Existing Chemical Secondary Notification Assessment Report ECSNA/1

November 2017

Australian Government
Department of Health
National Industrial Chemicals Notification and Assessment Scheme

α-D-Glucopyranoside, β-D-fructofuranosyl, octadecanoate

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

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Preface

This assessment was carried out under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). This scheme was established by the *Industrial Chemicals (Notification and Assessment) Act 1989* (the ICNA Act) to aid in the protection of the Australian people and the environment. This is achieved by assessing the risks of industrial chemicals, providing information and making recommendations to promote their safe use. NICNAS assessments are carried out by staff employed by the Australian Government Department of Health in conjunction with the Australian Government Department of the Environment and Energy.

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

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Contents

Overview

Background

α-D-Glucopyranoside, β-D-fructofuranosyl, octadecanoate, Chemical Abstracts Service Registry Number (CAS RN) 37318-31-3, is a UVCB substance consisting of C18 mono, di, tri and poly esters of sucrose. It was originally notified to and assessed by NICNAS in 2010 as an ingredient of imported, finished ink cartridges. The notified chemical is now listed on the Australian Inventory of Chemical Substances (AICS)

NICNAS was informed of an intended new use of the notified chemical in cosmetics, reformulation of the imported chemical into cosmetic products in Australia, the availability of new data on the human health hazards of the notified chemical and a proposed significantly increased introduction volume of the notified chemical to that previously assessed. This secondary notification assessment reassesses the risk posed to the public, workers and the environment based upon the new information provided.

Exempt Information (Section 75 of the Act)

No details are claimed exempt information.

Importation volume and uses

The notified chemical was originally imported into Australia as a minor ingredient (≤0.1%) of the ink used in finished inkjet printer cartridges. New information provided during the secondary notification indicates that the notified chemical will be imported at a concentration of up to 91% for reformulation into cosmetic products at a final concentration of between 0.5 and 5%. It will also be imported as an ingredient of finished cosmetic products (≤1%).

Although the volume of the chemical imported into Australia for use in inkjet printer inks remains unchanged from the original assessment at ≤250 kg per annum, an additional ≤1.5 tonnes per annum will be imported for cosmetic use.

Human health effects

No data to assess human health effects were provided in the original new chemical assessment. During the secondary notification, relevant data for the notified chemical were submitted for eye and skin irritation, skin sensitisation, and genotoxicity endpoints. As health data were not submitted for other endpoints, NICNAS identified suitable analogue data for toxicokinetics, acute and repeated dose oral toxicity as well as carcinogenicity.

When ingested, the notified chemical is expected to be predominately hydrolysed to sucrose and fatty acids and then share the same fate as other dietary sugars and fats. If absorbed intact through other non-oral routes of exposure, the notified chemical is also expected to be rapidly cleared from the body.

Due to its surfactant properties, the notified chemical may enhance the dermal absorption of other chemicals. The notified chemical has low acute and repeated dose oral toxicity as determined by studies using appropriate analogues. On the basis of data from substances with similar chemistry, the notified chemical is expected to have low acute and repeated dose dermal toxicity.

The notified chemical is not a skin irritant or skin sensitiser at a concentration of up to 17% in a human repeated insult patch test. At a concentration of 23%, the notified chemical is not irritating to the eyes as determined by the in vitro hen's egg test – chorioallantoic membrane (HET-CAM) test.

The notified chemical is not genotoxic in the bacterial reverse mutation test. Based upon analogue data, the notified chemical is not considered to be carcinogenic. The no observed adverse effect level (NOAEL) for the notified chemical is determined as 1970 mg/kg bw/day for males and 2440 mg/kg bw/day for females, from analogue subchronic and carcinogenicity studies.

Based on the toxicity data available on the notified chemical and suitable analogues, the notified chemical is not classifiable as hazardous under the *Globally Harmonized System of Classification and Labelling of Chemicals* (*GHS*) (United Nations, 2009), as adopted for industrial chemicals in Australia.

Public exposure and health risks

Exposure of the public to the notified chemical is expected to be very low when used as a component of inkjet printer cartridges. However, its use as an ingredient in cosmetics products has the potential for widespread and frequent public exposure. The public exposure is expected to occur at a significantly lower concentration (≤5%) than the level at which the notified chemical is likely to have adverse health effects. Based on the available information, the risk to the public associated with the use of the notified chemical in cosmetic products is considered to be low.

Occupational exposure and health risks

Occupational exposure during transport and warehousing is limited to accidental release from inkjet printer cartridge and cosmetic use. Reformulation of the notified chemical into cosmetics could result in a significant increase in worker exposure compared to its original use in finished inkjet printer cartridges. There is potential for dermal, ocular and inhalation exposure to the notified chemical (up to 91% concentration) during reformulation and associated activities at the blending sites. However, worker exposure is expected to be minimised through the use of automated processes and personal protective equipment (PPE). Considering the reported likely measures to reduce worker exposure and the relatively low toxicity of the notified chemical, the risk to workers from the reformulation of the notified chemical is considered to be low.

Environmental effects

Ecotoxicity data were not available in the original new chemical assessment and no new ecotoxicological studies were provided for the secondary notification assessment. The notified chemical is considered to be part of the polyglycoside surfactants group, and its environmental effects were predicted using the most toxic endpoints of the analogue chemical, ethyl glycoside fatty acid 6-O monoester (EGE) (C12). Based on the data for the analogue, the notified chemical is therefore considered to be harmful to aquatic life, with the predicted no-effect concentration (PNEC) calculated as 11 µg/L.

Although the notified chemical is considered to be harmful to aquatic life based on analogue data, in the absence of any measured ecotoxicity data for the chemical, it is not formally classified for acute or long-term hazards under the *GHS* Classification (United Nations, 2009).

No new environmental fate studies were submitted for the secondary notification assessment. Therefore, biodegradation was assessed using analogue data submitted for the new chemical assessment. On the basis of analogue data, the notified chemical is considered to be readily biodegradable. Based upon its ready biodegradation potential, relatively high molecular weight, and surface activity, the notified chemical is not considered to have a high potential to bioaccumulate.

Environmental exposure and risks

The notified chemical is imported as an ingredient in finished inkjet printer cartridges and cosmetics, and also for reformulation into cosmetics. No significant release of the chemical into the environment is expected during storage, transportation or reformulation. The majority of the notified chemical is expected to be released to sewers from cosmetic use, and also from recycling of paper printed with inkjet ink.

At sewage treatment plants, the notified chemical is expected to partition to sludge due to its surface activity. Based on the maximum import volume and assessed use pattern, the release of the chemical to

surface waters is not expected to reach ecotoxicologically significant quantities in the aquatic environment, with the total predicted environmental concentration (PEC) in river and ocean water calculated to be 1.02 µg/L and 0.102 µg/L, respectively.

On the basis of the PEC/PNEC ratio (0.093 for river and 0.0093 for ocean) and the assessed use pattern, the notified chemical is considered to pose a low risk to the environment.

Recommendations

This section provides the recommendations arising from the secondary notification assessment of the notified chemical, and incorporates the applicable recommendations from the new chemical assessment report.

