File No: LTD/1744
LTD/1745

September 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

2*H*-2,4a-Methanonaphthalene-8-ethanol, 1,3,4,5,6,7-hexahydro-β,1,1,5,5-pentamethyl- (LTD/1744)

2*H*-2,4a-Methanonaphthalene-8-ethanol, 1,3,4,5,6,8a-hexahydro-β,1,1,5,5-pentamethyl- (LTD/1745)

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.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1744 LTD/1745	Givaudan Australia Pty Ltd	2*H*-2,4a-Methanonaphthalene-8-ethanol, 1,3,4,5,6,7-hexahydro-β,1,1,5,5-pentamethyl- (LTD/1744) 2*H*-2,4a-Methanonaphthalene-8-ethanol, 1,3,4,5,6,8a-hexahydro-β,1,1,5,5-pentamethyl- (LTD/1745)	Yes	≤ 1 tonne per annum	Ingredient in cosmetics and household products

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Skin sensitisation (Category 1B)	H317 – May cause an allergic skin reaction

Based on the available information, the notified chemicals are recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase(s):

R38: Irritating to skin
R43: May cause sensitisation by skin contact

The environmental hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute Category 1	H400 – Very toxic to aquatic life
Chronic Category 1	H410 – Very toxic to aquatic life with long lasting effects

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

When used in the proposed manner, the notified chemicals are 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 chemicals are not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemicals should be classified as follows:
  - Skin sensitisation (Category 1B): H317 – May cause an allergic skin reaction

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.

- The Delegate (and/or the Advisory Committee on Chemicals Scheduling) should consider the notified chemicals for listing on the SUSMP.

Health Surveillance

- As the notified chemicals are skin sensitisers, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of skin sensitisation.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following isolation and engineering controls to minimise occupational exposure to the notified chemicals during reformulation processes:
  - Enclosed, automated processes, where possible
  - Ventilation system including local exhaust ventilation

- 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 chemicals during reformulation processes:
  - Avoid contact with skin and eyes
  - Avoid inhalation

- 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 chemicals during reformulation processes:
  - Coveralls, impervious gloves, goggles

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

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

- If products and mixtures containing the notified chemicals are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- The notified chemicals should be disposed of to landfill.

Storage

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

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the concentration of the notified chemical exceeds or is intended to exceed 0.075% in fine fragrances, 0.04% in other cosmetic products and 0.005% in fabric care and household products;
- further information on the repeat dose toxicity of the notified chemical becomes available.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemicals has changed from ingredients in cosmetics and household products, or is likely to change significantly;
- the amount of the chemicals being introduced has increased, or is likely to increase, significantly;
- the chemicals have begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemicals 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.

No additional secondary notification conditions are stipulated.

(Material) Safety Data Sheet
The (M)SDS of products containing the notified chemicals provided by the notifier was reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT
Givaudan Australia Pty Ltd (ABN: 87 000 470 280)
Unit 36/5 Inglewood Place
BAULKHAM HILLS NSW 2153

NOTIFICATION CATEGORY
LTD/1744: Limited-small volume – Chemical other than polymer (1 tonne or less per year)
LTD/1745: Limited-small volume (Reduced fee notification) – Chemical other than polymer (1 tonne or less per year) - Chemical is being notified at the same time as a similar chemical.

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU REACH (Notification No. 08-06-2060-00; REACH No. 01-0000020145-80-0001)
Switzerland (OCHEM) 2008

2. IDENTITY OF CHEMICAL

Note: The notified chemicals LTD/1744 and LTD/1745 are manufactured as a mixture and are not isolated as individual chemicals. All the physico-chemical and toxicological studies reported were carried out using a mixture of the two notified chemicals. All products containing the notified chemicals as components will have both chemicals in the formulated product.

MARKETING NAME(S)
LTD/1744: Component 1 in Ambermax
LTD/1745: Component 2 in Ambermax

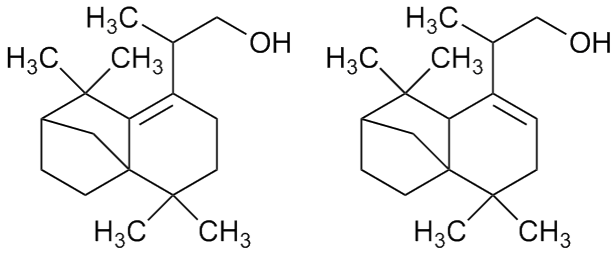
CAS NUMBER
LTD/1744: 929625-08-1
LTD/1745: 1001252-30-7

CHEMICAL NAME
LTD/1744: 2*H*-2,4a-Methanonaphthalene-8-ethanol, 1,3,4,5,6,7-hexahydro-β,1,1,5,5-pentamethyl-
LTD/1745: 2*H*-2,4a-Methanonaphthalene-8-ethanol, 1,3,4,5,6,8a-hexahydro-β,1,1,5,5-pentamethyl-

OTHER NAME(S)
GR-86-7554 (mixture of LTD/1744 & LTD/1745)

MOLECULAR FORMULA
$C_{18}H_{30}O$

STRUCTURAL FORMULA



LTD/1744 LTD/1745

MOLECULAR WEIGHT
262.4 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 90% (mixture of LTD/1744 and LTD/1745)

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: White paste – mixture of LTD/1744 and LTD/1745

Property	Value	Data Source/Justification
Melting Point/Freezing Point	56 °C	(M)SDS
Boiling Point	322 °C at 101.3 kPa	(M)SDS
Density	Not determined	Imported at low concentrations in solution.
Vapour Pressure	6×10^{-5} kPa at 20 °C	(M)SDS
Water Solubility	1.38×10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Contain no hydrolysable functional groups
Partition Coefficient (n-octanol/water)	log Pow ≥ 6.3	Measured
Adsorption/Desorption	log K_{oc} = 3.8 (MCI method) log K_{oc} = 3.6 (Kow method)	Calculated. KOCWIN v2.0, EPI Suite v 4.1 (US EPA, 2010)
Dissociation Constant	Not determined	Do not contain readily dissociable functionalities.
Flash Point	156 °C at 101.3 kPa	(M)SDS
Autoignition Temperature	270 °C	(M)SDS
Explosive Properties	Not expected to be explosive	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Not expected to be oxidising	Contains no functional groups that would imply oxidative properties.

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

Reactivity
The notified chemicals are expected to be stable under normal conditions of use. They are not explosive, non-oxidising and not auto-ignitable under normal conditions. The notified chemicals present no significant reactivity hazard by themselves or in contact with water. However, direct sources of heat and contact with strong acids, alkali or oxidising agents should be avoided.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified chemicals are not classified according to the Australian Dangerous Goods Code (NTC, 2007). However, the data above do not address all Dangerous Goods endpoints. Therefore, consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemicals.

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

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemicals will not be manufactured within Australia. The notified chemicals will be imported as components of fragrance formulations at concentrations up to 1.5%.

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

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

PORT OF ENTRY
Sydney (by sea or air)
Perth (by air)

IDENTITY OF MANUFACTURER/RECIPIENTS
Givaudan Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemicals will be imported as a component of fragrance formulations at a concentration ≤ 1.5% packaged in glass and lacquer-lined containers of 1, 5, 10, 25, 100 and 190 kg capacity.

