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May 2019

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Poly(oxy-1,2-ethanediyl), α-sulfo-ω-hydroxy-, C_{12-16}-alkyl ethers, zinc salts

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

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1620	Pierre Fabre Australia Pty Ltd	Poly(oxy-1,2-ethanediyl), α-sulfo-ω-hydroxy-, C_{12-16}-alkyl ethers, zinc salts	Yes	≤ 10 tonnes per annum	Cosmetic ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Skin corrosion/irritation (Category 2)	H315 – Causes skin irritation
Serious eye damage/eye irritation (Category 2A)	H319 – Causes serious eye irritation

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 and the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Skin corrosion/irritation (Category 2): H315 – Causes skin irritation
  - Serious eye damage/eye irritation (Category 2A): H319 – Causes serious eye irritation

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

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

- 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 contact with skin and eyes

- 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:
  - Safety glasses
  - Impervious gloves
  - Coveralls

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

- A copy of the 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.

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.

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
  - toxicological and ecotoxicological information becomes available for the notified chemical;
  - the concentration of the notified chemical in cosmetic products exceeds, or is intended to exceed 10%;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a cosmetic 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 and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Pierre Fabre Australia Pty Ltd (ABN: 30 098 999 850)
Suite 901, 1 Elizabeth Plaza
NORTH SYDNEY NSW 2060

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physico-chemical endpoints, acute toxicity, repeated dose toxicity, genotoxicity and bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Zetesol ZN

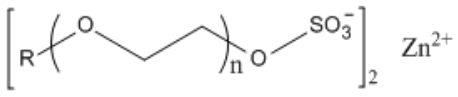
CAS NUMBER
224175-26-2

CHEMICAL NAME
Poly(oxy-1,2-ethanediyl), α-sulfo-ω-hydroxy-, C_{12-16}-alkyl ethers, zinc salts

OTHER NAME(S)
Zinc Coceth Sulfate (INCI name)

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



R = C12-16 alkyl

n = 3 (average)

MOLECULAR WEIGHT
860.48 Da (R = C_{12} and n = 3)
972.7 Da (R = C_{16} and n = 3)

ANALYTICAL DATA
Reference IR spectrum was provided.

3. COMPOSITION

DEGREE OF PURITY
23.5-25.5% (in ~75% water)

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS

Chemical Name	1,4-Dixoane		
CAS No.	123-91-1	*Weight %*	≤ 80 ppm
Hazardous Properties	H225 (Highly flammable liquid and vapour) H351 (Suspected of causing cancer) H319 (Causes serious eye irritation) H335 (May cause respiratory irritation)		
Chemical Name	Alcohols, C12-14, ethoxylated		
CAS No.	68439-50-9	*Weight %*	≤ 1%
Hazardous Properties	H302 (Harmful if swallowed) H318 (Causes serious eye damage) H315 (Causes skin irritation)		

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)

Chemical Name	Water		
CAS No.	7732-18-5	*Weight %*	~75%

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 C AND 101.3 kPa: colourless to yellow liquid

Property	Value	Data Source/Justification
Freezing Point	Not determined	Imported and used in solution
Boiling Point	> 100 °C	SDS
Density	1,040 kg/m^3 at 20 °C	SDS
Vapour Pressure	2.3 kPa at 20 °C	SDS
Water Solubility	Not determined	Expected to be water dispersible based on the amphiphilic structure of the notified chemical and its use as a surfactant
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionality but is unlikely to hydrolyse in the environmental pH range (4-9)
Partition Coefficient (n-octanol/water)	Not determined	Expected to partition to phase boundaries based on the surface activity of the notified chemical
Adsorption/Desorption	Not determined	May partition to the solid phase based on the surface activity of the notified chemical
Dissociation Constant	Not determined	Expected to be ionised in the environment
Flash Point	> 100 °C	SDS
Flammability	Not determined	Imported and used in solution
Autoignition Temperature	Not determined	Imported and used in solution
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

DISCUSSION OF PROPERTIES

Reactivity
The zinc salt is expected to be dissociated from the notified chemical in product formulations.

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

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured within Australia. It will be imported into Australia as the chemical itself (up to 25.5% in water) or as a component of cosmetic products at ≤ 10% 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
Sydney and Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Manufacturer: Zschimmer & Schwarz GmbH & Co. KG
Recipient: Pierre Fabre Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemical will be imported into Australia as the chemical itself (up to 25.5% in water) or as a component of cosmetic products at ≤ 10% concentration, packed in dozens inside a shipper. Finished consumer products will be packed in up to 500 mL bottles or tubes made mainly from plastics and will be transported primarily by road to retail stores.

USE
The notified chemical will be used as a cosmetic ingredient at ≤ 10% concentration.

OPERATION DESCRIPTION
The notified chemical will be imported as the chemical itself (up to 25.5% in water) for reformulation or as a component of cosmetic products at ≤ 10% concentration.