Recommendations are directed principally at importers and reformulators of the notified chemical.

Recommendations to importers and state and territory governments

Control measures

Occupational controls

No specific engineering controls, work practices or personal protective equipment (PPE) are required for the safe use of the notified chemical in print cartridges or the reformulation of cosmetics. However, use of automated processes for transfer and mixing during reformulation are to be considered consistent with the principles of best practice to minimise occupational exposure. PPE should be selected on the basis of all ingredients in the formulation.

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

Environment

It is recommended that any direct release of the notified chemical to surface waters should be avoided.

Disposal

Where reuse or recycling of the containers containing the notified chemical are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant government legislation.

Storage

Containers should be securely closed and stored according to container label instructions.

Emergency procedures

Spills or accidental release of the notified chemical should be handled by adsorbing with inert adsorbent material

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 Act), an introducer (importer or manufacturer) of the notified chemical has post-assessment regulatory obligations to notify NICNAS when any of these circumstances change.

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

- Data or other relevant information on the dermal toxicity or dermal absorption of the notified chemical becomes available.
- Ecotoxicology data for the notified chemical becomes available.

or

(2) Under Section 64(2) of the Act; if

- The function or use of the chemical has changed from an ingredient of printer inks or cosmetics, or is likely to change significantly.
- The amount of chemical being introduced has increased, or is likely to increase, significantly.
- If 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.

Abbreviations and acronyms

AICS	Australian Inventory of Chemical Substances
ALT	alanine transaminase
bw	body weight
C	concentration
CAS	Chemical Abstracts Service
CAS RN	Chemical Abstracts Service Registry Number
°C	degrees Celsius
CIR	Cosmetic Ingredient Review
cm	centimetre
DA	dermal absorption
Director	Director of National Industrial Chemicals Notification and Assessment Scheme (NICNAS)
EC50	median effective concentration or half maximal effective concentration
EFSA	European Food Safety Authority
EGE	ethyl glycoside fatty acid 6-O monoester
FAO	Food and Agriculture Organization of the United Nations
g	gram
GHS	Globally Harmonized System of Classification and Labelling of Chemicals (United Nations)
GRAS	Generally Recognised as Safe
h	hour
hazard	inherent property of an agent or situation having the potential to cause adverse effects when an organism, system, or sub(population) is exposed to that agent; intrinsic property of a substance to cause harm
HET-CAM	Hen's egg test - chorio-allantoic membrane test
ICNA Act	Commonwealth *Industrial Chemicals (Notification and Assessment) Act 1989*
JECFA	Joint FAO/WHO Expert Committee on Food Additives
kg	kilogram
kPa	kilopascal
L	litre
LC50	median lethal concentration
m^2	metre squared
m^3	cubic metre
µg	microgram
mg	milligram
mg/kg bw	milligram per kilogram bodyweight

mg/kg bw/d	milligram per kilogram bodyweight per day
mL	millilitre
ML	megalitre
MOE	margin of exposure
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
pH	potential of hydrogen
PNEC	predicted no effect concentration
PPE	personal protective equipment
Q	risk quotient (Q=PEC/PNEC)
Qir	irritation potential
RF	retention factor
risk	probability or likelihood of harm and the likely extent of the harm; the probability of an adverse effect in an organism, system or (sub)population caused under specified circumstances by exposure to an agent
SCCS	Scientific Committee on Consumer Safety
SDS	Safety data sheet
STP	sewage treatment plant
TG	test guideline
US FDA	Food and Drug Administration (United States)
UVCB	(chemical of) Unknown or Variable Composition, complex reaction products or Biological material
w/w	weight to weight
WHO	World Health Organization

1. Introduction

1.1 Background

The notified chemical is a UVCB substance consisting of C18 mono, di, tri and poly esters of sucrose. This chemical was originally assessed by NICNAS for use in printing applications, with no reformulation occurring in Australia. Subsequently, NICNAS became aware of the following information that may affect the risk posed by the chemical to human health and the environment:

- use as an ingredient in cosmetics, resulting in a significant increase in exposure of the public to the notified chemical
- reformulation now occurring in Australia, using ingredients containing a relatively high concentration of the notified chemical, resulting in a significant increase in the exposure of workers to the notified chemical
- an estimated import volume of up to 1.5 tonnes/annum, which is 6 times the import volume (≤250 kg per annum) considered in the original assessment
- the cosmetic use will result in the disposal of the notified chemical into the aquatic environment and not landfill as in the original assessment. Therefore, the proposed use will also lead to a significant change in environmental exposure to the notified chemical.
- new human health data for the notified chemical were provided by an applicant following a gazette notice indicating a secondary notification for the chemical. NICNAS also identified relevant human health analogue data for use in this assessment.

Therefore, the proposed significant change in use circumstances as described above warrants a reassessment of the risks to human health and the environment posed by the notified chemical.

Data submitted for the original new chemical assessment on use, exposure and toxicity are summarised in this report in the relevant sections. New data submitted for this secondary notification assessment are discussed in detail and identified by the abbreviation **ND**.

1.2 Notice Requiring Secondary Notification

A notice was published in the Chemical Gazette of September 2016, requiring secondary notification of the notified chemical by specified persons, in accordance with Section 65(2) of the Act. The notice required the provision of any information relevant to assessment of the chemical that was not covered in the new chemical assessment and included the following:

1) identity, properties and uses
    a. trade names under which the chemical is marketed by the introducers
    b. proposed uses of the chemical, including:
        i. description of end-use products
        ii. concentration in end-use products
        iii. types of end uses including whether in leave on or rinse off products.
    c. amount of the chemical introduced annually
    d. details of reformulation, including:
        i. concentration of the chemical that is imported and in resulting end-use products
        ii. package sizes imported
        iii. description of the reformulation and repackaging process and disposal of wastes.
    e. composition data for the UVCB chemical

f. description of transportation and storage.

2) human health and environment data
    a. physico-chemical data available for the notified chemical
    b. toxicology data available for the notified chemical or suitable analogue(s)
    c. ecotoxicology data available for the notified chemical or suitable analogue(s).

1.3 Objectives

The objectives of this assessment are to review the new data made available since the publication of the new chemical assessment report and, where appropriate, to revise the original assessment to:

- re-assess the human health hazards associated with the notified chemical
- re-assess the environmental hazards associated with the notified chemical
- re-assess the risks of adverse effects resulting from exposure to workers, the general public and the environment from the new use of the notified chemical
- make appropriate recommendations (based on the above) to control exposures and/or reduce potential health risks for workers, the general public and the environment, as required.

1.4 Peer review

During all stages of preparation, this report has been subject to internal peer review within NICNAS.

1.5 Applicant

Following the notice of secondary notification for the notified chemical, four companies applied for assessment. Three applicants were introducers of the chemical and one applicant had information relevant to the chemical.

The applicants details are as follows:

Ingredients Plus Pty Ltd
Ground Floor, Unit 3 Parklands Estate, 13 South Street
Rydalmere NSW 2116 Australia

BASF Australia Ltd
PO Box 4705
Melbourne VIC 3001 Australia

Unilever Australia & New Zealand
219 North Rocks Road
North Rocks NSW 2151 Australia

Ceechem Australia Pty Ltd
PO Box 517
Riverwood NSW 2210 Australia

In accordance with the Act, NICNAS provided the applicants with a draft copy of the report for comments during the corrections/variations phase of the assessment.