USE
The notified chemicals will be imported into Australia only within fragrance formulations at up to 1.5% concentration. The notified chemicals will then be reformulated and repackaged commercially by customers for public end-use. The notified chemicals will be used in cosmetics (including alcoholic perfumes, cosmetics, toiletries), and household products (including detergents and soaps). The following table shows the maximum concentration of the notified chemicals (as imported) in final consumer products.

Use	Maximum concentration of formulation	Mean concentration of formulation	Max. % of formulation in final product	Max. % chemicals in final product	Mean % chemicals in final product
Fine fragrance	1.5%	0.4%	5.0%	0.075	0.020
Cosmetics	1.0%	0.3%	4.0%	0.040	0.012
Household care	1.0%	0.2%	0.5%	0.005	0.001
Fabric care	1.0%	0.3%	0.5%	0.005	0.002

OPERATION DESCRIPTION
The notified chemicals will be imported as a formulated mixture and will be transported to the customers for reformulation and repackaging. The reformulated end-use consumer products such as alcoholic perfumes,

cosmetics, toiletries, household products, detergents and soaps will then be transported to retail outlets for sale to public.

Reformulation
The procedures for incorporating the notified chemicals (at ≤ 1.5% concentration) into end-use products (≤ 0.075% concentration) will likely vary depending on the nature of the reformulated products and may involve both automated and manual transfer steps. However, in general, it is expected that for the reformulation process, the notified chemicals will be weighed and added to the mixing tank where they will be blended with additional additives to form the finished cosmetic and household products. This is followed by automated filling of the reformulated products into retail packaging of various sizes. During the reformulation process, samples of the notified chemicals and the finished cosmetic products may be taken for quality control testing.

Household products
Household products containing the notified chemicals (≤ 0.005% concentration) may be used by consumers and professional workers. The products may be used in either closed systems with episodes of controlled exposure, for example automatic washing machines, or open processes and manually by rolling, brushing, spraying and dipping. The cleaning and washing liquids are completely discharged into industrial sewerage systems after use. In some cases, the cleaning product will be diluted with water prior to application. The dilution factor, which is often on the label, depends on the type of surface to be cleaned, the soil loading, and the type and method of application.

Cosmetics
The finished cosmetic products, including leave-on and rinse-off products, contain the notified chemicals at ≤ 0.04% concentration will be used by consumers and professionals (such as beauticians and hairdressers). Depending on the nature of the product, application of products could be by hand, sprayed or through the use of an applicator.

Fine fragrances
The finished fine fragrance products containing the notified chemicals at ≤ 0.075% concentration will be used by consumers. Depending on the nature of the product, application of products could be by pump or pressurised spray (manual or automatic).

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 Warehouse workers	none	Incidental exposure only
Mixer (plant operators)	4	2
Drum handling	4	2
Drum cleaning/washing	4	2
Maintenance	4	2
Quality control worker	4	2
Packager	4	2
End user (professionals)	1–8	200

EXPOSURE DETAILS
Transport and storage
At the notifier's facility, the primary work activity undertaken by transport and warehouse workers will include the handling, loading and off-loading of drums containing product with the notified chemicals at up to 1.5% concentration. Exposure of these workers will be limited to situations involving products sampling for quality control, or in the event of a discharge, clean up from a spill or leaking drum. If such an event occurs, a worker may be exposed through dermal or ocular contact. The notifier states that exposure will be minimised through the use of personal protective equipment (PPE) including overalls, hard hats, chemical resistant gloves and safety glasses.

Formulation of end products
During reformulation dermal, ocular and inhalation exposure of workers to the notified chemicals (at ≤ 1.5% concentration) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier anticipates that typical practices by cosmetic and consumer product manufacturers will include enclosed mixing vessels and filling areas, local ventilation, PPE such as overalls, safety glasses and impervious gloves, and a high degree of process automation. It is also expected that the workers will be provided the required training and education in proper handling of products containing the notified chemicals.

Beauty care and cleaning professionals
Exposure to the notified chemical in end-use products (at ≤ 0.04% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hair dressers, workers in beauty salons) or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use some PPE to minimise repeated exposure, but use is not expected. However, 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 up to 0.075% concentration) through the use of a wide range of cosmetic, personal care and household products. The main routes of exposure will be dermal, while ocular, oral (during facial use), and inhalation exposures (through the use of spray products) are also possible.

Data on typical use patterns of product categories in which the notified chemical may be used are shown in the following table (SCCS, 2012; Cadby *et al.*, 2002). For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. In the absence of dermal absorption data, the default dermal absorption of 100% was assumed for calculation purposes (European Commission, 2003a). For the inhalation exposure assessment (European Commission, 2003a; SDA, 2005), an adult inhalation rate of 23 m^3/day (enHealth, 2004) was used and it was assumed that the bioavailability of the notified chemical via the inhalation route is 100%. . An adult bodyweight of 60 kg has been used for calculation purposes.

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	0.04	1	0.052
Face cream	1540	0.04	1	0.010
Hand cream	2160	0.04	1	0.014
Fragrances	750	0.075	1	0.009
Liquid Foundation	510	0.04	1	0.003
Makeup remover	5000	0.04	0.1	0.003
Hair styling products	4000	0.04	0.1	0.003
Shower gel	18670	0.04	0.01	0.001
Hand wash soap	20000	0.04	0.01	0.001
Shampoo	10460	0.04	0.01	0.001
Hair conditioner	3920	0.04	0.01	0.000
Facial cleanser	800	0.04	0.01	0.000
Total				**0.099**

C = concentration; RF = retention factor based on 100% dermal absorption.
Daily exposure = mg/day × C (%) × RF
Daily systemic exposure = daily exposure × dermal absorption (%)/body weight (60 kg)

Household products (Indirect dermal exposure - from wearing clothes)

Product type	Amount	C	Product Retained	Percent Transfer	Daily systemic exposure
	(g/use)	(%)	(%)	(%)	(mg/kg bw/day)
Laundry liquid	230	0.005	0.95	10	0.0002
Fabric softener	90	0.005	0.95	10	0.0001
Total					**0.0003**

Daily systemic exposure = (Amount × C × PR × PT × dermal absorption)/body weight

Household products (Direct dermal exposure)

Product type	Frequency	C	Contact Area	Product Use C	Film Thickness	Time Scale Factor	Daily systemic exposure
	(use/day)	(%)	(cm^2)	(g/cm^3)	(cm)		(mg/kg bw/day)
Laundry liquid	1.43	0.005	1980	0.01	0.01	0.007	0.000
Dishwashing liquid	3	0.005	1980	0.009	0.01	0.03	0.000
All-purpose cleaner	1	0.005	1980	1	0.01	0.007	0.000
Total							**0.0001**

Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor x dermal absorption)/body weight

Aerosol products (Inhalation exposure)

Product type	Frequency	Amount	C	Inhalation Rate	Exposure Duration	Airspace Volume	Daily systemic exposure
	(use/day)	(g/use)	(%)	(m^3/day)	(min)	(m^3)	(mg/kg bw/day)
Hairspray	2	10	0.04	23	15	2	0.0160
Total							**0.0160**

Daily systemic exposure = (Frequency × Amount × C × Inhalation rate × Exposure duration × bioavailability via the inhalation route)/(body weight × Airspace volume)

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above table that contain the notified chemicals. This would result in a combined internal dose of 0.115 mg/kg bw/day.