Reformulation
The procedures for reformulating the notified chemical into cosmetic products will likely vary depending on the nature of the cosmetic products, and may involve both automated and manual transfer steps. In general, it is expected that the reformulation processes will involve blending operations that will normally be automated and occur in an enclosed system, followed by automated filling of the finished products into consumer containers of various sizes.

End-use
Finished cosmetic products containing the notified chemical at ≤ 10% concentration may be used by consumers and professionals such as hairdressers and workers in beauty salons. Depending on the nature of the products, these could be applied in a number of ways, such as by hand, using an applicator or by spray.

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)*
Transport and storage	4	12
Mixing	8	12
Quality control	3	12

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Packaging	8	12
Retail	4	12
Professional end users	8	365

EXPOSURE DETAILS

Transport and storage
Transport and storage workers may come into contact with the notified chemical itself (up to 25.5% in water) or at ≤ 10% concentration in consumer products only in the event of an unlikely accidental rupture of containers.

Reformulation
During reformulation into consumer products, dermal, ocular and inhalation exposure of workers to the notified chemical at ≤ 25.5% concentration may occur. As stated by the notifier, exposure is expected to be minimised through the use of exhaust ventilation and/or automated/enclosed systems as well as through the use of personal protective equipment (PPE) such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate).

End use
Exposure to the notified chemical in end-use products at ≤ 10% concentration may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. hair dressers, workers in beauty salons). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such workers may use some 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 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 ≤ 10% concentration through the use of cosmetic products. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

Data on typical use patterns of cosmetic products (SCCS, 2012; Cadby *et al.*, 2002; ACI, 2010; Loretz *et al.,* 2006) in which the notified chemical may be used are shown in the following tables. For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A dermal absorption (DA) of 2.4% was used for the notified chemical (for details of dermal absorption, see Section 6.2 Toxicokinetics). 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**	**Daily systemic exposure** (mg/kg bw/day)
Body lotion	7,820	10	1	0.2933
Face cream	1,540	10	1	0.0578
Hand cream	2,160	10	1	0.0810
Deodorant (non-spray)	1,500	10	1	0.0563
Fragrances	750	10	1	0.0281
Hair styling products	4,000	10	0.1	0.0150
Shower gel	18,670	10	0.01	0.0070
Hand wash soap	20,000	10	0.01	0.0075
Shampoo	10,460	10	0.01	0.0039
Hair conditioner	3,920	10	0.01	0.0015
Total				0.5513

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

Aerosol products (Inhalation exposure)

Product type	Amount (g/day)	C (%)	Inhalation Rate (m^3/day)	Exposure Duration (Zone 1) (min)	Exposure Duration (Zone 2) (min)	Fraction Inhaled (%)	Volume (Zone 1) (m^3)	Volume (Zone 2) (m^3)	Daily systemic exposure (mg/kg bw/day)
Hairspray	9.89	10	20	1	20	50	1	10	0.3219

Daily systemic exposure = [(Amount × C × Inhalation Rate × Fraction Inhaled × 0.1) / BW × 1440)] × [Exposure Duration (Zone 1)/Volume (Zone 1) + Exposure Duration (Zone 2)/Volume (Zone 2)]

The notified chemical is also proposed to be used in lipsticks where exposure is mainly through the oral route. The data is shown below (SCCS, 2012). A conservative 100% ingestion and gastrointestinal absorption rate was assumed for calculation purposes, with the use amount provided in the SCCS (2012) for lipsticks.

Cosmetic products (Oral exposure)

Product type	Amount (mg/day)	C (%)	Daily systemic exposure (mg/kg bw/day)
Lipstick	57	10	0.0891

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical. This would result in a combined internal dose of 0.9623 mg/kg bw/day. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic products (in addition to hair spray) may occur. However, it is considered that the combination of the conservative (screening level) hair spray inhalation exposure assessment parameters and the aggregate exposure from use of the dermally applied products is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic products with lower exposure factors (e.g., deodorant aerosol).

6.2. Human Health Effects Assessment

Only limited toxicity data were provided. The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Eye irritation (*in vitro* HET-CAM at 1%)	non-irritating
Eye irritation (*in vitro* HET-CAM at 1%, 5% 10%)	slightly irritating (1%), moderately irritating (5%), irritating (10%)
Eye irritation potential (*in vitro* NRR test at 23 %)	cytotoxic
Human, skin sensitisation – RIPT (5%)	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non-mutagenic

Use of Analogue Data in Human Health Effects Assessment

Only limited toxicological data were provided for the notified chemical. Adverse effects from Zn are not expected. Therefore, data on alcohol ethoxysulphates (AES) reported in a HERA report (HERA, 2003) were used to derive hazard conclusion for the notified chemical. The notified chemical belongs to the class of anionic surfactants known as AES. As the notified chemical contains a range of alkyl chains (C12-16) with average ethoxy (EO) groups of 3, analogues with an alkyl chain ranging from C12 to C16 and average ethoxy (EO) groups of 2 or 3 were considered for assessment on acute or local and repeated dose effects. Salts of AES are expected to be dissociated in any product formulation independent of whether the salt is sodium, ammonium, magnesium or zinc (CIR, 2010).