1.6 Exempt information

No details are claimed exempt information.

2. Chemical identity, physical and chemical properties

2.1 Chemical identity

Chemical name: α-D-Glucopyranoside, β-D-fructofuranosyl, octadecanoate

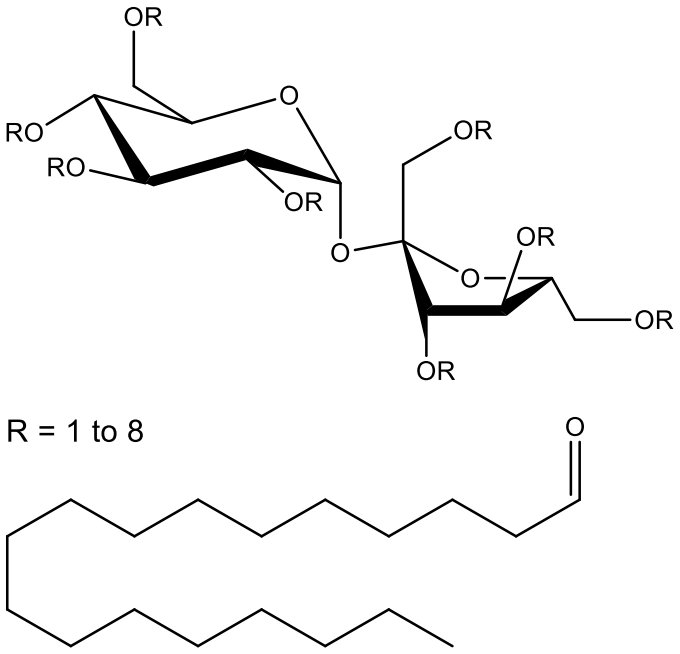
CAS number: 37318-31-3

Marketing name: Emulgade Sucro, Emulgade Sucro Plus, DK ESTER F-50, DK ESTER F-110, DK ESTER F-160, Sisterna SP-30C, Sisterna SP-50C, Sisterna SP-70C

Other names: Sucrose stearate, Sucrose octadecanoate

Molecular formula: $C_{18}H_{36}O_2.xC_{12}H_{22}O_{11}$

Structural formulae:



Molecular weight: Ranging from 608.76 for the monoester to 2473.99 for the octoester.

Analytical data: Analytical spectra were provided that confirm the identity and purity of the notified chemical.

2.2 Composition

CAS RN 37318-31-3 is a substance of unknown or variable composition (UVCB) consisting of one to eight 18-carbon octadecanoic (stearic) acids esterified to α-D-glucopyranoside, β-D-fructofuranosyl (sucrose).

The notified chemical is reported by one applicant as being produced overseas as a component of a reaction in which the composition of the product is approximately 51% esters of octadecanoic acid (C18, the notified chemical) and 49% hexadecanoic acid (C16). This notifier did not provide

information on the degree of esterification of the notified chemical or product specific composition of the notified.

The notified chemical is reported by another applicant as being a component of a substance produced overseas by transesterification of sucrose with stearic acid and palmitic acid derivatives.

The compositions of the products being introduced by the applicant are described below:

- DKS ESTER F50 and Sisterna SP-30C: Consists of 21-28% monostearate and 9-12% monopalmitate (monoesters), and approximately 60-70% of di, tri and poly esters of stearic and palmitic acid.
- DKS ESTER F110 and Sisterna SP-50C: Consists of 35% monostearate and 15% monopalmitate (monoesters), and approximately 50% of di, tri and poly esters of stearic and palmitic acid.
- DKS ESTER F160 and Sisterna SP-70C: Consists of 49% monostearate and 21% monopalmitate (monoesters), and approximately 30% of di, tri and poly esters of stearic and palmitic acid.

In the absence of complete information of the proportion of stearoyl versus palmoyl groups in the DKS ESTER/Sisterna mixed sucrose esters, it is conservatively assumed for the purposes of calculating the maximum purity (below) and import volume (Section 3) of the notified chemical, as well as rates of exposure (Section 4) and the risk characterisation (Section 6), that all di-, tri- and poly- esters are stearic acid esters. The product containing the greatest possible proportion of the notified chemical is DKS ESTER F50/Sisterna SP-30C, which contains a minimum of 9% sucrose monopalmitate and therefore a maximum of 91% mono, di, tri and poly sucrose stearate esters.

Degree of purity	≤91% (**ND**)
Impurities:	None identified

2.3 Physical and chemical properties

Relevant physical and chemical data of the notified chemical are shown in the table below.

Summary of the notified chemical's physical and chemical properties

Property	**Value**	**Data Source/Justification**
Appearance at 20ºC and 101.3 kPa	White waxy solid	Measured
Melting point	Between 40 and 70 °C	Measured
Boiling point	Not determined	Expected to decompose before boiling
Density	Between 0.80 and 1.2 at 16 °C	Measured
Vapour pressure	Not determined	Expected to have a low vapour pressure
Water solubility	< 0.1 g/L at pH 6.5	Company Technical Data Sheet
Hydrolysis as a function of pH	Not determined	Contains hydrolysable functional groups but significant hydrolysis is not expected at environmental pH range 4-9

Partition coefficient (n-octanol/water)	Not determined	The chemical is expected to be surface active and, therefore, is expected to accumulate at phase boundaries
Surface tension	Not determined	The chemical contains both hydrophilic and hydrophobic groups and, therefore, is expected to be surface active
Adsorption/desorption	Not determined	Expected to bind to soil based on its surfactant property
Dissociation constant	Not determined	Not expected to dissociate in the environmental pH range (4-9)
Particle size	Not determined	The chemical is not granular and is thus not suitable for analysis
Flash point	Between 200 and 300 °C	Measured
Autoignition temperature	Not determined	Expected to be high
Explosive properties	Not determined	Not estimated as explosive based on chemical structure

Comments on physical and chemical properties

Reactivity

The notified chemical is stable under normal conditions of use.

3. Importation and use

Information on the new use of the notified chemical provided for the secondary notification assessment is marked **ND**.

Importation

Existing use

The notified chemical was originally assessed for introduction into (Sydney) Australia as an ingredient comprising ≤0.1% of the ink in finished printer cartridges intended for use in inkjet printing. The capacity of the cartridges is <100 g. Cartridges are packed within sturdy shipment containers for transport by road. The chemical is not manufactured in Australia and reformulation does not occur in Australia.

*New use (**ND**)*

The chemical will now also be imported into Sydney either as an ingredient of finished cosmetic products at a concentration of ≤1%, or as a product used in the reformulation of cosmetics in which it is present at ≤91% **(ND).** The chemical will not be manufactured in Australia.

