the waterways with no removal in STPs. As the Q value is significantly less than 1, the notified chemical is unlikely to reach ecotoxicologically significant concentrations. Therefore, on the basis of the PEC/PNEC ratio, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point -10 °C

Method OECD TG 102 Melting Point/Melting Range
Remarks Determined by differential scanning calorimetry
Test Facility BASF (2018a)

Boiling Point 219.3 °C at 101.3 kPa

Method OECD TG 103 Boiling Point
Remarks Dynamic method
Test Facility BASF (2018a)

Density 1,012.7 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids
Remarks Determined using an oscillating density meter.
Test Facility BASF (2018a)

Viscosity 3.80 mPa·s at 20 °C
2.28 mPa·s at 40 °C

Method OECD TG 114 Viscosity of Liquids
Remarks Kinematic viscosity was measured using a capillary viscometer and density was measured using an oscillating density meter.
Test Facility BASF (2018a)

Vapour Pressure 6×10^{-3} kPa at 20 °C
9×10^{-3} kPa at 25 °C
7.5×10^{-2} kPa at 50 °C

Method OECD TG 104 Vapour Pressure
Remarks Dynamic method
Test Facility BASF (2018a)

Water Solubility 14.3 g/L at 20 °C

Method OECD TG 105 Water Solubility
Remarks Flask Method measured using HPLC-UV
Test Facility BASF (2017a)

Hydrolysis as a Function of pH

Method OECD TG 111 Hydrolysis as a Function of pH

pH	*T (°C)*	*$t_{½}$ hours*
4	50	Hydrolytically stable
7	50	Hydrolytically stable
9	20	281.8
9	25	149.9

Remarks Measured using HPLC-UV
Test Facility BASF (2018b)

Adsorption/Desorption – main test Average log K_{oc} = 3.08

Method OECD TG 106 Adsorption – Desorption Using a Batch Equilibrium Method

Soil Type	*Organic Carbon Content (%)*	*pH*	*Koc (cm^3/g)*	*Log Koc*
Loam	6.54	7.28	664	2.82
Silt load	1.36	4.60	1988	3.30
Silt clay loam	5.36	6.81	1126	3.05
Silt loam	1.39	7.84	1724	3.23
Silt loam	6.85	6.85	650	2.81

Remarks Analysis by gas chromatography
Test Facility Jiangsu (2019a)

Flash Point 99 °C at 101.3 kPa

Method DIN EN ISO 2719
Remarks Closed cup procedure
Test Facility BASF (2018c)

Autoignition Temperature 415 °C

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Remarks Flask heater procedure
Test Facility BASF (2018c)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain	Rat/Wistar
Vehicle	Corn oil
Remarks – Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	3 F	300	0/3
2	3 F	2,000	0/3
3	3 F	2,000	0/3

LD50	> 2,000 mg/kg bw
Signs of Toxicity	Piloerection, impaired general state and dyspnea were observed in all animals. Animals in groups 1 and 2 also displayed cowering positions.
Effects in Organs	No abnormalities were observed at necropsy.
Remarks – Results	Two females from group 1 and one female from group 2 displayed slow weight gains during the second week. This was not considered by the study authors to be test substance-related.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	Bioassay (2018a)

B.2. Acute Dermal Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test
Species/Strain	Rat/Wistar
Vehicle	None
Type of dressing	Semi-occlusive
Remarks – Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5 M	2,000	0/5
2	5 F	2,000	0/5

LD50	> 2,000 mg/kg bw
Signs of Toxicity – Local	No signs of local skin effects were observed.
Signs of Toxicity – Systemic	No signs of systemic effects were observed.
Effects in Organs	No macroscopic pathologic abnormalities noted at necropsy.
Remarks – Results	All animals showed expected body weight gains during the study period.
CONCLUSION	The notified chemical is of low acute toxicity via the dermal route.
TEST FACILITY	Bioassay (2018b)

B.3. Skin Irritation – *In Vitro* EpiDerm™ Reconstituted Human Epidermis Test

TEST SUBSTANCE	Notified chemical

METHOD

OECD TG 431 *In vitro* Skin Corrosion: Reconstructed Human Epidermis (RHE) Test Method
OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human Epidermis Test Method

Vehicle: None

Remarks – Method: No significant protocol deviations. In a preliminary test the test substance was shown to reduce MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolim bromide] directly. Therefore, the study was performed in parallel on viable and freeze-killed control (KC) tissues.