Alkyl chain length	Structure	Short name
C12	$CH_3(CH_2)_{10}CH_2(OCH_2CH_2)_nOSO_3$	C12AE2S
		C12AE3S
C12-C14	$CH_3(CH_2)_{10\text{-}12}CH_2(OCH_2CH_2)_nOSO_3$	C12-C14AE2S
C12-C15	$CH_3(CH_2)_{10\text{-}13}CH_2(OCH_2CH_2)_nOSO_3$	C12-15AE3S

Toxicokinetics

Dermal absorption of the notified chemical is expected to be relatively poor as expected from ionic molecules. In a study conducted in rats, C12AE3S had a low percutaneous absorption rate of 0.0163 µg/cm^2/h (HERA, 2003). In a dermal absorption study conducted in guinea pigs, 2.4% of a ^{14}C labelled sodium laureth sulphate applied cutaneously penetrated the skin during 24 hours exposure (CIR, 1983).

Acute toxicity
Analogues C12-C14AE2S (triisopropanolamine salt, 90% active material) and NaC12-14AE2S (70% active material) were found to have a low order of acute oral toxicity in rats (LD50 > 2,000 mg/kg bw and > 2,500 mg/kg bw, respectively) (HERA, 2003). C12-C14AE2S (triisopropanolamine salt, 90% active material) also showed low dermal toxicity in rats (LD50 > 2,000 mg/kg bw) (HERA, 2003). Based on the analogue data, the notified chemical is not expected to be acutely toxic via the oral and dermal routes. There is no data available on the inhalation toxicity of the notified chemical or suitable analogues.

Irritation
The skin irritation potential of AES is concentration dependent. C12-C14AE2S (triisopropanolamine at 90% concentration) was found to be moderately irritating in rabbits (HERA 2003). NaC12-14AE2S (70%) showed moderate to severe irritation in two skin irritation studies conducted in rabbits (HERA, 2003). At 10-30% concentrations AES are slightly to moderately irritating and at < 1% concentrations AES are non-irritating (HERA, 2003).

The eye irritation potential of AES is also concentration dependent. C12-C14AE2S (triisopropanolamine at 90% concentration) and C12-14AE2S (28%) were found to be moderately to severely irritating in two independent eye irritation studies conducted in rabbits (HERA 2003). AES at 1-10% concentrations are slightly to moderately irritating to eyes and at < 1% concentrations AES are non-irritating (HERA, 2003).

The skin and eye irritation potential of the notified chemical is expected to be concentration-dependent, similar to other AES. The notified chemical was considered to be non-irritating to eyes at 1% concentration in a hen's egg test – chorioallantoic membrane (HET-CAM). In another HET-CAM test, 1%, 5% and 10% solutions of the notified chemical were reported as a mild irritant, a moderate irritant and an irritant, respectively. The eye irritation potential of the notified chemical was further supported by the cytotoxic result in a neutral red release (NRR) test. The notified chemical is classified as a skin irritant and a severe eye irritant by the notifier in the SDS provided.

Mild skin irritation effects were observed in a skin irritation study conducted in 12 human subjects with a detergent formulation containing 11.4% of NaC12-14ES (CAS No. 68891-38-3) (HERA, 2003).

Sensitisation
In a human repeat insult patch test (HRIPT) completed in 25 subjects, the notified chemical at 5% concentration was found to be non-sensitising. Analogue NaC12-14AE2S (27% or 28%) did not cause skin sensitisation in guinea pigs in either of two studies according to the Magnusson-Kligman protocol (HERA 2003). C12-C14AE2S (triisopropanolamine salt) showed no sensitising effects on guinea pigs when tested according to the Buehler method at a challenge concentration of 25% (HERA, 2003). Although weak skin sensitisation responses have been reported, AES are not considered to be skin sensitisers based on the weight of evidence (14 out of 15 AES studies according to Magnusson-Kligman protocol and 6 out of 8 studies according to the Buehler method revealed no evidence of sensitisation) (HERA, 2003). Based on the HRIPT data for the notified chemical and the data of the analogues, the notified chemical is expected to be non-sensitising.

Repeated dose toxicity
A number of close analogues (with an alkyl chain ranging from C12 to C16 and average EO groups of 3) of the notified chemical were evaluated in repeated dose oral toxicity studies (HERA, 2003).