It is imported in finished cosmetic products in 50 g containers. When imported as part of a product for reformulation into cosmetics, the notified chemical is packaged in ≤25 kg containers. It will be transported by road to reformulators and stored at warehouses **(ND).**

Maximum introduction volumes (100%) over next 5 years:

Existing use

Year	*1*	*2*	*3*	*4*	*5*
Kg	≤250	≤250	≤250	≤250	≤250

*New use (**ND**)*

Year	*1*	*2*	*3*	*4*	*5*
Kg	1000-1500	1000-1500	1000-1500	1000-1500	1000-1500

Use

Existing use

The notified chemical continues to be imported as an ingredient of the ink used in sealed printer cartridges for inkjet printing.

*New use (**ND**)*

The chemical is used as an emulsifier in leave-on and rinse-off cosmetics. While one of the applicants reported importation of finished cosmetic products containing the notified chemical at ≤1%, two others will supply the chemical to third parties for reformulation into cosmetic products at between 0.5 and 5%. The total amount used as a cosmetic ingredient is approximately 6 times that used in inkjet printer cartridges.

4. Exposure

New information on the use of the chemical reported for the secondary notification assessment has significantly altered the public, occupational and environmental exposure that was originally assessed. Therefore, the public, occupational and environmental exposure sections have been updated from the new chemical assessment report. New information related to exposure of the notified chemical for the secondary notification assessment are marked **ND**.

4.1 Occupational exposure

4.1.1 Operational description

Existing use:
The notified chemical is imported as an ingredient of the ink in sealed printer cartridges designed for use in certain models of inkjet printing machines in the workplace and also by the general public.

*New use (**ND**)*
Finished cosmetic products containing the notified chemical and the chemical intended for reformulation will be transported by road to warehouse facilities for temporary storage until shipment to end users. Transportation and warehouse workers will only be exposed to the chemical in the case of accidental spills.

The chemical will be reformulated by third parties in batches using heating to emulsify the oil and water phases. The applicants reported that reformulation is expected to occur in a closed vessel and workers are expected to wear PPE during reformulation. The time taken to complete reformulation of a batch is estimated as 1 hour. No information was provided regarding transfer of the notified chemical into reformulation vessels and packaging of the reformulated materials into cosmetic products.

Finished cosmetic products containing the notified chemical will be distributed for sale to both businesses and the general public.

4.1.2 Estimates of occupational exposure

Existing use:
Dermal and ocular exposure to the notified chemical is possible for workers in the supply and use chain for inkjet printer cartridges, such as: transport and storage workers; service technicians; engineers; printer operators; and commercial and retail suppliers. Inhalation exposure from printer cartridges and printing is expected to be negligible due to low vapour pressure of the notified chemical, enclosed nature of the printer cartridges and print machines, and workplace ventilation.

The most widespread, albeit extremely minor, exposure is expected in printer operators (>1000 workers). Service technicians and engineers have the potential for the highest exposure of up to 8 hours daily for 200 days/annum, although the likelihood of such an exposure is expected to be extremely low. Worker exposure is unlikely in other scenarios except in the case of an accident where the cartridges are damaged and the contents are exposed.

*New use (**ND**)*
Although the information provided by the applicants for secondary notification assessments of the notified chemical does not allow for the detailed estimation of duration and frequency of worker exposure, the maximum potential exposure of workers to the chemical has been reported to be 12 hours/day on 240 days/annum. Transportation and warehouse workers may be exposed to the notified chemical at a concentration of up to 91% in the case of an accidental spill. However, the likelihood of such an event is expected to be low.

Exposure is also expected to be low during reformulation as reformulation is expected to occur within

closed vessels and workers are expected to wear PPE during reformulation. No information was provided on the mode of transfer of the chemicals into the closed vessel for mixing, as applicants are not involved in the reformulation process. If it is a manual process, then potential exposure may occur during the transfer. If automated, then exposure is likely to be minimal.

4.2 Public exposure

Existing use:

The public may be occasionally exposed to the notified chemical at ≤0.1% of the ink in finished printer cartridges during its use and replacement. However, the exposure of the public from the use of printer ink cartridges containing the notified chemical will be low as the chemical is present at very low concentrations in sealed ink cartridges and it is expected to remain bound to the substrate.

*New use (**ND**):*

Public exposure has the potential to be widespread and frequent through the daily use of cosmetics containing the notified chemical at a concentration of up to 5%.The primary route of exposure is expected to be dermal, although ocular and oral exposure is also possible. As the notified chemical is not proposed to be used in spray products, inhalation exposure is not anticipated.

Data on the typical use patterns of cosmetics containing the notified chemical identified during secondary notification are shown in the table below. They are based upon guidance provided by the European Commission (SCCS, 2016). The use patterns of cosmetics in Australia and Europe are assumed to be similar for the purposes of assessing dermal exposure. Dermal absorption (DA) of 100% of the notified chemical is assumed on the basis of the chemical's physicochemical properties. A lifetime average female body weight (bw) of 64 kg and the maximum reported concentration of the chemical in the product (5%) were used for the calculations below.

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Hand wash soap	20000	5	0.01	0.156
Hair conditioner	3920	5	0.01	0.031
Hair styling products	4000	5	0.1	0.313
Body lotion	7820	5	1	6.109
Face cream	1540	5	1	1.203
Hand cream	2160	5	1	1.688
Liquid foundation	510	5	1	0.398
Make-up remover	5000	5	0.1	0.391
Total				10.289

C = concentration of the notified chemical
RF = retention factor (unit-less)
Daily systemic exposure = (Amount × C × RF × DA)/bw

The worst case scenario estimation using these assumptions is for a person who uses all products listed in the above table that contain the notified chemical. This would result in a combined internal dose of 10.289 mg/kg bw/day.

4.3 Environmental exposure

4.3.1 Releases

Release of chemical at site

The notified chemical will be imported into Australia as a component of raw material for reformulation into cosmetic products, in addition to the use as an ingredient in finished ink cartridges as reported in the original new chemical assessment.

As no reformulation of the chemical occurs for its use in inkjet ink cartridges, it is not expected to be released into the environment.

There is unlikely to be any significant release to the environment from transport and storage during either use in ink cartridges or in cosmetic products, except in the case of accidental spills and leaks. In the event of spills, the product containing the chemical is expected to be collected with adsorbents, and disposed of to landfill in accordance with local government regulations.

The chemical will be reformulated locally to prepare cosmetic products. The reformulation process is a batch production involving heating, and is expected to occur within a fully enclosed environment. Therefore, significant release of the chemical to the environment is not expected.

Wastes containing the notified chemical generated during reformulation include equipment wash water, empty import containers and spilt materials. Wastes may be collected and released to sewers in a worst case scenario, or disposed of to landfill in accordance with local government regulations. The applicants have not provided any information regarding packaging processes.

Release of chemical from use

Release from ink products: Release of ink containing the notified chemical to the environment is not expected under normal conditions of use. Ink cartridges are designed to prevent leakage and will not be opened during use, installation or replacement. In the unlikely case of spills arising during installation and replacement, it is expected that the ink containing the chemical will be contained and collected with absorbent material and be subsequently disposed of to landfill.

Release from cosmetic products: All of the notified chemical is assumed to be released to the aquatic compartment through sewers during its use as a cosmetic.