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOAEL 1,000 mg/kg bw
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	non genotoxic

Toxicokinetics, metabolism and distribution.

Based on the lipophilicity of the notified chemicals (water solubility 1.38×10^{-3} g/L at 20 °C; log Pow > 6.3) dermal absorption is expected to be slow, with the rate of transfer between the stratum corneum and the epidermis limiting absorption across the skin. However, given the low molecular weight (262.4 Da) of the notified chemicals and the skin irritation findings, it is possible that the notified chemicals may be dermally absorbed. Absorption across the gastrointestinal tract in rats was confirmed by the systemic effects seen in the 28 day repeated dose toxicity study.

Acute toxicity.
A mixture of the notified chemicals was found to be of low toxicity via the oral and dermal routes.

Irritation and sensitisation.
A dermal irritation study carried out on rabbits indicated that the mixture of notified chemicals was irritating to the skin with erythema and scaling observed in all animals during the study period. The mixture of notified chemicals was found to be slightly irritating to the eyes of rabbits.

The mixture of notified chemicals was found to be a skin sensitizer in a local lymph node assay (LLNA) in mice, with reported stimulation indices of 1.1, 6.5, 11.0 and 5.9 at 1%, 10%, 30% and 'neat' concentration, respectively. The calculated EC3 value was reported to be 4.2%.

Repeated dose toxicity.
In a 28-day oral toxicity study on rats a mixture of the notified chemicals was administered at 50, 200 and 1,000 mg/kg bw/day. There were a range of treatment related effects seen in the 200 and 1,000 mg/kg bw/day dose groups that were deemed by the study authors to not be adverse. Treatment related effects included one mortality near the beginning of the study in the high dose group, a range of clinical observations (including statistically significant body weight decreases in the 1,000 mg/kg bw/day dose group), changes in blood and biochemistry parameters (at 1,000 mg/kg bw/day) and changes in the organs (liver weight increases with hepatocellular hypertrophy). A NOAEL of 1,000 mg/kg bw/day was established by the study authors, based on their determination of an absence of adverse effects.

Mutagenicity/Genotoxicity.
The mixture of notified chemicals was not mutagenic in an in vitro bacterial mutation test. The mixture of notified chemicals did not demonstrate clastogenic potential to Chinese Hamster V79 cells derived from lung tissue.

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

Hazard classification	***Hazard statement***
Skin sensitisation (Category 1B)	H317 – May cause an allergic skin reaction

Based on the available information, the notified chemicals are recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase(s):

R38: Irritating to skin
R43: May cause sensitisation by skin contact

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Reformulation
Exposure of workers to the notified chemicals (at ≤ 1.5% concentration) may occur during blending operations. While the notified chemicals may be harmful to human health via the oral route, ingestion is unlikely under the occupational settings described. The notified chemicals are considered to be skin irritants and skin sensitisers. Therefore, caution should be exercised when handling the notified chemicals during reformulation processes. However, provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to the health of workers from use of the notified chemicals is not considered to be unreasonable.

End-use
Cleaners and beauty care professionals will handle the notified chemicals at ≤ 0.04% concentration, similar to public use. Therefore, the risk to workers who regularly use products containing the notified chemicals is expected to be of a similar or lesser extent than that experienced by members of the public who use such products on a regular basis. For details of the public health risk assessment see Section 6.3.2.

6.3.2. Public Health

Repeated-dose toxicity

Members of the public may experience repeated exposure to the notified chemicals (at ≤ 0.075% concentration) through the use of cosmetic and household products.

The repeat dose toxicity potential was estimated by calculation of the margin of exposure (MoE) of the notified chemicals using the worst case exposure scenario from use of multiple products of 0.115 mg/kg bw/day (see Section 6.1.2) and the NOAEL of 1,000 mg/kg bw/day, as determined by the study authors in a 28-day repeated dose toxicity study on the notified chemical. Using the abovementioned NOAEL, the MoE was estimated to be 8,696. A MoE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences; therefore, the MoE is considered to be acceptable. However, if the treatment related effects such as the liver weight increases and changes in the biochemical parameters in both sexes in the 1,000 and 200 mg/kg bw/day dose groups are considered adverse and the next lowest dose of 50 mg/kg bw/day is used as the NOAEL the MOE estimate would still be > 100 (435).

Irritation

The notified chemicals are considered to be skin irritants. Skin irritation effects are not expected from use of the notified chemicals at the proposed concentrations in cosmetic and household products.

Sensitisation

A mixture of the notified chemicals was found to be a skin sensitiser in an LLNA in mice. Methods for the quantitative risk assessment of dermal sensitisation have been proposed and been the subject of significant discussion (see for example, Api et al., 2008 and RIVM, 2010). Using a deodorant (containing 0.04% notified chemical) as an example product that may contain the notified chemical, as a worst case scenario, the Consumer Exposure Level (CEL) is estimated to be 2.86 μg/cm^2 (Cadby et al., 2002). When tested in an LLNA study, the notified chemical was a skin sensitiser with an EC3 value of 4.2%. Consideration of the study details and application of appropriate safety factors allowed the derivation of an Acceptable Exposure Level (AEL) of 3.5 μg/cm^2. In this instance, the factors employed included an interspecies factor (3), intraspecies factor (10), a matrix factor (3.16) and a use and time factor (3.16), giving an overall safety factor of 300. As the AEL > CEL, the risk to the public of the induction of sensitisation that is associated with the use of deodorants (a worst case example of a leave-on cosmetic product) at ≤ 0.04% concentration is not considered to be unreasonable. All other cosmetic products that may contain the notified chemicals were calculated to have a lower CEL than deodorants and based on the significantly lower expected exposure level from household and fabric care products (≤ 0.005% notified chemicals) the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable. It is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on the aggregate exposure has not been conducted.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 0.075% in fine fragrances, ≤ 0.04% in other cosmetic products, ≤ 0.005% in fabric care products and ≤ 0.005% in household products, is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemicals will be imported as a formulated mixture and will be transported to the customers for reformulation and repackaging into cosmetic and household products. Accidental spills of the notified chemicals will be collected and disposed of to landfill.

For a typical reformulation process, the notified chemicals will be weighed and added to the mixing tank where they will be blended with additional additives to form the finished cosmetic and household products. Waste waters containing the notified chemicals from cleaning of the blending equipment may be disposed of to the sewer for the worst case. Up to 1% of the notified chemicals may remain in containers and be disposed of to landfill with the empty containers.

RELEASE OF CHEMICAL FROM USE

It is expected that most of the imported notified chemicals will be washed down to sewers after use.
RELEASE OF CHEMICAL FROM DISPOSAL

It is expected that up to 1% of the notified chemicals will be lost as residues in consumer containers, which are primarily sent to landfill.

7.1.2. Environmental Fate

The notified chemicals are considered neither to be readily nor inherently biodegradable based on the provided studies. The notified chemicals degraded rapidly by irradiation in aqueous systems with a maximum half-life of 5.2 days in natural light. The notified chemicals are not expected to be bioaccumulative based on the measured low bioconcentration factor (BCF) of 57.4 in fish. For the details of the environmental fate studies please refer to Appendix C. The half-life of the notified chemicals in air is calculated to be 1.3 hours based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). Therefore, in the event of release to atmosphere, the notified chemicals are not expected to persist in the atmospheric compartment.