Test Material	Study summary and Estimated LOEL/NOAEL/NOEL
NaC12-15AE3S	21 Day dietary rat study at 0.023%, 0.047%, 0.094%, 0.188%, 0.375%, 0.75%, 1% and 1.5%. No effects were noted at or below 0.188% level (254 mg/kg bw/day). The Lowest Observed Effect Level (LOEL) was established as 0.375% (487 mg/kg bw/day) based on hepatocyte hypertrophy. Significantly increased organ weights (liver, kidney, brain) were noted at doses equal to or higher than the LOEL.
NH4C12-15E3S	21 Day dietary rat study at 0.023%, 0.047%, 0.094%, 0.188%, 0.375%, 0.75%, 1% and 1.5%. No effects were noted at or below 0.188% (232 mg/kg bw/day). The LOEL was established as 0.375% (465 mg/kg bw/day) based on significant increases in plasma alkaline phosphatase activity. Significantly increased liver weight was noted at doses higher than the LOEL.
NaC12-15E3S	21 Day dietary rat study at 0.023%, 0.047%, 0.094%, 0.188%, 0.375%, 0.75%, 1% and 1.5%. No effects were noted at or below 0.094% level (108 mg/kg bw/day). The LOEL was established as 0.188% (217 mg/kg bw/day) based on significant increases in plasma alkaline

	phosphatase activity. Significantly increased liver weight was noted at doses equal to or higher than the LOEL.
NH4C13-15E3S	21 Day dietary rat study at 0.023%, 0.047%, 0.094%, 0.188%, 0.375%, 0.75%, 1% and 1.5%. No effects were noted at or below 0.375% (461 mg/kg bw/day). The LOEL was established as 0.75% (857 mg/kg bw/day) based on hepatocyte hypertrophy. Significantly increased organ weights (liver, testes, brain) were noted at doses higher than the LOEL.
C12AE3S	2-Year rat study at 0.1% or 0.5% in the diet. The results suggested a NOAEL of greater than 250 mg/kg bw/day.
C12AE3S	2-Year rat study at 0.1% in the drinking water. The NOAEL was estimated as greater than 75 mg/kg bw/day (equivalent to tested dose of 0.1% in the drinking water).

Repeated dose dermal studies on two liquid dishwashing detergents containing C12-14AES at 23% and 27% concentrations were conducted in rabbits, in which the test substance was administered at 0.5%, 1%, 2.5% for 6 hours per day and 5 days a week for a total of 91 days. The test substance caused no adverse systemic effects, slight to moderate dermal irritation was observed at the detergent application sites in both studies.

Mutagenicity/Genotoxicity
The notified chemical was negative in a bacterial reverse mutation assay. A structure activity analysis on AES didn't reveal functional groups that were associated with mutagenic or genotoxic properties (HERA, 2003). In all available *in vitro* and *in vivo* mutagenicity/genotoxicity assays on AES (analogues of the notified chemical), there is no indication of mutagenic/genotoxic potential (HERA, 2003). Therefore, the notified chemical is expected to be non-genotoxic.

Carcinogenicity
A close analogue of the notified chemical, C12AE3S, was evaluated in carcinogenicity studies (HERA, 2003).

C12AE3S	2-year rat study with 0.1% in the drinking water. The only unusual finding was slight but consistently higher water consumption by test-substance treated rats and a significant difference on the empty cecum to body weight ratio of female animals. Various types of benign and malignant tumours were found in both treatment and control groups, with no significant difference in frequency of tumours between the groups.
C12AE3S	2-year rat feeding study at 0.1 or 0.5% in the diet. No indications of an increased incidence in tumours were reported.
C12AE3S	Applied as a 5% aqueous solution twice weekly on the skin of 30 female mice with no papillomas or other tumours observed.

It is concluded in the HERA report (HERA, 2003) that there is sufficient evidence that AES is not carcinogenic in the tested species under the conditions described.

Toxicity for reproduction
In available studies on various AES (NaC12-14AE2S, C12-CaC15AE3S, C12AE3S), the primary sex organs of the animals did not show evidence of treatment-related adverse effects at the highest tested exposure level of 250 mg/kg bw/day (HERA, 2003).

Developmental toxicity/teratogenicity
A number of close analogues (with an alkyl chain ranging from C12 to C16 and average EO groups of 3) of the notified chemical were evaluated in developmental toxicity/teratogenicity studies (HERA, 2003).

NaC12-15AE3S	Gavage administration to pregnant rats at 375 and 750 mg/kg bw/day once daily from day 6 to 15 of gestation. The NOAEL for maternal toxicity was established as 375 mg/kg bw/day and the NOAEL for teratogenic effects or developmental toxicity was estimated to be greater than 750 mg/kg bw/day.
NaC12-14AE3S	Gavage administration to pregnant rats at 93, 187, 375 and 750 mg/kg bw/day once daily from day 6 to 15 of gestation. The NOAEL for maternal toxicity was established as 375 mg/kg bw/day and the NOAEL for teratogenic effects or developmental toxicity was estimated to be greater than 750 mg/kg bw/day.
NaC12-15E3S	Gavage administration to pregnant rats at 125, 250, 500 and 1000 mg/kg bw/day once daily from day 6 to 15 of gestation. Maternal toxicity indicated by a significant reduction in body weight gain

was noted at 1000 mg/kg bw/day but no evidence of treatment-related developmental toxicity or teratogenic effects were noted.

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

Hazard classification	*Hazard statement*
Skin corrosion/irritation (Category 2)	H315 – Causes skin irritation
Serious eye damage/eye irritation (Category 2A)	H319 – Causes serious eye irritation

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available toxicological information on the notified chemical and analogues, the notified chemical may cause skin irritation and severe eye irritation. Systemic toxicity effects are not expected from exposure to the notified chemical.