Negative control: deionized water (corrosion test), PBS, sterile (irritation test)
Positive Control: 8N potassium hydroxide solution (corrosion test), 5% sodium dodecyl sulphate in water (irritation test)

RESULTS

Corrosion test

Test material	*Test 1 (3 minute exposure period)*		*Test 2 (1 hour exposure period)*	
	Mean OD_{570} of duplicate tissues	*Relative mean viability (%)*	*Mean OD_{570} of duplicate tissues*	*Relative mean viability (%)*
Negative control				
Viable	1.533	100	1.506	100
KC	0.079	5.2	0.072	4.75
Test substance				
Viable	1.518	99	1.384	91.9
KC	0*	0*	0.007	0.45
Positive control	0.181	11.8	0.078	5.2

OD = optical density; * Negative values set to zero for further calculation

Irritation test

Test material	*Test 1*			*Test 2*		
	Mean OD_{570} of triplicate tissues	*Relative mean Viability (%)*	*SD of relative mean viability*	*Mean OD_{570} of triplicate tissues*	*Relative mean Viability (%)*	*SD of relative mean viability*
Negative control						
Viable	1.776	100	8.9	1.845	100	2
KC	0.056	3.2	0.2	0.047	2.5	0.1
Test substance						
Viable	1.193	67.2	14.7	1.37	74.3	22.6
KC	0.001	0.034	0.03	0.001	0.042	0.0
Positive control	0.045	2.50	0.3	0.046	2.5	0.3

OD = optical density; SD = standard deviation

Remarks – Results: Mean tissue viability after KC correction was 99% and 91.4% for the 3 minute and 1 hour corrosion tests respectively for the test substance. Based on the mean tissue viability of > 55% after 3 min exposure and > 20% after 1 h exposure, the test substance was not classified as a skin corrosive according to the test guidelines, using GHS criteria.

Mean tissue viability for the irritation test after KC correction was 67.1% and 74.2% for the 1st and 2nd test runs respectively for the test substance. Based on the mean tissue viability of > 50%, the test substance is not classified as a skin irritant according to the test guidelines, using GHS criteria.

A high inter-tissue variability in the irritation test warranted the addition of a 2nd test run. The 2nd test run also displayed a high inter-tissue variability. The SD of % viability of the test substance-treated tissues was

	outside of the acceptance range for the test. However, this deviation was not considered by the study authors to affect the evaluation adversely since all other quality criteria of the test were met and the viability values of four out of the six tissues were above the cut-off for skin irritation and the two tissues that were not above the cut-off were within the borderline threshold. Positive and negative controls performed as expected.
CONCLUSION	The notified chemical was considered non-corrosive and non-irritating to the skin under the conditions of the test, not requiring classification of it as an eye irritant according to the GHS criteria.
TEST FACILITY	BASF (2018d)

B.4. Eye Irritation – *In Vitro* EpiOcular™ Reconstructed Human Cornea-like Epithelium (RhCE)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG No. 492 Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage
Vehicle	None
Remarks – Method	No significant protocol deviations. In a preliminary test the test substance was shown to reduce MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolim bromide] directly. Therefore, the study was performed in parallel on viable and freeze-killed control (KC) tissues. Negative Control: deionized water Positive Control: methyl acetate

RESULTS

Test Material	*Mean OD_{570} of Duplicate Tissues*	*Relative Mean Viability (%)*	*SD of relative mean viability*
Negative Control			
Viable	1.66	100	8
KC	0.039*	2.3*	N/A
Test Substance			
Viable	1.219	73.4	1.8
KC	0#	0#	N/A
Positive Control	0.445	23.2	7.2