Most of the notified chemicals will be released to the sewer after use and directed to sewage treatment plants (STPs) national wide. A small amount of the notified chemical may be sent to landfill as collected spills or container residues. In STPs, the majority of the notified chemicals are expected to be removed from the water column, via adsorption to sediment sludge, based on their high log P_{OW} ($\geq$ 6.3) and sent to landfill. In landfill, the notified chemicals are expected to undergo biotic or abiotic degradation processes, forming water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated assuming entire release of the notified chemicals to the sewer system. Using the maximum log P_{OW} of 6 and vapour pressure (6.1×10^{-2} Pa) and no degradation, the SimpleTreat model (European Commission, 2003b) predicted removal of the notified chemicals by volatilisation (1%) and partitioning to sludge (85%) during STP processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	86%	**Mitigation**
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.08	µg/L
PEC - Ocean:	0.01	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 5.15 mg/kg (dry wt). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified chemicals may approximate 0.03 mg/kg in applied soil. This assumes that degradation of the notified chemicals occurs in the soil within 1 year from application. Assuming accumulation of the notified chemicals in soil for 5 and 10 years under repeated biosolids application, the concentration of notified chemicals in the applied soil in 5 and 10 years may approximate 0.2 mg/kg and 0.3 mg/kg, respectively.

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 chemicals in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.1 µg/L may potentially result in a soil concentration of approximately 0.5 µg/kg. Assuming accumulation of the notified chemicals in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemicals in the applied soil in 5 and 10 years may be approximately 2.8 µg/kg and 5.7 µg/kg, respectively.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemicals 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 = 0.3 mg/L*	Very toxic to fish
Daphnia Toxicity	48 h EC50 > 0.26 mg/L*	Not harmful to aquatic invertebrates up to their limit of water solubility
Algal Toxicity	72 h EC50 > 0.14 mg/L*	Not harmful to algae up to their limit of water solubility
Inhibition of Bacterial Respiration	3h EC50 > 100 mg/L	Do not inhibit to microbial respiration up to their limit of water solubility

* Measured concentration for the nominal loading rate of 100 mg/L

Based on their toxicities, the notified chemicalss are considered to be very toxic to fish and, not harmful to aquatic invertebrates and algae up to their limit of water solubility. Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemicals are very toxic to aquatic organisms and are formally classified as 'Acute Category 1: Very toxic to aquatic life. On the basis of the acute toxicity and the lack of ready biodegradability, the notified chemicals are classified as 'Chronic Category 1: Very toxic to aquatic life with long lasting effects.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) was calculated using the most sensitive endpoint for fish as shown below. A safety factor of 100 was used as the acute toxicity values from three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
NOEC (algae)	0.3	mg/L
Assessment Factor	100	
PNEC:	3	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.08	3	0.028
Q - Ocean	0.01	3	0.003

The risk quotient (RQ = PEC/PNEC) for discharge of treated effluents containing the notified chemicals to the aquatic environment indicates that the notified chemicals are unlikely to reach ecotoxicologically significant concentrations based on its annual importation quantity. Therefore, on the basis of the PEC/PNEC ratio and the assessed use pattern, the notified chemicals are not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 1.38 mg/L at 20 °C

Method	OECD TG 105 Water Solubility.
Remarks	Column Elution Method
Test Facility	Givaudan (2011)

Partition Coefficient (n-octanol/water) log Pow ≥ 6.3 at 20 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water), High Performance Liquid Chromatography (HPLC) Method
Remarks	HPLC Method
Test Facility	Notox (2007a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical mixture (LTD/1744 & LTD/1745)
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/ HanRCC:WIST (SPF)
Vehicle	Polyethylene Glycol 300
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
A	3 female	2000	0/3
B	3 female	2000	0/3

LD50	> 2000 mg/kg bw
Signs of Toxicity	There were no unscheduled deaths during the study. Slightly ruffled fur was observed in all animals.
Effects in Organs	No adverse macroscopic findings were recorded at necroscopy.
Remarks - Results	The body weights of the animals were within the range commonly recorded for this strain and age, and no reductions were recorded during the observation period. .
CONCLUSION	The mixture of the notified chemicals is of low toxicity via the oral route.
TEST FACILITY	RCC (2007a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical mixture (LTD/1744 & LTD/1745)
METHOD	OECD TG 402 Acute Dermal Toxicity.
Species/Strain	Rats/HanRcc:WIST (SPF)
Vehicle	Polyethylene glycol 300
Type of dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	All animals had slight to moderate erythema, scaling and crusts starting from around day 5 and persisting to the end of the observation period in some animals.
Signs of Toxicity - Systemic	There were no signs of systemic toxicity observed in any of the test animals.
Effects in Organs	No adverse macroscopic findings were recorded at necropsy.
Remarks - Results	The body weight of the animals was within the range commonly recorded for this strain and age.
CONCLUSION	The mixture of the notified chemicals is of low toxicity via the dermal route.
TEST FACILITY	RCC (2007b)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical mixture (LTD/1744 & LTD/1745)
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbits/ New Zealand White
Number of Animals	3 (1 male and 2 females)
Vehicle	Water
Observation Period	14 days
Type of Dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	2	1.3	2	2	< 7 days	0.00
Oedema	0	0	0	0	-	0.00

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

Remarks - Results	Slight to well defined erythema was present in all animals at all observations up to day 7 when the effects had resolved. Scaling was present on all animals from the 72 hour observation and was still apparent at the end of the observation period.
CONCLUSION	The mixture of the notified chemicals is irritating to the skin.
TEST FACILITY	RCC (2007c)

B.4. Irritation – eye

TEST SUBSTANCE	Notified chemical mixture (LTD/1744 & LTD/1745)
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 (1 male and 2 females)
Observation Period	72 hours
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.33	0	0.33	1	< 48 hours	0
Conjunctiva: chemosis	0	0	0	0	-	0
Conjunctiva: discharge	0	0	0	0	-	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results	A slight reddening of the conjunctivae was observed in two animals at the 1 and 24 hour observations. Additionally the same two animals expressed a slight reddening of the sclera at the 1 hour observations. All effects had resolved by the 48 hour observation.
CONCLUSION	The mixture of the notified chemicals is slightly irritating to the eye.

TEST FACILITY RCC (2007d)

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

TEST SUBSTANCE Notified chemical mixture (LTD/1744 & LTD/1745)

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)
Species/Strain Mouse/CBA/CaHsdRcc(SPF)
Vehicle Acetone / olive oil (4/1 v/v)
Remarks - Method A concurrent positive control study was not run, but had been conducted previously in the test laboratory using α-hexylcinnamaldehyde.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	586	-
1%	619	1.1
10%	3820	6.5
30%	6463	11.0
100% (undiluted)	3463	5.9
Positive Control		
α-Hexylcinnamaldehyde		
0	314	-
5%	910	2.9
10%	1223	3.9
25%	2725	8.7

Remarks - Results All treated animals survived the scheduled study period, and no signs of systemic toxicity were noted.
The stimulation index at ≥ 10% concentration was > 3, indicating a positive response. Based on these results, the EC3 value was calculated to be 4.2%.