Reformulation
Dermal, ocular and inhalation exposure of workers to the notified chemical at various concentrations up to 25.5% may occur during formulation of cosmetics. As stated by the notifier, the use of personal protective equipment (PPE) such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate), and engineering controls including automated/enclosed blending processes and local exhaust ventilation should minimise the risk for workers. Provided that the protective measures and engineering controls are used, the notified chemical is not expected to pose an unreasonable risk to workers during formulation of products.

End use
Store persons and workers involved in professions where the services provided involve the application of cosmetic products containing the notified chemicals to clients (such as beauticians and hairdressers) may come into contact with the notified chemical at ≤ 10% concentration. The risk to workers who regularly handle these products is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health
There will be widespread and repeated exposure of the public to the notified chemical through the use of cosmetic products at proposed concentrations of ≤ 10% in individual products. The principal route of exposure will be dermal, while ocular exposure and inhalation exposure (in spray applications) is also possible.

Based on the available information on the notified chemical and analogues, the potential to cause skin and eye irritation effects at up to 10% concentration cannot be ruled out. The irritation potential is expected to vary depending on the cosmetic formulation.

Repeated dose toxicity
The repeated 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 containing the notified chemical (0.9623 mg/kg bw/day) (see Section 6.1.2). Using a NOAEL of 375 mg/kg bw/day derived from reproductive toxicity studies in rats (HERA, 2003), the margin of exposure (MoE) was estimated to be 389. A MoE value greater than or equal to 100 is generally considered acceptable to account for intra- and inter-species differences.

Based on the available information, the risk to the public associated with use of the notified chemical at ≤ 10% concentration in cosmetic 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 will be imported as ~25.5% aqueous solution for reformulation into finished cosmetic products, or as a component of finished cosmetic formulations. There is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the product containing the notified chemical is expected to be collected with inert material, and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve both automated and manual transfer of the raw material containing the notified chemical into blending vessels, followed by blending operations that are expected to be highly automated and occur within a fully enclosed environment. The process will be followed by automated filling of the finished products into end-use containers of various sizes. Wastes containing the notified chemical generated during reformulation include equipment wash water, residues in empty import containers (estimated by the notifier to be 1% of the import volume of the notified chemical) and spilt materials. Wastes may be collected and released to sewers, or disposed of to landfill in accordance with state and local government regulations.

RELEASE OF CHEMICAL FROM USE

The notified chemical is expected to be released to the aquatic compartment through sewers during its use in various leave on and rinse off cosmetic products.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated by the notifier that 3% of the import volume of the notified chemical may remain in end-use containers once the consumer products are used up. Wastes and residues of the notified chemical in empty containers are likely to either share the fate of the container and be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in cosmetic formulations, the majority of the notified chemical is expected to enter the sewer system, before potential release to surface waters nationwide. The notified chemical is expected to ionise into inorganic zinc (II) and organic components which are expected to follow different pathways during sewage treatment plant (STP) processes. The results of submitted biodegradability study suggest that the notified chemical is considered to be readily biodegradable (83% in 28 days). This is consistent with published literature (HERA, 2004, Madsen et al., 2001).

Zinc is ubiquitous in the environment with concentrations of 0.9 µg/L common in fresh water (ANZECC/ARMCANZ 2000). The majority of zinc from the notified chemical is expected to partition to biosolids during STP processes and either be disposed of to landfill or applied to agricultural soils. In sewage treatment plants (STPs) the notified chemical (organic moiety) is expected to be efficiently removed from influent via biodegradation and only a small portion may be released to surface waters and is unlikely to significantly alter the environmental concentrations of zinc.

The high removal efficiency of the organic moiety of the notified chemical is expected based on rapid biodegradation. A proportion of the notified chemical may be applied to land when effluent is used for irrigation, or disposed of to landfill as waste. Alkyl ether sulfates are generally considered to have low bioaccumulation potential in aquatic organisms (Madsen et al., 2001). In surface waters and landfill, the notified chemical is expected to degrade through biotic and abiotic processes to form water and oxides of carbon and sulfur.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume a realistic case scenario, with 100% release of the notified chemical into sewer systems nationwide and 87% removal within sewage treatment plants (STPs) was assumed based on the SimpleTreat model (Struijs, 1996).

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:	27.40	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	87%*	**Mitigation**
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.73	µg/L
PEC - Ocean:	0.07	µg/L

The SimpleTreat model was used to estimate the removal of the notified chemical within STPs based on its ready biodegradability and modelled physico-chemical properties submitted by the notifier (Struijs, 1996).

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 1500 kg/m3). Using these assumptions, irrigation with a concentration of 0.73 µg/L may potentially result in a soil concentration of approximately 4.87 µg/kg.

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	96 h LC50 = 10-100 mg/L*	Harmful to fish
Algal Toxicity	72 h EC50 < 1.5 mg/L*	Potentially very toxic or toxic to algae

* The results should be interpreted with care due to deviations from standard OECD TGs.