OD = optical density; SD = standard deviation; * Single tissue sample; # Negative values set to zero for further calculation

Remarks – Results	Mean tissue viability after KC correction was 73.4% (> 60%) for the test substance.
CONCLUSION	The notified chemical was considered non-irritating to the eye under the conditions of the test, not requiring classification of it as an eye irritant according to the GHS criteria.
TEST FACILITY	BASF (2018e)

B.5. Skin Sensitisation – *In Chemico* DPRA Test

TEST SUBSTANCE	Notified chemical

METHOD	OECD TG 442c *In Chemico* Skin Sensitisation: Direct Peptide Reactivity Assay (DPRA) (2015)
Vehicle	Acetonitrile
Remarks – Method	No significant protocol deviations

RESULTS

Sample	*Cysteine Peptide Depletion (% ± SD)*	*Lysine Peptide Depletion (% ± SD)*
Negative Control	0.00*	0.00*
Test Substance	0.67 ± 5.43	0.62 ± 1.13
Positive Control - ethylene glycol dimethacrylate	67.63 ± 3.65	13.64 ± 0.15

SD = Standard Deviation; * Normalised

Remarks – Results	The mean depletion of cysteine and lysine peptides was 0.64%, indicating minimal or no reactivity of the test substance with peptides. Positive and negative controls performed as expected. All quality criteria were met.
CONCLUSION	The notified chemical was predicted as negative for the first key event (molecular initiating) of the adverse outcome pathway (AOP) for skin sensitisation.
TEST FACILITY	BASF (2018f)

B.6. Skin Sensitisation – *In Vitro* ARE-Nrf2 Luciferase Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 442d *In Vitro* Skin Sensitisation Assays Addressing the AOP Key Event on Keratinocyte Activation (2015) - The ARE-Nrf2 luciferase LuSens test method
Negative Control	5 mM DL-Lactic acid in 1% DMSO (in culture medium)
Vehicle Control	1% DMSO in culture medium
Positive Control	Ethylene glycol dimethacrylate in 1% DMSO (in culture medium)
Remarks – Method	No significant protocol deviations

RESULTS

Sample	*Concentration (µM)*	*Mean Cell viability (% ± SD)(Exp 1/Exp 2)*	*Mean Luciferase Induction (fold ± SD) (Exp 1/Exp 2)*
Vehicle Control	-	100*	1.00*
Negative Control	5000	99.0 ± 8.48	1.11 ± 0.021
Test substance			
Dose Level 1	564	96.5 ± 6.36	0.76 ± 0.233
Dose Level 2	676	93.0 ± 8.49	0.99 ± 0.000
Dose Level 3	812	94.5 ± 6.36	1.09 ± 0.099
Dose Level 4	974	93.5 ± 6.36	1.13 ± 0.134
Dose Level 5	1169	93.5 ± 0.71	1.10 ± 0.042
Dose Level 6	1403	85.5 ± 4.95	1.13 ± 0.071
Dose Level 7	1683	86.5 ± 6.36	1.17 ± 0.148
Dose Level 8	2020	81.0 ± 5.65	1.28 ± 0.177
Positive Control	90.8	82.5 ± 0.71	4.54 ± 1.061

SD: Standard Deviation; * Normalised

	$EC_{1.5}$ (µM)	*IC50 (µM)*	*Imax*
Experiment 1	N/A	N/A	1.4 at 2020 µM
Experiment 2	N/A	N/A	1.15 at 2020 µM

EC1.5 – concentration resulting in 1.5-fold induction of luciferase activity relative to vehicle control

IC50 – concentration resulting in 50% reduction in cell viability relative to vehicle control
I_{max} – maximal fold induction of luciferase activity relative to vehicle control

Remarks – Results	Cells treated with the test substance displayed cell viabilities > 50% in both experiments, hence, an IC50 could not be determined. Cells treated with the test substance produced an Imax ≤ 1.4, hence, an EC1.5 could not be obtained. Acceptance criteria were met for all experiments in this study.
CONCLUSION	The test substance was negative for the second key event (keratinocytes response) of the adverse outcome pathway (AOP) for skin sensitisation.
TEST FACILITY	BASF (2018f)