Release of chemical from disposal

Release from ink products: Following its use in printer ink, the notified chemical is anticipated to be disposed of to landfill or subjected to paper recycling processes. Up to half of the printed paper is expected to be recycled. Therefore, 50% of the notified chemical used in ink products is expected to be released to sewage treatment plants (STPs) during these processes.

The used cartridges are expected to be collected for reuse, recycling or be disposed directly to landfill. The ink residues separated from the recycled cartridges are expected to be disposed of under relevant local regulations. Residual ink remaining in the used ink cartridges is expected to be disposed of to landfill along with the used items if the used ink cartridges are not reused or recycled.

Release from cosmetic products: A small proportion of the notified chemical may remain in end-use containers once the consumer products are used up. Wastes and residues of the chemical in empty containers are likely either to share the fate of the containers and be disposed of to landfill, or to be released to sewer when containers are rinsed before recycling through an approved waste management facility.

For the purposes of the environmental risk assessment, it is assumed that all of the imported chemical for cosmetic uses is released to sewer at end use, and Section 4.3.3 below provides a detailed estimation of the release of the notified chemical into the environment.

4.3.2 Fate

No new environmental fate studies were submitted for this secondary notification assessment and, therefore, biodegradation was assessed using analogue data submitted in the new chemical assessment. Based on the results of a ready biodegradability study on an analogue, α-D-glucopyranoside, β-D-fructofuranosyl, monohexadecanoate (CAS RN 26446-38-8), indicating 98% biodegradation in 7 days, the notified chemical is considered to be readily biodegradable.

Half the amount of the chemical used in ink products is expected to be released to sewer from paper recycling processes, with the other half being disposed of to landfill along with the used paper. During

the paper recycling process, waste paper is repulped using a variety of chemical treatments that result in fibre separation and ink detachment from the fibres. The waste water is expected to go to sewers.

Following use in cosmetic products, all of the notified chemical is expected to enter sewer systems before potential release to surface waters on a nationwide basis.

Based on its surface activity, most of the notified chemical is expected to adsorb to suspended matter or sludge at wastewater treatment plants when it enters sewer systems. Any chemical that remains in treated waste water and then enters receiving waters is expected to rapidly biodegrade.

Sludge containing the chemical may be applied to agricultural soils or be disposed of to landfill as waste. In soil or land, the chemical is not expected to be mobile based on its low water solubility and surface activity.

The notified chemical is not expected to have a high potential to bioaccumulate based on its ready biodegradation, relatively high molecular weight and surface activity. In water, soil or landfill, the chemical is expected to degrade through biotic and abiotic processes to form water and oxides of carbon.

4.3.3 Predicted environmental concentration (PEC)

Predicted Environmental Concentration (PEC) from use in ink products

Up to 250 kg of the notified chemical is reported to be introduced annually in ink products. Based on the environmental release information discussed above, the predicted environmental concentration (PEC) has been calculated by assuming that 50% of the notified chemical used in ink products will be released to sewer from the paper recycling process.

For the worst case scenario, it is assumed that no removal of the notified chemical occurs during sewage treatment processes. The nationwide release is assumed to be over 260 working days per year. The calculation is summarised in the table below:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment from ink use	
Total Annual Import/Manufactured Volume	250 kg/year
Proportion expected to be released to sewer	50%
Annual quantity of chemical released to sewer	125 kg/year
Days per year where release occurs	260 days/year
Daily chemical release	0.48 kg/day
Water use	200.0 L/person/day
Population of Australia (Millions)	22.613 million
Removal within STP	0% mitigation
Daily effluent production	4,523 ML
Dilution Factor - River	1.0
Dilution Factor - Ocean	10.0
PEC - River	0.11 µg/L
PEC - Ocean	0.01 µg/L

Predicted Environmental Concentration (PEC) from use in cosmetic products

The amount of notified chemical introduced in cosmetic products is reported to be 1,500 kg (1.5 tonnes) per year. For the cosmetic use pattern, the predicted environmental concentration (PEC) has been calculated by assuming a worst case scenario of 100% release of the notified chemical into sewer systems with none removed by sewage treatment processes. The release is assumed to be nationwide, over 365 days per year.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment	
Total Annual Import/Manufactured Volume	1,500 kg/year
Proportion expected to be released to sewer	100%
Annual quantity of chemical released to sewer	1,500 kg/year
Days per year where release occurs	365 days/year
Daily chemical release	4.11 kg/day
Water use	200.0 L/person/day
Population of Australia (Millions)	22.613 million
Removal within STP	0% Mitigation
Daily effluent production	4,523 ML
Dilution Factor - River	1.0
Dilution Factor - Ocean	10.0
PEC - River:	0.91 µg/L
PEC - Ocean:	0.091 µg/L

Combined Predicted Environmental Concentration (PEC) from both ink and cosmetic uses

Based on the above calculations, the total predicted environmental concentration (PEC) in river and ocean water are calculated to be:

$PEC_{river,\ total} = 0.11 + 0.91 = 1.02$ µg/L

$PEC_{ocean,\ total} = 0.011 + 0.091 = 0.102$ µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified 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 1.02 µg/L may potentially result in a soil concentration of approximately 6.8 µg/kg per year.

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 34 µg/kg and 68 µg/kg, respectively.

5. Hazard assessment

5.1 Physicochemical and human health hazard assessment

This section contains a summary of all of the data relevant to the physicochemical and human health hazard assessment of the notified chemical. No new studies relevant to the physiochemical hazards of the chemical were submitted for the secondary notification assessment. Therefore, the physicochemical hazard assessment is based upon information from the new chemical assessment report. The robust summaries of the new human health studies on the notified chemical submitted for the secondary notification assessment are summarised in this section and designated as **ND**.

5.1.1 Physicochemical effects assessment

Based upon the available physicochemical data, the notified chemical is not recommended for hazard classification according to the *GHS (United Nations, 2009)*, as adopted for industrial chemicals in Australia.

5.1.2 Human health effects assessment

No data were provided for the original new chemical human health effects assessment of the notified chemical. This secondary notification assessment uses relevant toxicological studies of both the chemical submitted for secondary notification assessment and appropriate analogues identified by NICNAS. The following table summarises these results, which are also all denoted as **ND**.

Endpoint	Result	Test Chemical
Rodent, acute oral	LD50 >20,000 mg/kg bw,	Analogue (sucrose monostearate, stearic acid)
Human skin irritation and skin sensitisation - RIPT (17%)	No evidence of irritation or sensitisation	Notified chemical
Eye irritation (in vitro) (HET-CAM Assay)	Not irritating	Notified chemical
Rat repeated dose oral (dietary, fed as 5%), 2 years	NOAEL = 1970 mg/kg bw/day	Analogue (S-570)
Genotoxicity - bacterial reverse mutation	Not genotoxic	Notified chemical
Carcinogenicity - feeding studies	Not carcinogenic	Analogue (S-570)

Use of analogue data in the human health effects assessment

Toxicological studies were not available for all relevant endpoints of the notified chemical. As a result, available data from appropriate analogues identified by NICNAS were used to support human health hazard conclusions.