As there are no specific ecotoxicity endpoints for the notified chemical, it is not appropriate, in this case, to classify the notified chemical for acute or long-term aquatic hazards under the Globally Harmonised System of Classification and Labelling of Chemicals (United Nations, 2009).

Generally, the measured data is consistent with the published literature. The toxicity of alkyl ether sulfate seems to peak at alkyl chain length of C_{16} (Madsen et al., 2001). EC50 endpoints for algae to alkyl ether sulfates are in the range between 4 and 65 mg/L (Madsen et al., 2001). The closest analogue chemical to the notified chemical in the structures considered by Madsen et al. is a $C_{10\text{-}15}$ hydrophobe and 3 ethoxylate units and one sulfate $C_{10\text{-}15}AE_3S$. The 48 h EC50 for *Selenastrum capricornutum* was 65 mg/L (Madsen et al., 2001). A 72 h NOEC value of 0.9 mg/L was reported for $C_{12\text{-}15}AE_3S$ to *Scenedesmus subspicatus* (HERA, 2004). EC50 for the acute toxicity for alkyl ether sulfates to daphnids ranges between 1 and 50 mg/L (Madsen et al., 2001). However, an EC50 of 0.37 mg/L and NOEC of 0.27 mg/L for $C_{13\ 67}AE_{2\ 25}S$ was observed in a 21-day reproduction test with *Daphnia magna* (Madsen et al., 2001). LC50 values for alkyl ether sulfate to fish are in the range between 0.39 and 450 mg/L (Madsen et al., 2001). The 96 h LC50 for $C_{12\text{-}15}AE_3S$ to fish ranges between 1.0 and 8.9 mg/L (Madsen et al., 2001). A NOEC of 0.12 mg/L was reported for $C_{12\text{-}15}AE_3S$ to *O. mykiss* in a 28-day study (HERA, 2004). Hence the lowest endpoint from the provided studies and published literature will be used as a lower limit for the calculation of the Predicted No-Effect Concentration below. This is a conservative estimate for the notified chemical.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) for the notified chemical has been calculated from the most sensitive chronic endpoint for fish. An assessment factor of 100 was used given chronic endpoints for three trophic levels are available based on published literature, but without a review of the primary study.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
NOEC (Fish).	0.12	mg/L
Assessment Factor	100.00	
Mitigation Factor	1.00	
PNEC:	1.20	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	*Q*
Q - River:	0.73	1.2	0.609
Q - Ocean:	0.07	1.2	0.061

The Risk Quotients (Q = PEC/PNEC) for discharge of treated effluents containing the notified chemical have been calculated to be < 1 for both river and ocean compartments indicating that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters based on its maximum annual importation quantity and ready biodegradability. On the basis of the PEC/PNEC ratio and assessed use pattern in cosmetic formulations, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – eye (in vitro)

TEST SUBSTANCE	Notified chemical (1% aqueous solution)
METHOD	No test guideline or test protocol details were provided in the report. The potential of the notified chemical to cause serious damage to the eye/mucous membranes was assessed by a single topic application of 0.2 mL of the test substance at 1% concentration to the chorionallantoic membrane (CAM) of fertilised and incubated hen eggs. Four eggs were treated with the test substance, 2 eggs were treated with the negative control (0.2 mL demi water) and 2 eggs were treated with the positive control (0.2 mL Resconicol 5%). The eggs were observed immediately prior to administration and at 30 seconds, 2 minutes and 5 minutes after exposure. Irritation effects (hyperemie, haemorrhage and coagulation) in response to the test substance were recorded.
RESULTS	
Remarks - Results	The test substance solution showed no irritation effects (score of 0). The positive and negative controls gave a satisfactory response confirming the validity of the test system.
CONCLUSION	The notified chemical at 1% concentration was considered to be non-irritating under the conditions of the test.
TEST FACILITY	Biolab (2000a)

B.2. Irritation – eye (in vitro)

TEST SUBSTANCE	Notified chemical (10% aqueous solution)
METHOD	No test guideline or test protocol details were provided in the report. The concentration of the test substance resulting in 50% cell death (CI 50%) was determined using the technique of neutral red release (NRR) from 10% pre-loaded cells. Positive controls were 0.01%, 0.05% and 0.2% sodium dodecyl sulphate.
RESULTS	

Concentration tested	*20%*	*25%*	*30%*	*35%*
% Cellular mortality	26.06	50.65	60.87	68.55
CI 50%			25.15	
Classification			Moderate cytotoxicity	

Remarks - Results	A brief study report was provided. The CI 50% for the test substance used at 23% concentration was determined to be 25.15% (equivalent to 5.8% concentration) and the test substance was classified as moderately cytotoxic. The CI 50% for the positive control was determined to be 0.033 – 0.045%, indicating the expected severe cytotoxicity.
CONCLUSION	The notified chemical at 5.8% concentration was cytotoxic under the conditions of the test.