B.7. Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (2016)
Species/Strain	Rats/Wistar
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 14 days pre mating and 14 days mating period in both male and female animals, and during gestation (up to 20 days) and lactation (up to 13 days) for females Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	Corn oil
Remarks – Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	10 per sex	0	0/20
Low Dose	10 per sex	100	0/20
Mid Dose	10 per sex	300	0/20
High Dose	10 per sex	1,000	0/20
Control Recovery	5 per sex	0	0/10
High Dose Recovery	5 per sex	1,000	0/10

Mortality and Time to Death
There were no unscheduled deaths.

Effects on parental animals
Salivation in the mid and high dose groups was attributed to the unpleasant taste of the test substance. No test substance-related effects were seen in functional and behavioural examinations. Food and water consumption was not impacted by the treatment.

Slightly reduced mean body weight was seen in the male recovery group on day 13 and the mean body weight gain was reduced in males during the recovery between study days 38 to 45. The effects were considered by study authors to be test substance-related but not adverse.

Haematology and clinical chemistry
Statistically significantly reduced prothrombin times were reported in high dose males at the end of the administration period. This change combined with the statistically significantly increased cholesterol levels in the same individuals was considered by the study authors as test substance-related and adverse.

In the recovery group, males had increased absolute basophil cell counts and females had increased absolute and relative large unstained cell (LUC) counts at the end of the administration, however, these values were within the historical control range. At the end of recovery, males in the recovery group had increased haemoglobin values (within the historical control range).

Increased albumin values (above the historical control range) and sodium levels were reported in the recovery males but not in the high dose males.

There were decreased alkaline phosphatase (ALP) levels in recovery females (compared to historical control data), but these changes were not considered by the study authors to be test substance-related as animals of the historical controls were 6 weeks younger when compared with the rats of this study.

Pathology for test groups

Compared with the control mean, slightly increased mean absolute weight of epididymides (6% for low dose group, 0.9% for mid dose group and 8.3% for high dose group) and statistically significantly increased mean absolute weight of prostate (16.8% for low dose group, 23.8% for mid dose group and 24.6% for high dose group) were reported in treated males. There were also increased mean absolute weight of thymus in the mid dose females and reduced mean absolute weight of thymus in the high and low dose females (statistically significant; considered by the study authors as accidental as there was no dose-response relationship).

The mean absolute weight (1.24 g) of epididymides in males of high dose group was slightly above the historical control range (1.102 – 1.230 g) but the mean relative weight of epididymides (0.30%) was within the historical control range (0.272 – 0.32%) and there were no test substance-related histopathological findings. Therefore, the slightly increased mean absolute weight of epididymides was considered by the study authors as incidental.

The mean absolute and relative prostate weights of males in low dose group (1.13 g, 0.27%), mid dose group (1.19 g, 0.29%), and high dose group (1.20 g, 0.29%) were within the range of historical control data (1.01 - 1.274 g, 0.244 - 0.315%), whereas the mean absolute and relative prostate weights of control males (0.96 g, 0.24%) were below the historical control range. Furthermore, there were no test substance-related histopathological findings in the prostate. Based on these, the statistical increase of prostate weights in males of all treatment groups were considered by the study authors to be attributed to the comparable low prostate weight in concurrent control males.

No treatment related effects were noted for gross lesions and histopathological investigations.

Pathology for recovery groups

Compared with the control, there is no significant difference for all mean absolute and relative organ weights except for a statistically significant increase in the relative heart weights in males. The increase of the relative heart weights in males was associated with the slightly but not significantly reduced terminal body weight. No significant changes of the heart weights were noted in males in the corresponding test group.

No treatment related effects were noted for gross lesions and histopathological investigations.

Reproductive effects

There were no test substance-related effects for estrous cycle, male reproduction data (including male mating and fertility indices) and female reproduction and delivery data (including female mating and fertility indices, gestation index, live birth indices and postimplantation loss).