The notified chemical, sucrose stearate, is expected to be hydrolysed to sucrose and stearic acid when ingested, which are then absorbed by the gastrointestinal tract. Therefore, for endpoints determined by oral dosing, sucrose, stearic acid and sucrose esters in which stearic acid is the major acid component of the esters were considered as appropriate analogues.

Substances with sufficient structural similarity to the notified chemical were considered as appropriate analogues for non-orally dosed endpoints if:

- the substance consists of sucrose esterified to one or more fatty acids

- the chain length of the fatty acid is between 16 and 20 carbons, noting that stearic acid is 18 carbons
- the fatty acid chain may or may not contain double bonds, noting that stearic acid does not contain double bonds.

Information originating from studies of the analogues listed in the table below was used as part of the human health effects assessment of the notified chemical.

Analogue	**Description**	**Endpoint**
Stearic acid CAS RN 57-11-4	Chemical formed from the hydrolysis of the notified chemical.	Acute oral toxicity, Repeat dose oral toxicity, Carcinogenicity
P-1670 CAS RN 26446-38-8	Sucrose esters of primarily palmitic acid consisting of approximately 80, 17 and 3% of mono, di and tri esters respectively.	Dermal penetration, skin irritation
S-570* CAS RN 27195-16-0	Sucrose esters of fatty acids consisting of 29, 35, 25 and 11% of mono, di, tri and poly esters respectively, and a fatty acid composition of approximately 70% stearic acid, 30% palmitic acid and small amounts of oleic acid.	Repeat dose oral toxicity, Carcinogenicity
S-970* CAS RN 37318-31-3	Sucrose esters of primarily stearic acid consisting of approximately 48, 34 and 14% of mono, di and tri esters respectively.	Dermal penetration, skin irritation
S-1170 * CAS RN 37318-31-3	Sucrose esters of fatty acids consisting of 57, 28, 10 and 1% of mono, di, tri and poly esters respectively, and a fatty acid composition of 70% stearic acid and 30% palmitic acid.	Toxicokinetics
Sucrose oleate CAS RN 52683-61-1	Sucrose esterified to between 1 and 8 oleic acids (18:1), which may also include esters of fatty acids other than oleic acid.	Dermal penetration
Sucrose monostearate* CAS RN 25168-73-4	Sucrose esterified to an average of one molecule of stearic acid, which may also contain esters with more than one fatty acid, and fatty acid chains other than stearic acid.	Toxicokinetics, acute oral toxicity, repeat dose oral toxicity
Sucrose distearate* CAS RN 27195-16-0	Sucrose esterified to an average of two molecules of stearic acid, which may also contain esters with more or less than two fatty acids, and fatty acid chains other than stearic acid.	Toxicokinetics
Mixed sucrose esters of stearic and palmitic acids*	Sucrose esters of fatty acids containing primarily esters of stearic and palmitic acid, whereby individual sucrose molecules are esterified to both stearic and palmitic acids.	Repeat dose oral toxicity

Note: A number of the analogues identified contain chemical entities that are chemically identical to some of the chemical entities comprising the notified UVCB chemical. For these analogues, a significant portion of the substance consists of sucrose esterified to one or more stearic acid molecules, and are denoted in the table above with the symbol (*). For example, the notified chemical and the analogues S-570, S-970, S-1170, sucrose monostearate and mixed sucrose esters of stearic and palmitic acids are all expected to contain CAS RN 13039-42-4 as a component, which consists of a single stearic acid esterified to a specific position on the sucrose molecule. The significant overlap in chemical composition is also

reflected by the fact that two of the analogues identified for the assessment (S-970 and S-1170) are also most appropriately described by the CAS descriptor used for the notified chemical, CAS RN 37318-31-3.

Toxicokinetics

Data from analogues were used to assess the toxicokinetics of the notified chemical.

The pattern of radioisotope excretion from rats orally administered ^{14}C labelled S-1170 indicated that sucrose stearate and sucrose palmitate are hydrolysed to sucrose and fatty acid prior to absorption by the gastrointestinal tract (Shigeoka et al, 1984).

In human volunteers who consumed either 1-3 g in a single dose or 2 g twice a day for 5 days of S-1170, the rate of hydrolysis of the ingested sucrose esters was estimated to be between 70-80% (JECFA, 1996).

Radiolabelled (^{14}C) sucrose monostearate or sucrose distearate was administered orally to rats as a single dose of 100 mg/kg bw. Radioisotope in the blood peaked at 3 hours and was cleared in a biphasic fashion, with elimination from the body occurring primarily through the faeces and expired air.

At 24 hours after oral administration of ^{14}C labelled sucrose monostearate or sucrose distearate, the majority of the radioisotope was present in the liver, followed by skin, muscle, white adipose tissue, blood and kidney. At 168 hours, remaining radioisotope from sucrose monostearate was present in white adipose tissue (6.11%), muscle (4.97%), skin (2.66%), liver (0.42%), kidney (0.18%) and pancreas (0.16%), with radioisotope from sucrose distearate present in white adipose tissue (2.87%), muscle (2.31%), skin (1.57%), liver (0.25%) and pancreas (0.09%) (EFSA, 2004).

Sucrose monostearate injected intravenously at 1 mg/kg bw was undetectable in the plasma 24 hours after injection. Following intraperitoneal injection of up to 100 mg/kg bw of radiolabelled sodium tallowate, 80% of the radioisotope was excreted 19 hours after the injection (EFSA, 2004; Daniel et al, 1979). This suggests that intact sucrose esters of fatty acids and sucroglycerides are rapidly cleared from the body.

Based on the above data, the notified chemical is expected to be predominantly hydrolysed to sucrose and fatty acid in the gastrointestinal tract following ingestion, and then absorbed, metabolised and excreted in the same fashion as dietary sucrose and fatty acids. Any intact non-hydrolysed notified chemical present in the body is also expected to be rapidly cleared.

Dermal penetration

Various formulations containing sucrose esters of fatty acids (C16-C18 chain length), including S-970, P-1670 and sucrose oleate, have been shown to enhance the dermal penetration of drugs such as progesterone, aceclofenac and 4-hydroxy benzonitrile (Ayala-Bravo et al, 2003; Klang et al, 2010; Isailovic et al, 2016; CIR, 2016).

Based upon analogue data, the notified chemical is expected to enhance the dermal absorption of other chemicals.

Acute toxicity

Data from analogues were used to assess the acute oral toxicity of the notified chemical.

Oral doses of 20,000 mg/kg bw sucrose monostearate administered to rats or mice in 10 equal doses with intervals of up to an hour did not did not lead to death in any of the dosed animals (JECFA, 1974).

A number of acute oral toxicity studies in various strains of rats are described for the analogue stearic acid (CIR, 1987). Upon oral administration, deaths occurred in 40% of rats in one study at 4,640 mg/kg bw, 10-20% of rats in two studies at 5,000 mg/kg bw, 20% of rats in two studies at 10,000 mg/kg bw, and 10% of rats in one study at 15,000 mg/kg bw. No deaths occurred in a number of other studies in which animals were dosed at up to 15,000 mg/kg bw. Transient toxic effects were observed in rats at doses of 4,640 and 10,000 mg/kg bw, and were characterised by slight depression, depressed righting and placement reflexes, oily and unkempt fur, diarrhoea, excess salivation, and discharge from the nose and eyes.