CONCLUSION There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the mixture of the notified chemicals.

TEST FACILITY RCC (2005)

B.6. Repeat dose toxicity

TEST SUBSTANCE Notified chemical mixture (LTD/1744 & LTD/1745)

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).
Species/Strain Rat/Han:Rcc:WIST(SPF)
Route of Administration Oral – gavage
Exposure Information Total exposure days: 28 days
Dose regimen: 7 days per week
Post-exposure observation period: none
Vehicle Corn oil
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
Control (Vehicle only)	5 per sex	0	0/10

low dose	5 per sex	50	0/10
mid dose	5 per sex	200	0/10
high dose	5 per sex	1,000	1/10

Mortality and Time to Death

One female animal that had been dosed with 1,000 mg/kg/day was killed in extremis on day 2 due to its poor condition and severe clinical signs including ruffled fur, visible weight loss, hunched posture, salivation and decreased temperature. No other animals showed such severe effects, and all the remaining animals survived to the end of the 28 day study.

Clinical Observations

Clinical signs noted during the study included salivation in both male and females in the 200 and 1,000 mg/kg/day dose groups. At the end of treatment pale ears and/or appendages were observed in all males in the 1,000 mg/kg/day dose group. One female from the 1,000 mg/kg/day dose group had adhesions at the lower mandible and a different female at the same dose showed ruffled fur at the end of treatment period. Male animals in the 50 and 200 mg/kg/day dose groups showed significantly increased locomotor activity, however as there was no dose response relationship the study authors considered the findings to be of no toxicological relevance. Body weights in the 1,000 mg/kg/day dose group were significantly decreased for both male and female animals.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Female animals treated with 1000 mg/kg/day showed significantly increased absolute white blood cell counts, absolute neutrophils, eosinophils, basophils, lymphocytes, monocytes and large unstained cell counts. Male animals in the 1000 mg/kg/day dose group showed an increase in the platelet count and a decrease in the partial thromboplastin time.

Biochemistry parameters observed in animals treated with 1000 mg/kg/day include increased cholesterol values (males 40% and females 42%), increased triglycerides (females 30%), increased alanine aminotransferase (females 70%), increased protein values (females 7%), increased potassium (males 10%), decreased chloride (females 5%) and increased creatine kinase (females 82%). There were a range of other statistically significant clinical changes recorded, however as they showed no dose response relationship or histopathological correlations they were considered to be incidental by the study authors.

Effects in Organs

There was a dose related increase in liver weights for animals of both sexes across all of the treatment groups with statistical significance achieved for both sexes in the 1000 mg/kg/day dose group (28% increase for both sexes). Statistically significant increases in the liver/body weight ratios were observed in both the 200 and 1000 mg/kg/day dose groups and liver/brain weight ratios in the 1000 mg/kg/day dose group. At the end of the treatment period, enlarged livers were observed in males and females that had been treated with 1000 mg/kg/day. In addition, histopathology indicated minimal to moderate hepatocellular hypertrophy of the livers of both sexes treated with 200 and 1000 mg/kg/day. The observed liver changes were considered to be adaptive by the study authors as these types of changes are often seen in the rodent liver following treatment with xenobiotics, and in the absence of any associated degenerative or inflammatory changes are not considered to be adverse. Other microscopic changes observed included statistically significant decreases in the body, heart and thymus weight in female animals dosed with 1000 mg/kg/day. Minimal to moderate histiocytic aggregation in females treated with 200 mg/kg/day and in both sexes treated with 1000 mg/kg/day and an increased incidence and mean severity grade of hyaline droplets in the kidneys of males that had been treated with 200 and 1000 mg/kg/day. Female rats were not tested for hyaline droplets formation in the kidneys.

Remarks – Results

The effects noted for animals in the mid and high dose groups were not considered by the study authors to be toxicologically significant. Therefore, the No Observed (Adverse) Effect Level (NO(A)EL) was established by the study authors as 1,000 mg/kg, based on their determination of an absence of adverse effects.

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) was established as 1,000 mg/kg bw/day in this study, based on the determination by the study authors of an absence of adverse effects at all doses.

TEST FACILITY RCC (2007e)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical mixture (LTD/1744 & LTD/1745)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure and Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98 & TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphtoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 3–5000 µg/plate b) Without metabolic activation: 3–5000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	No significant protocol deviations. Test 1 was conducted as a plate incorporation assay and test 2 was undertaken as a pre-incubation assay. Concurrent untreated and solvent controls were performed as negative control. Sodium azide, 4-nitro-o-phenylene-diamine and methyl methane sulfonate were used as positive controls in test without metabolic activation and 2-aminoanthracene used as positive control for test with metabolic activation.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000	> 5,000	≥ 2,500	Negative
Test 2	> 5,000	> 5,000	≥ 5,000	Negative
Present				
Test 1	> 5,000	> 5,000	≥ 2,500	Negative
Test 2	> 5,000	> 5,000	≥ 5,000	Negative

Remarks - Results	No significant increase in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose, either with or without metabolic activation. The positive controls produced satisfactory responses, thus confirming the activity of S9-mix and the sensitivity of the bacterial strains.
CONCLUSION	The mixture of the notified chemicals was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC-CCR (2006)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical mixture (LTD/1744 & LTD/1745)
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain	Chinese Hamster
Cell Type/Cell Line	V79 cells derived from lung tissue
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphtoflavone induced rat liver
Vehicle	Ethanol
Remarks - Method	No significant protocol deviations. Vehicle and positive controls (ethylmethane sufonate without metabolic activation and cyclophosphamide with metabolic activation) were used in parallel with the test substance.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0.8, 1.6, 3.1, 6.3*, 12.5*, 25.0*, 50.0, 100.0	4 h	18 h
Test 2a	1.6*, 3.1*, 6.3*, 12.5, 25.0, 50.0	18 h	18 h
Test 2b	6.3*, 12.5*, 25.0, 50.0	28 h	28 h
Present			
Test 1	0.8, 1.6, 3.1, 6.3*, 12.5*, 25.0*, 50.0, 100.0	4 h	18 h
Test 2	3.1, 6.3*, 12.5*, 25.0*, 50.0, 100.0	4 h	28 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 22.0	≥ 25.0	> 100	Negative
Test 2a	≥ 22.0	≥ 25.0	> 50	Negative
Test 2b		≥ 25.0	> 50	Negative
Present				
Test 1	≥ 44.1	≥ 50.0	≥ 25	Negative
Test 2		≥ 50.0	≥ 50	Negative

Remarks - Results

The positive controls showed increased mutation frequency, confirming the validity of the test system. The mutation frequencies in the test groups did not show a biologically relevant increase, compared to the controls. In test 1 in the presence of metabolic activation the number of aberrant cells exceeded the historical controls, however as the increase was not statistically significant and showed no dose dependency the study authors did not consider it to be biologically relevant.

CONCLUSION

The mixture of the notified chemicals was not clastogenic to Chinese hamster V79 cells treated in vitro under the conditions of the test.