Effects on pups

There were no test substance-related effects for litter data (including pup number and status at delivery, pup viability index/mortality and sex ratio), pup clinical observations, pup body weight data, anogenital distance and anogenital distance index, nipple/areola and pup necropsy observations.

Remarks – Results

There were signs of systemic toxicity in the high dose group males at the end of the administration period (reduced prothrombin times and increased cholesterol values), but disappeared after the recovery period. There were no test substance-related adverse findings in males in the low and mid dose groups and in all female parental animals (F0) and all pups (F1).

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day for systemic toxicity for females (based on the absence of test substance-related adverse effects up to the highest dose tested) and 300 mg/kg bw/day for males (based on significantly reduced prothrombin time combined with significantly increased cholesterol values observed in males treated at 1,000 mg/kg bw/day at the end of administration period).

The NOAEL for reproductive/developmental toxicity was established as 1,000 mg/kg bw/day based on there were no test substance-related reproductive/developmental effects up to the highest dose tested.

TEST FACILITY BASF (2019)

B.8. Genotoxicity – Bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test
Plate incorporation (Test 1) and Pre incubation procedure (Test 2)

Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100 *Escherichia coli*: WP2uvrA
Metabolic Activation System	S9 mix from phenobarbital/β-naphthoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 33 – 5000 µg/plate b) Without metabolic activation: 33 – 5000 µg/plate
Vehicle	DMSO
Remarks – Method	The dose selection for Test 2 was based on the toxicity observed in a preliminary test (reported as Test 1) carried out at 33 – 5000 µg/mL. Positive controls: With metabolic activation: 2-aminoanthracene Without metabolic activation: 4-nitroquinoline-N-oxide (WP2 uvrA); N-methyl-N′-nitro-N-nitrosoguanidine (TA1535, TA100); 4-nitro-o-phenylene-diamine (TA98); 9-aminoacridine (TA1537)

RESULTS

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

Remarks – Results No significant increases in the frequency of revertant colonies were observed for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation.

The positive and negative controls gave a satisfactory response confirming the validity of the test system.

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

TEST FACILITY BASF (2017b)

B.9. Genotoxicity – *In Vitro* Mammalian Cell Gene Mutation

TEST SUBSTANCE Notified chemical

METHOD	OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test
Species/Strain	Chinese hamster
Cell Type/Cell Line	Chinese hamster ovary (CHO)
Metabolic Activation System	S9 fraction from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	DMSO (at 1% (v/v) in culture medium)
Remarks – Method	No significant protocol deviations
	Negative control: culture medium (Ham's F12 medium). Positive control: Without S9: ethyl methanesulfonate (EMS) With S9: 7,12-dimethylbenz[a]anthracene (DMBA)

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	14.8, 29.7, 59.4, 118.8, 237.5*, 475*, 950*, 1900*	4 h	7-9 days	6-7 days
Present				
Test 1	14.8, 29.7, 59.4, 118.8, 237.5*, 475*, 950*, 1900*	4 h	7-9 days	6-7 days

*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	-	> 1900	> 1900	negative
Present				
Test 1	-	> 950	> 1900	negative

Remarks – Results	The test substance did not cause any biologically relevant increases in the mutant frequencies either with or without metabolic activation. The positive and negative controls gave a satisfactory response confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to CHO cells treated *in vitro* under the conditions of the test.
TEST FACILITY	BASF (2018g)

B.10. Genotoxicity – *In Vitro* Mammalian Cell Micronucleus Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 487 In vitro Mammalian Cell Micronucleus Test (2014)
Species/Strain	Human
Cell Type/Cell Line	Peripheral lymphocytes
Metabolic Activation System	S9 mix from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	DMSO (at 0.5% (v/v) in culture medium) (Test 1 and 3) Culture medium (Test 2 and 4)
Remarks – Method	Additional studies were conducted on the positive controls to ensure that the mutagenic responses were statistically significant. Based on these results, the recovery phase and harvest time was modified. Negative control: culture medium (Ham's F12 medium) Positive control: Without S9: mitomycin C (Test 1 and 3) and demecolcine (Test 2 and 4) With S9: cyclophosphamide