TEST FACILITY	CEPC (2000a)

B.3. Irritation – eye (in vitro)

TEST SUBSTANCE	Notified chemical (1%, 5% and 10% aqueous solution)
METHOD	No test guideline or test protocol details were provided in the report. The test substance at three concentrations (1%, 5% and 10%) was applied to the chorionallantoic membrane (CAM) of fertilised and incubated hen eggs. Physiological serum was used as a negative control at 0.9% concentration and lauryl betaine sulphate was used as a positive control at 0.4%.
RESULTS	
Remarks - Results	A brief study report was provided. The 1%, 5% and 10% solutions gave scores of 1.3, 7.5 and 10.8 respectively and were reported as a mild irritant, a moderate irritant and an irritant respectively. The negative control and positive control showed the expected results with scores of 0.8 and 17.3 respectively.
CONCLUSION	The notified chemical was considered to be slightly irritating to eyes at 1% concentration, moderately irritating to eyes at 5% and irritating to eyes at 10% concentration, under the conditions of the test.
TEST FACILITY	CEPC (2000b)

B.4. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical (5% aqueous solution)
METHOD	Repeated insult patch test with challenge
Study Design	Induction Procedure: A patch test was conducted, followed by 4 more patch tests in the following 4 weeks. The test substance was in contact with the skin for 48 hours and skin reactions were evaluated 15 minutes, 1 hour and 24 hours after patch removal. Rest Period: information not provided Challenge Procedure: the test substance was in contact with the skin for 48 hours and skin reactions were evaluated 15 minutes, 1 hour and 24 hours after patch removal.
Study Group	20 F, 5 M; age range18-70 years
Vehicle	Information not provided
Remarks - Method	Occluded. The test substance was spread on a 0.7 cm aluminium disk.
RESULTS	
Remarks - Results	A brief study report was provided. After the initial patch 8/25 subjects showed light erythema at the 15 minute observation, 12/25 subjects showed light to moderate erythema at the 1 hour observation and 8/25 subjects showed light to visible erythema at the 24 hour observation. After the final patch 9/25 subjects showed light to visible erythema at the 15 minute observation, 11/25 subjects showed light to visible erythema at the 1 hour observation and 4/25 subjects showed light erythema at the 24 hour observation. There were no signs of oedema observed. Total irritation index was 0.45 during the induction and challenge procedures and the test substance was considered as non-irritating (meeting the criterion of irritation index < 0.5 for non-irritants). The test substance was considered to be non-sensitising by the study authors.

CONCLUSION	The test substance was non-sensitising under the conditions of the test.
TEST FACILITY	University of Pavia (2000)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical (25% aqueous solution)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure
Species/Strain	*Salmonella typhimurium*: TA1538, TA1535, TA1537, TA98, TA100
Metabolic Activation System	S9 mix from Araclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 10 – 100,000 µg/plate b) Without metabolic activation: 10 – 100,000 µg/plate
Vehicle	Demi water
Remarks - Method	No preliminary tests were conducted. Positive controls were 9-aminoacridine, sodium azide, 2-nitrifluorene and 2-aminoanthracene.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	not provided	not provided	not provided
Present			
Test 1	> 100,000	not provided	negative

Remarks - Results	The report stated that the test substance was not a mutagen at all dilutions with or without metabolic activation.
CONCLUSION	The notified chemical (25% aqueous solution) was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Biolab (2000b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical (25% aqueous solution)
METHOD	OECD TG 301 C Ready Biodegradability: Modified MITI Test (I).
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Respirometer
Remarks - Method	GLP is not claimed for this test. Samples were collected from sewage treatment plant, river and industrial treatment plant. No chemical analysis was undertaken. The test was conducted at a concentration of 100 mg test substance /L. Deviations from the Modified MITI procedure were: the pH of the contents of the bottles were not reported, the percentage biodegradation was determined based on COD rather than ThOD.

RESULTS

Test substance		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	30	7	48
14	42	14	69
21	83	21	87
28	83	28	87

Remarks - Results	The percentage degradation of the reference compound, sodium benzoate surpassed the threshold level of 40% within 7 days and 65% within 14 days indicating the suitability of the inoculums. The degree of degradation of the notified chemical after 28 days was 83%. The 10-d window does not apply to the MITI method.
CONCLUSION	The notified chemical is considered to be readily biodegradable.
TEST FACILITY	Biolab (1999)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical (24% aqueous solution)
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Static.
Species	*Brachydanio Rerio*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	180 mg $CaCO_3$/L
Analytical Monitoring	None
Remarks – Method	The stock solution of 100 mg/L was prepared and diluted further. No chemical analysis was undertaken.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*					
Nominal	*Actual*		*2-4h*	*8 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	ND*	10	0	0	0	0	0	0

40	ND	10	0	0	0	0	0	0
46	ND	10	0	2	1	0	0	0
53	ND	10	2	1	1	0	0	0
61	ND	10	3	1	1	0	0	0
70	ND	10	5	NR	NR	NR	NR	NR

*ND = not determined
§ NR = not reported

LC50 10-100 (51.6 mg/L) at 96 hours.