Based upon the available information, the notified chemical is expected to have very low acute oral toxicity.

No dermal toxicity data are available for either the notified chemical or analogues. While metabolism may differ when administered either orally or dermally, the Generally Recognised as Safe (GRAS) notifications for various sucrose esters of fatty acids suggest low dermal toxicity. Further, sucrose acetate isobutyrate has low acute dermal toxicity and glycerol fatty acid esters (glycerides) have low acute subcutaneous toxicity; these substances share structural similarity with the notified chemical (CIR, 2001; CIR, 2016). Considering the evidence available for substances with similar chemistry, the notified chemical is expected to have low acute dermal toxicity.

Skin irritation and skin sensitisation

A human repeat insult patch test with the notified chemical was submitted for secondary notification.

Skin sensitisation - human volunteers

TEST SUBSTANCE	The notified chemical is present at 34% in the undiluted product, and the product is diluted with vehicle to give a final concentration for the notified chemical of 17%.
METHOD	Repeated insult patch test with challenge – In-house method.
Study Design	Induction Procedure: Patches containing 0.2 mL test substance were applied 3 times/week for a total of 9 applications. Patches were removed after 24 h of each application and the test sites were evaluated prior to each re-application. Rest Period: approximately 2 weeks Challenge Procedure: A challenge patch was applied to a naïve site adjacent to the original induction site. The patch was removed after 24 h and the site was evaluated 24 h and 72 h post-application.
Study Group	112 subjects, male and female; 104 subjects completed the test Age group: 16-78 years
Vehicle	Cetiol CC
Remarks - Method	Occluded. The test substance was spread on a 1.9 cm × 1.9 cm absorbent pad portion of an adhesive dressing. Not a validated method.
RESULTS	
Remarks - Results	Eight (8) subjects discontinued participation for non-test substance related reasons. There was no evidence of irritation during the study in any test subject.
CONCLUSION	The test substance was non-sensitising and non-irritating under the conditions of the test.
TEST FACILITY	Consumer Product Testing (2004)

The data submitted indicate that, at a concentration of 17%, the notified chemical does not cause skin irritation or skin sensitisation.

Nanoemulsions containing up to 1% S-970 and 2% P-1670 were not irritating to the skin following a 24 hour occluded application, as determined by the erythema index (Isailovic et al, 2016).

Based upon the available information, the notified chemical is not expected to be a skin irritant or skin sensitiser at concentrations up to 17%.

Eye irritation

An in vitro eye irritation study on the notified chemical using the HET-CAM model was submitted for secondary notification.

In vitro Eye Irritation Test

TEST SUBSTANCE	The notified chemical is present at 34% in the undiluted product, and the product is diluted with the vehicle to give a final concentration for the chemical of 23%.
METHOD	Hen's egg test - chorio-allantoic membrane (HET-CAM) test: End Point Method
Vehicle	Cetiol CC, present in test substance at 32%
Remarks - Method	Not a validated method.
RESULTS	
Test material	Qir is the irritation potential expressed as the sum of irritation scores for 6 eggs. A semiquantitative score of 0 (none), 1 (weak), 2 (moderate), or 3 (strong) is assigned to haemorrhage, lysis and protein coagulation reactions.
Test substance	Qir = 0 (not irritant)
Positive control	Qir = 12 (moderately irritant)
Remarks - Results	The notified chemical did not exhibit eye irritation potential under the conditions of the test.
CONCLUSION	According to the classification criteria provided in the study report, the test substance is not irritating.
TEST FACILITY	Institute Dr. Schrader (2004)

The submitted data indicate that, at a concentration of 23%, the notified chemical is not irritating to the eyes.

Based upon the available information, the notified chemical is not expected to be an eye irritant at concentrations up to 23%.

Repeated dose oral toxicity

A number of repeat dose studies using analogues of the notified chemical have been described in assessments conducted by:

- the Joint FAO/WHO Expert Committee on Food Additives (JECFA)
- the European Food Safety Authority (EFSA)

- the Cosmetic Ingredient Review (CIR)
- GRAS submissions to the U.S. Food and Drug Administration (US FDA).

Relevant studies from these assessments are discussed below.

Analogue S-570

Analogue S-570 was administered to Fischer 344/DuCrj rats at 1, 3 or 5% of the diet in a 13 week subchronic study (Takeda and Flood, 2002).

As no significant effects were noted, the NOAEL for this study was the highest concentration tested, 5%. This corresponds to 1970 mg/kg bw/day in males and 2440 mg/kg bw/day in females.

Sucrose esters of fatty acids and sucroglycerides

Rats were orally dosed daily with sucrose monostearate up to 2000 mg/kg bw/day for 60 days without adverse effects on weight gain or organ weights.

Daily oral dosing of rats with mixed sucrose esters of stearic and palmitic acid up to 6000 mg/kg bw/day did not affect weight gain and no pathology was evident in any of the organs examined.

No effects were observed on growth rate, food intake, organ weights or haematological parameters in mice fed a diet containing up to 3% of mixed sucrose esters of stearic and palmitic acids for 76 weeks.

No dogs died when fed a diet of up to 3% mixed sucrose esters of stearic and palmitic acid for 26 weeks. Body weight, food and water intake, clinical chemistry, haematological parameters and urinalysis remained within the normal range (JECFA, 1974; JECFA, 1990).

Stearic acid

A report on stearic acid describes studies in which animals were maintained on diets containing the fatty acid. Adverse health effects occurred in a number of these studies, including abnormal blood clotting, hyperlipidaemia, atherosclerosis, pathology in various organs and death (CIR, 1987). However, the diets described are relatively high in fat, and high fat diets are known to be associated with numerous adverse health effects (Panchal and Brown, 2011). Therefore, it is unclear whether direct toxic effects of stearic acid contributed to the pathology observed in these studies.

Repeated dose dermal toxicity

There are no data available for repeated dose toxicity via the dermal route for either the notified chemical or a suitable analogue. Similar to acute dermal toxicity, the 'Generally Recognised as Safe' (GRAS) status of the notified chemical also suggests low repeated dose dermal toxicity.

Genotoxicity

A bacterial reverse mutation assay on the chemical was submitted for the secondary notification assessment.

TEST SUBSTANCE	Notified chemical (34% final concentration in a mixture with other ingredients of the product tested)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation (Test 1) and pre-incubation (Test 2) procedures
Species/Strain	*S. typhimurium*: TA 1535, TA 1537, TA 98, TA 100, TA 102
Metabolic Activation System	S9 fractions from phenobarbitone/ β-naphthoflavone induced rat liver

Concentration Range in Main Test	33, 100, 333, 1000, 2500 and 5000 µg/plate (with/without metabolic activation)
Vehicle	Tetrahydrofuran
Remarks - Method	A preliminary toxicity test (3-5000 µg/plate) was performed using the strains TA 98 and TA 100 to determine the toxicity of the test material. No toxicity was observed and the results were incorporated into Test 1. The test material formulations and vehicle control were dosed by the plate incorporation and pre-incubation methods. This procedure was repeated, in triplicate, for each bacterial strain and for each concentration of test material both with and without S9-mix. The positive and untreated controls were dosed using the plate incorporation and pre-incubation methods.