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	14.3, 25.0, 43.7, 76.4, 134, 234, 410, 717*, 1255*, 1882*	4 h	40 h
Test 2	76.4, 134, 234, 410, 717*, 1255*, 1882*	20 h	40 h
Test 3	65.5, 115, 201, 351, 615*, 1075*, 1882*	4 h	40 h
Test 4	134, 234, 410, 717*, 1255*, 1882*	20 h	40 h
Present			
Test 1	14.3, 25.0, 43.7, 76.4, 134, 234, 410, 717*, 1255*, 1882*	4 h	40 h
Test 3	65.5, 115, 201, 351, 615*, 1075*, 1882*	4 h	40 h

*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	> 1882	> 1882	> 1882	negative
Test 2	> 1882	> 1882	> 1255	positive
Test 3	> 1882	> 1882	> 1882	negative
Test 4	> 1882	> 1882	> 1882	negative
Present				
Test 1	> 1882	> 1882	> 1882	negative
Test 3	> 1882	> 1882	> 1882	negative

Remarks – Results

In Test 1 (with metabolic activation), a statistically significant increase in the frequencies of micronucleated cells was noted at the 1225 µg/mL concentration. However, this increase was not considered by the study authors to be biologically relevant as the increase was within the range of the historical control data and no dose-dependency via trend test was observed.

In Tests 1 and 2 (in the absence of metabolic activation), statistically significant increases (clearly exceeded the range of the historical control data) in the frequencies of micronucleated cells were noted at 717 (test 2), 1225 (test 1) and 1882 µg/mL (test 2). However, the increases were not considered by the study authors to be biologically significant as no dose-dependency via trend test was observed.

Apart from these observations, the test substance did not induce a statistically or biologically significant increase in the number of micronucleated cells at all other test concentrations in each exposure group, with or without metabolic activation.

The positive controls performed as expected, confirming the validity of the test system.

CONCLUSION

The test chemical was not genotoxic to human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY

BASF (2018h)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO2 Evolution Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	DOC
Remarks – Method	Aniline was used as a reference substance. A toxicity test was also run.

RESULTS

Test Substance		*Aniline*		*Toxicity Test*	
Day	*% Degradation*	*Day*	*% Degradation*	*day*	*% Degradation*
0	0	0	0	0	0
5	6	5	38	5	32
14	76	14	83	14	75
21	82	21	89	21	81
28	84	28	93	28	85

Remarks – Results	All validity criteria were met. The difference in extremes between replicates was less than 20%, the inorganic carbon in test suspension was < 5% of total carbon and the total CO_2 evolution in the control sample was less than 39 mg/L. The toxicity test indicated that the test substance was not considered inhibitory as the control sample reached 61% degradation after 8 days.
CONCLUSION	Test substance is readily biodegradable.
TEST FACILITY	BASF (2018i)

C.1.2. Ready Biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	BOD
Remarks – Method	Sodium benzoate was used as a reference substance. A toxicity test was also run.

RESULTS

Test Substance		*Sodium benzoate*		*Toxicity test*	
Day	*% Degradation*	*Day*	*% Degradation*	*Day*	*% Degradation*
0	0	0	0	0	0
7	25	7	66.5	7	18.9
14	42.5	14	83.4	14	40.6
21	62.4	21	88.5	21	42.3
28	77.4	28	86.5	28	46.9

Remarks – Results	All validity criteria were met. The difference in extremes between replicates was less than 7.44%, the oxygen uptake of the inoculum blank was 29.6 mg/L and the pH was maintained between 6.92 and 7.88. The toxicity test indicated that the test substance was not considered inhibitory as the control sample reached 40% degradation after 14 days.
CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	Jiangsu (2019b)

C.2. Ecotoxicological Investigations

C.2.1. Acute Toxicity to Fish

TEST SUBSTANCE	Notified chemical
METHOD	Equivalent to OECD TG 203 Fish, Acute Toxicity Test – semi static
Species	*Gobiocypris rarus* (Rare minnow)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	142 mg $CaCO_3$/L
Analytical Monitoring	GC
Remarks – Method	The species used is the only difference that deviated from the OECD test guideline. Based on a range finding study, test concentrations (detailed below) were prepared from dilution of a stock solution. Test solutions were renewed after 48 hours. A reference test was conducted, less than one month prior to the definitive study using potassium dichromate.