TEST FACILITY

RCC-CCR (2007)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Fresh activated sludge
Exposure Period	28 days
Auxiliary Solvent	Not applied
Analytical Monitoring	The amount of oxygen taken up by the micro-organisms was expressed as a percentage of theoretical oxygen demand (ThOD)
Remarks - Method	The above test guideline and good laboratory practice (GLP) were followed. The test was conducted at a concentration of 100 mg/L. Deionised water containing less than 10 mg/L dissolved organic carbon was used.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
5	0	5	70
14	1	7	77
28	1	28	90

Remarks - Results	All the test validity criteria were met. The toxicity control test indicates that the notified chemicals did not show toxic effects to the micro-organisms at the test concentration. A degradation of 1% was achieved by 28 day of the test. Therefore, the notified chemicals were considered not to be readily biodegradable.
CONCLUSION	The notified chemicals are not readily biodegradable
TEST FACILITY	Givaudan (2007)

C.1.2. Ready biodegradability

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Natural river water only was used without addition of any mineral salts.
Exposure Period	28 days
Auxiliary Solvent	Not applied
Analytical Monitoring	Not applied
Conclusion	A biodegradation degree of 14% was determined by day 28 of the test. The test did not follow the test guideline and good laboratory practice (GLP). Instead of deionised water (required in the test guideline), natural water only was used. Therefore, this study is not considered for risk assessment purposes.
TEST FACILITY	Givaudan (2010)

C.1.3. Ready biodegradability

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Sewage sludge micro-organisms

Exposure Period	28 days
Auxiliary Solvent	Acetone
Analytical Monitoring	The total amount of amount of oxygen taken up by the micro-organisms was expressed as a percentage of theoretical oxygen demand (ThOD)
Remarks - Method	The above test guideline and good laboratory practice (GLP) were followed. The test was conducted at a concentration of 1.0 mg/L. The test substance was added to the test vessels using an inert support glass fibre filter paper due to the low water solubility.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
3	9	3	32
14	10	11	60
28	12	28	78

Remarks - Results	All the test validity criteria were met. The toxicity control test indicates that the notified chemicals did not show toxic effects to the micro-organisms at the test concentration. A degradation of 12% was achieved by 28 day of the test. Therefore, the notified chemicals were considered not to be readily biodegradable.

CONCLUSION The notified chemicals are not readily biodegradable.

TEST FACILITY Harlan (2009)

C.1.4. Ready biodegradability

TEST SUBSTANCE Notified chemicals

METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Sewage effluent mirco-organisms
Exposure Period	28 days
Auxiliary Solvent	Acetone
Analytical Monitoring	Biological Oxygen Demand (BOD) was determined and expressed as a percentage of theoretical oxygen demand (ThOD)
Remarks - Method	The test was conducted following the test guideline and the national certificated laboratory practice. The test was conducted at a concentration of 2.0 mg/L.

RESULTS

Test substance		*Sodium lauryl sulfate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	0.49	7	60.4
14	0.82	14	72.4
28	1.15	28	74.5

Remarks - Results	All the test validity criteria were met. A degradation of 1.15% was achieved by 28 day of the test. The toxicity control test was not conducted. This is considered to be acceptable since the previous degradability studies indicated that the notified chemicals were not toxic to micro-organisms. The notified chemicals were considered not to be readily biodegradable.

CONCLUSION The notified chemicals are not readily biodegradable.

TEST FACILITY SAES (2007a)

C.1.5. Inherent biodegradability

TEST SUBSTANCE	Notified chemicals
METHOD	OECD Guideline for the Testing of Chemicals No. 302C, Paris, 1992; EC Council Regulation 2008/440/EC: C.4. Determination of Ready Biodegradability, Part V., Manometric Respirometry Test (Method C.4-D); OECD Guideline for Testing of Chemicals, Draft for Guideline 302D: Inherent Biodegradability: CONCAWE Test; EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.3100 Aerobic Aquatic Biodegradation.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	Not applied
Analytical Monitoring	The total amount of amount of oxygen taken up by the micro-organisms was expressed as a percentage of theoretical oxygen demand (ThOD).
Remarks – Method	The above test guideline and good laboratory practice (GLP) were followed. A measured volume of inoculated mineral medium, containing the test substance (30 mg/L) as the nominal sole source of organic carbon, was stirred in a closed flask at a constant temperature for 28 days or more. The consumption of oxygen was determined by measuring the quantity of oxygen required to maintain constant the gas volume in the respirometer flask. Evolved carbon dioxide was absorbed in soda lime pellets.
RESULTS	
Remarks – Results	All the test validity criteria were met. A toxicity test indicated no toxicity to the inoculum at the test concentration (30 mg/L). At the end of the experiment, the test flasks were extracted with an appropriate solvent, and analysed by gas chromatography. 75 % to 95 % of the test substance was recovered, showing that it underwent no significant primary degradation. Based on the oxygen uptake, the notified chemicals reached 5 % biodegradation after 28 days (5 % biodegradation after 29 days) in the test conditions. No further detailed data were provided in the test report. Thus, the notified chemicals should be regarded as not inherently biodegradable according to this test method.
CONCLUSION	The notified chemicals are not inherently biodegradable.
TEST FACILITY	Givaudan (2009)

C.1.6. Bioaccumulation

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 305B Bioconcentration: Semi-static Fish Test (Adopted: 12 May 1981)
Species	
Exposure Period	Exposure: 28 days Depuration: not reported
Auxiliary Solvent	Acetone
Concentration Range	Nominal: 0.01 and 0.015mg/L Actual: not reported
Analytical Monitoring	GC with FID and DB-WAX column was used in this study to determine the

	concentrations in fish and water samples.
Remarks - Method	The bioaccumulation test was performed in triplicate at nominal concentrations of 0.01 mg/L and 0.015 mg/L with renewal of test solution every 24 hours. The stock solution was prepared with acetone. Each test vessel contained 10 fish. New test media were prepared one day early to reach equilibrium between test substance and dilution water. No depuration period was reported.
RESULTS	
Bioconcentration Factor	57.4 (average value of two concentrations)
LC50	0.178 mg/L (96 h, 95% CI 0.157-0.202 mg/L)
Remarks - Results	All the test validity criteria were met. The recoveries in dilution water were 80.4% – 84.9% with relative standard deviations of 0.4% – 1.1%. The recoveries in fish were 91.5% – 100% with relative standard deviations of 4.5% – 6.7%. The limit of detection was 0.033 ng/L and the limit of quantification was 1.65 pg/L in water and 0.198 mg/kg in fish, respectively for this analytical method. Steady state was reached after day 27 of the test. The BCF for the notified chemicals on zebra fish was 48.4 for the 0.010 mg/L level and 66.5 for the 0.015 mg/L level. The overall average BCF was determined to be 57.4 and the relative standard deviation was 18.3%. Lipid concentration and lipid level correction was not discussed in the test report.
CONCLUSION	The notified chemicals are not bioaccumulative in fish
TEST FACILITY	Supervision and Test Center (2008)