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	≥ 2500	Negative
Test 2	N/A	≥ 2500	≥ 1000	Negative
Present				
Test 1	> 5000	≥ 5000	≥ 1000	Negative
Test 2	N/A	≥ 2500	≥ 1000	Negative
Remarks - Results	No change in growth of the background bacterial lawn was evident at a concentration of up to 5000 µg/plate and regardless of metabolic activation. A minor toxic effect (reduction in the number of revertants) was observed in TA 98 at 5000 µg/plate (Test 2 with metabolic activation), and in TA 102 at 5000 µg/plate (Test 1 with and without metabolic activation), and at 2500 and 5000 µg/plate (Test 2 with and without metabolic activation). The test substance precipitated in the overlay agar at 2500 µg/plate in Test 1 without metabolic activation, and under all other experimental conditions at 1000 µg/plate. The precipitate had no effect on the recording of data. The test substance did not cause a marked increase in the number of revertants per plate of any of the tester strains either in the presence or absence of S9. Negative controls were within historical limits. Positive controls confirmed the sensitivity of the test system.			
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.			
TEST FACILITY	RCC (2004)			

The notified chemical was negative in the bacterial reverse mutation assay and the chemical is not expected to be genotoxic.

Carcinogenicity

In a carcinogenicity study, Fischer 344/DuCrj rats were maintained on a control diet or diets containing 1, 3 or 5% (w/w) of the analogue S-570. There was no difference in the survival rate between the treated and control animals. The incidence of tumours observed in this study was within the historical range expected for this strain of rat. Tumour incidence and the time taken for tumours to develop also did not significantly differ between the control and treatment groups (Takeda and Flood, 2002).

In another study, female CH3 mice were fed diets supplemented with stearic acid and the incidence of spontaneous mammary tumours examined. Increasing levels of this fatty acid correlated with a decrease in tumour incidence and an increased time for development of tumours (Tinsley et al, 1981).

There is no evidence of carcinogenicity in the studies described above. Therefore the chemical is not considered to be carcinogenic.

Selection of NOAEL

A NOAEL of 1970 mg/kg bw/day in male rats and 2440 mg/kg bw/day in females were identified from the subchronic and carcinogenicity studies using the analogue S-570, for quantitative risk assessment purposes.

5.1.3 Hazard classification

Based on the available information the notified chemical is not classified as hazardous according to the *GHS (United Nations, 2009)*, as adopted for industrial chemicals in Australia.

5.2 Environmental hazard assessment

Ecotoxicity data were not submitted, either for the assessment of the notified chemical as a new chemical, or for this secondary assessment. Therefore, the environmental effects of the notified chemical are conservatively predicted using the most toxic endpoints reported for an acceptable analogue chemical, ethyl glycoside fatty acid 6-O monoester (EGE) (C12), as part of the alkyl polyglycoside surfactants group (Madsen et al. (2001, p 65)). The ecotoxicity results are summarised in the table below.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LC50 (96 h) = 11-17 mg/L	Predicted to be harmful to fish
Daphnia Toxicity	EC50 (48 h) = 21-25 mg/L	Predicted to be harmful to aquatic invertebrates
Algal Toxicity	EC50 (72 h) = 37-38 mg/L	Predicted to be harmful to algae
Algal Toxicity	NOEC (72 h) = 11 mg/L	Not classified for long term hazard

The notified chemical and the analogue chemical, EGE, can be considered as belonging to the polyglycoside surfactants group based on their structures and functional groups. Therefore, the ecotoxicological endpoints measured for the analogue chemical are considered acceptable for the purpose of regulatory risk assessment.

However, as the toxicity of these surfactants is expected to vary with surfactant tail length and structure, these endpoints are not expected to be entirely representative for the purposes of classification under the *GHS (United Nations, 2009)*. Thus, the notified chemical is not classified under the *GHS* for acute or long-term aquatic hazards (United Nations, 2009).

5.2.2 Predicted no-effect concentration

The predicted no-effect concentration (PNEC) is calculated from the most toxic endpoint of fish determined for the analogue. An assessment factor of 1000 is used as there are no measured data for the notified chemical and analogue data are used instead.

PNEC for the Aquatic Compartment		
NOEC (Fish, 96h)	11	mg/L
Assessment Factor	1,000	
PNEC	11	µg/L

5.2.3 Hazard classification

The notified chemical is not classified for short and long term hazard under the *GHS (United Nations, 2009)* as no measured endpoints were available.

6. Risk characterisation

6.1 Public health risk characterisation

Frequent and widespread public exposure to the notified chemical is likely through the use of cosmetics containing the chemical at a concentration of up to 5%. There will be negligible exposure to the public through the use of the chemical in inkjet printer inks.

The potential systemic exposure to the public from the use of the notified chemical in cosmetic products was estimated to be a maximum of 10 mg/kg bw/day, as a worst case scenario based upon a dermal absorption of 100%. Using a NOAEL of 1970 mg/kg bw/day in male from a subchronic and a 2 year oral feeding study with an analogue (S-570), the margin of exposure (MOE) was estimated to be 197. An MOE of 244 was calculated with the NOAEL in female rats from this study of 2440 mg/kg bw/day. A MOE greater than or equal to 100 (to account for intra- and inter-species differences) is considered acceptable.

Upon ingestion, the majority of the notified chemical is hydrolysed to sucrose and stearic acid prior to absorption, and very little of the chemical is absorbed intact in the gastrointestinal tract. Therefore, since the NOAEL used in the MOE calculation was derived from an orally dosed study, the calculated MOE may be an overestimation given the main absorption route in the public will be dermal. It is also noted that, while the public may use multiple cosmetics containing the notified chemical on a daily basis, the exposure estimate is conservative; as it assumes a dermal absorption of 100%.

The notified chemical has the potential to enhance dermal absorption of other chemicals on the basis of its surfactant activity and supporting analogue data. With cosmetic use, the notified chemical is mixed with other chemicals and purposely applied to the skin. Therefore, there is the possibility of potentiating the biological effect of other chemicals through increasing uptake and concentration within the body.

Based on the available information, the risk to the public associated with the use of the notified chemical at ≤5% in cosmetic products is considered to be low.

6.2 Occupational health risk characterisation

Workers may be exposed to the notified chemical at a concentration of up to 91% during reformulation. The use of enclosed automated processes and PPE should minimise the potential for exposure. Based upon the expected control measures in place to minimise worker exposure and the overall low toxicity of the notified chemical, the risk to workers from the use of the notified chemical is considered to be low.

6.3 Environmental risk characterisation

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the predicted PEC and PNEC. The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment (0.093 to river and 0.0093 to ocean) indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters. This is based on its maximum annual importation quantity. The notified chemical is expected to be readily biodegradable, and is expected to have a low potential for bioaccumulation.

On the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic and inkjet printing products, the notified chemical is expected to pose a low risk to the environment at the maximum annual importation quantity.

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	**PEC/PNEC**
River:	1.02	11	0.093
Ocean:	0.102	11	0.0093

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