RESULTS

Concentration (mg/L)		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	-	7	0	0	0	0	0
10	9.62	7	0	0	0	0	0
20	18.9	7	0	0	0	0	0
40	38.4	7	0	0	2	3	3
80	78.3	7	0	7	7	7	7
100	94.0	7	0	7	7	7	7

LC50	54.8 mg/L at 24 hours 40.4 mg/L at 96 hours
NOEC (or LOEC)	18.9 mg/L at 96 hours
Remarks – Results	All validity criteria were met. The dissolved oxygen content was maintained at > 60% of the air saturation value and the concentration of the test substance was analysed. LC50 values were calculated based on the measured test concentrations. The results from the reference study showed an LC50 of 346 mg/L, which is consistent with previous results.
CONCLUSION	Test substance is harmful to fish.
TEST FACILITY	Jiangsu (2019c)

C.2.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE	Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – semi-static

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	252 mg $CaCO_3$/L
Analytical Monitoring	GC-MS
Remarks – Method	Based on a range finding study, test concentrations (detailed below) were prepared from dilution of a stock solution. Test solutions were renewed after 24 hours.

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	0	0
13.1	11.8	20	0	2
28.9	26.5	20	0	1
63.6	57.4	20	0	0
140	146	20	8	13
308	330	20	10	20

LC50	330 mg/L at 24 hours 116 mg/L at 48 hours
NOEC (or LOEC)	57 mg/L at 48 hours
Remarks – Results	All validity criteria were met. Dissolved oxygen was maintained between 7.85 – 9.6 mg/L, pH was maintained between 7.40 and 7.90 and temperature was maintained at 20°C ± 1°C. Due to variability in test substance concentration the EC50 was calculated based on nominal concentrations.

CONCLUSION The test substance is not harmful to aquatic invertebrates.

TEST FACILITY Smithers Viscient (2018a)

C.2.3. Algal Growth Inhibition Test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test

Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 125 mg/L Actual: 143 mg/L
Auxiliary Solvent	None
Water Hardness	39 - 85 mg $CaCO_3$/L
Analytical Monitoring	GC-MS
Remarks – Method	A limit test only was conducted. A reference study was conducted within one year prior to the definitive study using potassium dichromate.

RESULTS

Growth rate		*Yield*	
ErC50 (mg/L)	*NOEC (mg/L)*	*EyC50 (mg/L)*	*NOEC (mg/L)*
> 143	> 143	> 143	< 143

Remarks – Results	The reference study indicated an ErC50 of potassium dichromate of 0.875 mg/L, which was within the expected range.

	All validity criteria were met. The control cell density increased by a factor of 102, the mean coefficient of variation for section-by-section specific growth was 0.96% and the coefficient of variation for the average specific growth rates was 7.52%.
CONCLUSION	Test substance is not harmful to algal growth.
TEST FACILITY	Smithers Viscient (2018b)

C.2.4. Inhibition of Microbial Activity

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test
Inoculum	
Exposure Period	3 hours
Concentration Range	Nominal: 62.5 - 1000 mg/L
Remarks – Method	A reference test was conducted using 3,5 dichlorophenol.
RESULTS	
IC50	> 1,000 mg/L
IC10	> 1,000 mg/L
Remarks – Results	The reference test showed 3,5 dichlorophenol IC50 of 7.6 mg/L which is within the expected range of 2 – 25 mg/L. All validity criteria were met. The oxygen uptake of the controls was 22 mg/g×h and the coefficient of variation between replicates was 5.2%.
CONCLUSION	Test substance is not inhibitory to microbial respiration.
TEST FACILITY	BASF (2018j)