C.1.7. Photodegradation

TEST SUBSTANCE	Notified chemical
METHOD	OECD Guideline 316 for Testing of Chemicals: Photo-transformation of Chemicals in Water – Direct Photolysis. Adopted: October 03, 2008.
Light source and Spectrum	"Suntest" apparatii, equipped with xenon lamps, with filters to remove wavelengths below 290 nm.
Relative Intensity	46 W/m^2 (within 300 to 400 nm, mean value, penetrating the surfaces of the aqueous solutions).
Spectrum of Test Substance	Not provided
Exposure Period	3 days for buffer solutions and 2 days for natural water
Remarks – Method	The test was conducted following the above test guideline. This study was not conducted under Good Laboratory Practice (GLP) status. The general performance of the study (maintenance of records during experimental and reporting phase, preparation of materials, etc.) respected the general guidelines of GLP. The notified chemicals were irradiated with a xenon arc light source at about 25 °C in sterile aqueous buffer solution at pH 7, natural pond water and sterile natural pond water in duplicate. The test concentrations were 0.188 mg/L, 0.25 mg/L and 0.265 mg/L, respectively for the three systems. The 3 days irradiation time corresponded to 4.4 days of midsummer sunlight at latitudes 30-40°N and 4.6 days at latitude 50°N. Dark control solutions were treated in the same way as the irradiated solutions, except that they were protected from light. Acetonitrile was used as a co-solvent at 1%. The test solutions were analysed using LC-MS analysis. The rates of photo-degradation of the notified chemicals in the different systems were described using single first-order kinetics.

RESULTS

Remarks - Results

The test quality criteria were met. In the irradiated buffer solution the mean amounts of the notified chemicals decreased from initially 100% to 27.3% within 3 days of irradiation. In the buffered dark control samples 67.3% of the notified chemicals were detected after 3 days of incubation. Losses in the dark controls were mainly due to volatilisation of the test item. Evaporation of water from the systems was not an issue, since the test systems were entirely closed. Adsorption of the test item to the walls of the test vessels was ≤ 5.5% of the applied amount. In the irradiated natural water system the concentration of the notified chemicals decreased to 44.8% within 2 days. The corresponding value for the dark control was 69.1%. In sterile natural water 42.5% of the test item was detected after 2 days of irradiation, whereas the test item still represented 75.1% in the respective dark control. The amounts of test item adsorbed to the walls of the test vessels were below the detection limit of 0.005 µg/mL.

In conclusion, the notified chemicals degraded rapidly by irradiation in all three aqueous systems showing a maximum half-life of 2.9 days in artificial sunlight corresponding to 5.2 days at latitude 50°N. Observed losses in the dark control samples were due to volatilisation and were corrected for in the kinetics calculations for the irradiated samples.

CONCLUSION The notified chemicals degraded rapidly by irradiation in aqueous systems with a maximum half-life of 5.2 days at latitude 50°N

TEST FACILITY IES (2010)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to Fish

TEST SUBSTANCE Notified chemicals

METHOD OECD TG 203 Fish, Acute Toxicity Test – Semi-Static Test

Species Carp (*Cyprinus carpio*)

Exposure Period 96 hours

Auxiliary Solvent Not reported

Water Hardness 180 mg $CaCO_3$/L

Analytical Monitoring Gas Chromatography (GC) Analysis

Remarks – Method The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

The fish ecotoxicity test was conducted in water accommodated fractions (WAFs) of the test substance. A WAF of nominal loading of 100 mg/L was prepared by stirring the test substance in ISO-medium for 48 hours. The WAF solution was then filtered through a membrane filter (0.45 µm). The clear and colourless filtered WAF was used for the test. Two lower concentrations of WAFs were prepared by subsequent dilutions of the filtrate in ISO-medium.

RESULTS

Concentration ((mg/L;WAF)		*Number of Fish*	*Cumulative Mortality (%)*				
Nominal	*Measured*		*2 1/2 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	-	7	0	0	0	0	0
10	0.046	7	0	0	0	0	0
32	0.16	7	0	0	0	0	0
100	0.57	7	0	0	100	100	100

LL50	0.3 (0.16 – 0.57) mg/L at 96 hours
NOEL	0.16 mg/L at 96 hours.
Remarks – Results	All validity criteria for the test were satisfied. The actual concentrations of the test substance in WAFs were measured periodically at 0 and 24 hours. The test solutions were renewed every 24 hours during the 96-h test period. The median lethal loading rate (LL50) and no observed effect loading rate (NOEL) values were calculated based on the measured treatment concentrations.
CONCLUSION	The notified chemicals are very toxic to fish (carp)
TEST FACILITY	Notox (2007b)

C.2.2. Acute toxicity to Fish

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-Static Test
Species	Zebra fish (*Brachydanio rerio)*
Exposure Period	96 hours
Auxiliary Solvent	Not reported
Water Hardness	Not reported
Analytical Monitoring	Gas Chromatography (GC) Analysis
Remarks – Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported. The fish ecotoxicity test was conducted in water accommodated fractions (WAFs) of the test substance. A WAF of nominal loading of 100 mg/L was prepared by stirring the test substance for 4 hours. The WAF solution was then filtered through a membrane filter (0.45 µm). The clear and colourless filtered WAF was used for the test.

RESULTS

Concentration (mg/L; Filtered WAF)		*Number of Fish*	*Cumulative Mortality (%)*				
Nominal	*Measured*		*2 1/2 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	-	10	0	0	0	0	0
100	0.63 (0 h) 0.18 (96 h)	10	0	0	0	0	0

LL50	> 100 mg/L at 96 hours (nominal concentration)
NOEL	100 mg/L at 96 hours.
Remarks – Results	All validity criteria for the test were satisfied. The test treatment was renewed at every 24 hours. The actual concentrations of the test substance in WAFs were measured at 0 and 24 hours from day 0 to until the end of the test. The median lethal loading rate (LL50) and no observed effect loading rate (NOEL) values were determined based on the nominal loading rate. Acute toxicity for the test substance was not observed at the loading rate tested.
CONCLUSION	The notified chemicals were not harmful to zebra fish up to the limit of their water solubility
TEST FACILITY	SAES (2007b)

C.2.3. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – Static Test
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Not reported
Water Hardness	180 mg $CaCO_3$/L
Analytical Monitoring	Gas Chromatography (GC) Analysis
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported. The daphnia ecotoxicity test was conducted in water accommodated fractions (WAFs) of the test substance. A WAF of nominal loading of 100 mg/L was prepared by stirring the test substance in ISO-medium for 48 hours. The WAF solution was then filtered through a membrane filter (0.45 µm). The clear and colourless filtered WAF was used for the test. A lower concentrations of WAF (10% concentration) was prepared by dilution of the filtrate in ISO-medium.