Remarks – Results Total mortality was reported to be 60% at 53 mg/L, 80% at 61 mg/L and 100% at 70 mg/L which is not consistent with mortality numbers shown in the table above. The statistical method to determine LC50 was not described. Therefore, LC50 value of 51.6 mg/L should be interpreted with great care.

CONCLUSION The notified chemical is considered to be harmful to fish.

TEST FACILITY Biolab (2000c)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE Notified chemical (25% aqueous solution)

METHOD OECD TG 201 Alga, Growth Inhibition Test.

Species *Selenastrum capricornutum*

Exposure Period 72 hours

Concentration Range Nominal: 1.5 mg/L
Actual: unknown

Auxiliary Solvent None

Water Hardness Not reported

Analytical Monitoring None

Remarks - Method The test was performed at one concentration (1.5 mg/L). No chemical analysis was undertaken.

RESULTS

Biomass		*Growth*	
EC50	*NOEC*	*EC50*	*NOEC*
mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
Not determined	Not determined	Not determined	Not determined

Remarks - Results The algae growth inhibition was 73% at 1.5 mg/L. EC50 is expected to be < 1.5 mg/L.

CONCLUSION The notified chemical is potentially toxic to algae.

TEST FACILITY Biolab (2005)

BIBLIOGRAPHY

ANZECC & ARMCANZ (Australian and New Zealand Environment and Conservation Council and Agriculture and Resource Management Council of Australia and New Zealand), (2000). *Australian and New Zealand Guidelines for Fresh and Marine Water Quality.*

Biolab (1999) Evaluation of Aerobic Biodegradability Modified MITI Test (Study No. M99/517.A, October, 1999). Vimodrone (Milano) Italy, Biolab Spa (Unpublished report submitted by the notifier).

Biolab (2000a) Zinc Coceth Sulfate: HET CAM Test (Report No. 00/13525, June, 2000). Vimodrone, Italy, Biolab S.p.A. di Vimodrone (Unpublished report submitted by the notifier).

Biolab (2000b) Zetesol ZN: Salmonella Typhimurium Bacterial Reverse Mutation Assay (Report No. 99/29313-1, April, 2000). Vimodrone, Italy, Biolab S.p.A. di Vimodrone (Unpublished report submitted by the notifier).

Biolab (2000c) Acute Fish Toxicity (Study No. M00/0481.0MI, June, 2000). Vimodrone (Milano) Italy, Biolab Spa (Unpublished report submitted by the notifier).

Biolab (2005) Assay of Inhibition of Algae Growth (Study No. M04/2187.1MI, May, 2005). Vimodrone (Milano) Italy, Biolab Spa (Unpublished report submitted by the notifier).

CEPC (2000a) Zetesol ZN: Evaluation of the Potential Irritant *in vitro*, by the Method of "Neutral red Release" Assay (Study No. 00-0350, December, 2000). Castres, Cedex, France, Experimental and Pharmacocinetic Centre of Campans (Unpublished report submitted by the notifier).

CEPC (2000b) Zetesol ZN: Evaluation of the Potential Irritating by Application on the horionallantoic Membrane of Chicken Egg (Study No. 00-0351, December, 2000). Castres, Cedex, France, Experimental and Pharmacocinetic Centre of Campans (Unpublished report submitted by the notifier).

CIR (1983) Final Report on the Safety Assessment of Sodium Laureth Sulfate and Ammonium Laureth Sulfate. . Cosmetic Ingredient Review, International Journal of Toxicology, Volume 2, Number 5.

CIR (2010) Final Report of the Amended Safety Assessment of Sodium Laureth Sulfate and Related Salts of Sulfated Ethoxylated Alcohols. Cosmetic Ingredient Review, International Journal of Toxicology, Volume 29, Supplement 3, 151S-161S.

HERA (2003) Alcohol Ethoxysulphates: Human Health Risk Assessment Draft (January 2003). Human and Environmental Risk Assessment on Ingredients of Household Cleaning Products.

HERA (2004) Alcohol Ethoxylsulphates Environmental Risk Assessment (June, 2004). Human & Environmental Risk Assessment on ingredients of European household cleaning products. Accessed 19 April 2017 at http://www.heraproject.com/files/1-E-04-HERA%20AES%20ENV%20%20web%20wd.pdf.

Madsen T, Boyd HB, Nylén D, Pederson AR & Simonsen F (2001). Environmental Project No. 615; Environmental and Health Assessment of Substances in Household Detergents and Cosmetic Detergent Products. CETOX, Miljøprojekt, pp 201, http://www2 mst.dk/udgiv/publications/2001/87-7944-596-9/pdf/87-7944-597-7.pdf.

Struijs J (1996). *SimpleTreat 3.0: a model to predict the distribution and elimination of chemicals by sewage treatment plants*. National Institute of Public Health and the Environment, Bilthoven, The Netherlands.

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 >.

University of Pavia (2000) Eveluation of Possible Irritating or Sensitising Effects of a Cosmetic Product through Repaeted Skin Tests (Shelanski and Shelanski test with some changes in it) (January, 2000). Pavia, Italy, University of Pavia (Unpublished report submitted by the notifier).