BIBLIOGRAPHY

BASF (2017a) Water Solubility of "Neopentylglycol diacetate" (Study No. 17L00105, March, 2017). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2017b) Neopentylglycol diacetate *Salmonella Typhimurium/Escherichia Coli* Reverse Mutation Assay (Study No. 40M0090/17M042, October, 2017). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018a) Physico-chemical properties of "Neopentylglycol diacetate" (Study No. 17L00397, January, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018b) Hydrolysis as a Function of pH of "Neopentylglycol diacetate" (Study No. 17L00398, January, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018c) Evaluation of Physical and Chemical Properties according to Regulation (EC) No 440/2008 (Study No. SIK-Nr.18/0926, July, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018d) Neopentylglycol Diacetate In vitro Skin Irritation and Corrosion Turnkey Testing Strategy Including Transport Classification (Study no. 70V0090/17A076, June, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018e) Neopentylglycol Diacetate In Vitro Eye Irritation Turnkey Testing Strategy (Study No. 71V0090/17A077, June, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018f) Neopentylglycol Diacetate In Vitro Skin Sensitization Turnkey Testing Strategy (Study No. 67V0090/17V040, June, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018g) Neopentylglycol diacetate In Vitro Gene Mutation Test in CHO Cells (HPRT Locus Assay) (Study No. 50M0090/17M314, November, 2018) Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018h) Neopentylglycol diacetate Micronucelus Test In Human Lymphocytes In Vitro (Study No. 31M0090/17X303, November, 2018) Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018i) Determination of the Ready Biodegradability in the CO2-Evolution Test (Study No. 22G0090/17G454, July, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2018j) Determination of the Inhibition of Oxygen Consumption in the Activated Sludge Respiration Inhibition Test (Study No. 08G0090/17G607, July, 2018). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

BASF (2019) Neopentylglycol diacetate Combined Repeated-Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test in Wistar Rats and Recovery Period of 2 Weeks Oral Administration (Gavage) (Study No. 85R0090/17C054, May, 2019). Ludwigshafen, Germany, BASF SE (Unpublished report submitted by the notifier).

Bioassy (2018a) Neopentylglycol diacetate acute oral toxicity study in rats (Study No. 17-BF-OT132, January, 2018). Heidelberg, Germany, Bioassay Labor fur biologische Analytik GmbH (Unpublished report submitted by the notifier).

Bioassay (2018b) Neopentylglycol diacetate acute dermal toxicity study in rats (Study No. 18-BF-DT007, August 2018). Heidelberg, Germany, Bioassay Labor fur biologische Analytik GmbH (Unpublished report submitted by the notifier).

Jiangsu (2019a) Report for the Adsorption-Desorption Test (Batch Equilibrium Method) (Study No. S2018NC006-03, August, 2019). Nanjing, China, Jiangsu Yaxin Tech. Co. Ltd. (Unpublished report submitted by the notifier).

Jiangsu (2019b) Report for Ready Biodegradability by the Manometric Respirometry Test (Study No. S2018NC006-02, August, 2019). Nanjing, China, Jiangsu Yaxin Tech. Co. Ltd. (Unpublished report submitted by the notifier).

Jiangsu (2019c) Report for Acute Toxicity to Fish (*Gobiocyprius rarus)* (Study No. S2018NC006-01, August, 2019). Nanjing, China, Jiangsu Yaxin Tech. Co. Ltd. (Unpublished report submitted by the notifier).

Smithers Viscient (2018a) Acute Toxicity to *Daphnia magna* (Study No. 3202084, July, 2018). North Yorkshire, United Kingdom, Smithers Viscient (ESG) Ltd. (Unpublished report submitted by the notifier).

Smithers Viscient (2018b) Inhibition of Growth to the Alga *Pseudokirchneriella subcapitata* (Study No. 3202083, July, 2018). North Yorkshire, United Kingdom, Smithers Viscient (ESG) Ltd. (Unpublished report submitted by the notifier).

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