RESULTS

Concentration (filtered WAF; mg/L)		*Number of D. magna*	*Cumulative Immobilised (%)*	
Nominal	*Measured*		*24 h*	*48 h*
Control	Control	20	0	0
10	Not determined	10	0	0
100	0.264	20	0	0

EL50	> 100 mg/L at 48 hours (nominal concentration); > 0.26 mg/L at 48 hours (measured concentration)
NOEL	100 mg/L at 48 hours (nominal concentration)
Remarks - Results	All validity criteria for the test were satisfied. The actual concentrations of the test substance in WAFs were measured at 0 and 48 hours within the 48-h test period. EL50 and NOEL values were calculated based on the initial measured concentration as the measured concentration remained constant during the exposure period.
CONCLUSION	The notified chemicals are not harmful to aquatic invertebrates up to the limit of their water solubility
TEST FACILITY	Notox (2007c)

C.2.4. Algal growth inhibition test

TEST SUBSTANCE	Notified chemicals
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	96 hours
Concentration Range	Nominal: 4.6, 10, 22, 46, and 100% Measured: 0.0061, 0.014, 0.018, 0.052, 0.14 mg/L
Auxiliary Solvent	Not reported
Water Hardness	Not reported
Analytical Monitoring	Gas Chromatography (GC) Analysis
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

The algae ecotoxicity test was conducted in water accommodated fractions (WAFs) of the test substance. A WAF of nominal loading rate of 100 mg/L was prepared by stirring the test substance in M2-medium for 50 hours. The WAF solution was then filtered through a membrane filter (0.45 µm). The clear and colourless filtered WAFs were used for the test. Lower concentrations of WAFs were prepared by dilution of the filtrate in M2-medium. The exponentially growing algae cultures were exposed to five treatment concentrations which were filtered prior to the toxicity test. All the exposure treatments (loading rates) were clear and colourless. The treatment WAF solutions were prepared in algal test medium.

RESULTS

Biomass (72 h) (filtered WAF; mg/L)		*Growth (72 h) (filtered WAF; mg/L)*	
E_yL50 (mg/L)	*NOE_yL (mg/L)*	*E_rL50 (mg/L)*	*NOE_rL (mg/L)*
0.1 – 0.35	0.052	> 0.14	0.05

Remarks - Results

All validity criteria for the test were satisfied. Chemical analyses of the test substance in WAFs were conducted at 0, 24 and 72 hours of the test. Therefore, toxicity endpoints were calculated based on the measured concentrations. It was noted in the study report that the toxicity endpoint for biomass was reported as a range. It is likely that the extrapolated results for the upper and lowers confident intervals were presented in the study. Statistically significant reduction of growth rate was found at the highest treatment, which was at the loading rate of 100 mg/L (measured concentration of 0.14 mg/L). The endpoints were calculated using Analysis of Variance (ANOVA). The median toxicity values were above the solubility limit of the test substance.

CONCLUSION

The notified chemicals are not harmful to algae up to the limit of their water solubility

TEST FACILITY

Notox (2007d)

C.2.5. Inhibition of microbial activity

TEST SUBSTANCE

Notified chemicals

METHOD

OECD TG 209 Activated Sludge, Respiration Inhibition Test.

Inoculum: Activated sludge

Exposure Period: 3 hours

Concentration Range: Nominal: 100 mg/L

Remarks – Method: The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

RESULTS

EC20: Not reported

EC50: > 100 mg/L

Remarks – Results: All validity criteria for the test were satisfied. A loading rate of 100 mg/L was tested in duplicate. The EC50 exceeded the tested concentration (> 100 mg/L). The duplicate measurement confirmed the test result from the preliminary test. Therefore, no further testing was needed.

CONCLUSION

The notified chemicals do not inhibit to microbial respiration up to their limit of water solubility

TEST FACILITY

Notox (2007e)

BIBLIOGRAPHY

Api AM, Basketter DA, Cadby PA, Cano MF, Ellis G, Gerberick GF, Griem P, McNamee PM, Ryan CA and Safford R (2008) Dermal Sensitization Quantitative Risk Assessment (QRA) for Fragrance Ingredients. Regul. Toxicol. Pharm., 52:3-23.

Cadby, P.A., Troy, W.R. and Vey, M.G.H. (2002) Consumer Exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation. Regulatory Toxicology and Pharmacology, 36: 246-252.

enHealth (2004) Environmental Health Risk Assessment, Guidelines for Assessing Human Health Risks from Environmental Hazards. Canberra, Department of Health and Ageing and enHealth Council, Commonwealth of Australia.

European Commission (2003a) Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances and Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market – Part I. Institute for Health and Consumer protection, European Chemicals Bureau, European Communities.

European Commission (2003b). Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances and Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market – Part II. Institute for Health and Consumer protection, European Chemicals Bureau, European Communities.

Givaudan (2007) Ready Biodegradability of GR-86-7554 according to OECD Guideline No. 301F (Study No. 07-E020, June, 2007). Switzerland, Givaudan Suisse SA, Ecotoxicological Laboratory (Unpublished report submitted by the notifier).

Givaudan (2009) Inherent biodegradability of GR-86-7554 (Study No. 08-E094, February, 2009). Switzerland, Givaudan Suisse SA, Ecotoxicological Laboratory (Unpublished report submitted by the notifier).

Givaudan (2010) Ready biodegradability of GR-86-7554 (Study No. 10-E065/P, April, 2009). Switzerland, Givaudan Suisse SA, Ecotoxicological Laboratory (Unpublished report submitted by the notifier).

Givaudan (2011) Water solubility of GR-86-7554 (Study No. 11-E197, October, 2011). Switzerland, Givaudan Suisse SA, Ecotoxicological Laboratory (Unpublished report submitted by the notifier).

Harlan (2009) Ambermax: Assessment of Ready Biodegradability; Closed Bottle Test (Project No. 1895/0018, August, 2009). Derbyshire, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

IES (2010) Ambermax: Aqueous Photolysis in Buffer Solution at pH 7, Natural Water and Sterile Natural Water (Study No. 50501131, August, 2010). Vernier, Switzerland, Innovative Environmental Services Ltd (Unpublished report submitted by the notifier).

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

Notox (2007a) Determination of the Partition Coefficient (N-Octoanol/Water) of GR-86-7554 (Project No. 485878, August, 2007). The Netherland, Totox B. V. (Unpublished report submitted by the notifier).

Notox (2007b) 96-Hour Toxicity Study in Carp with GR-86-7554 (Semi-Static) (Project No. 484740, December, 2007). The Netherland, Totox B. V. (Unpublished report submitted by the notifier).

Notox (2007c) Acute Toxicity Study in *Daphnia magna* with GR-86-7554 (Static) (Project No. 484739, October, 2007). The Netherland, Totox B. V. (Unpublished report submitted by the notifier).

Notox (2007d) Freshwater Algal Growth Inhibition Test with GR-86-7554 (Project No. 484741, December, 2007). The Netherland, Totox B. V. (Unpublished report submitted by the notifier).

Notox (2007e) Activated Sludge Respiration Inhibition Test with GR-86-7554 (Project No. 486295, October, 2007). The Netherland, Totox B. V. (Unpublished report submitted by the notifier).

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia

RCC (2005) GR-86-7554: Local Lymph Node Assay (LLNA) in Mice (Identification of Contact Allergens) (Study No. A36674, December, 2005). Füllinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by the notifier).

RCC (2007a) GR-86-7554: Acute Oral Toxicity Study in Rats (Study No. B27450, June, 2007). Füllinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by the notifier).

RCC (2007b) GR-86-7554: Acute Dermal Toxicity Study in Rats (Study No. B43773, September, 2007). Füllinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by the notifier).

RCC (2007c) GR-86-7554: Primary Skin Irritation Study in Rabbits (4-Hour Semi-Occlusive Application) (Study No. B27461, June, 2007). Füllinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by the notifier).

RCC (2007d) GR-86-7554: Primary Eye Irritation Study in Rabbits (Study No. B27472, June, 2007). Füllinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by the notifier).

RCC (2007e) GR-86-7554: 28-Day Oral Toxicity (Gavage) Study in the Wistar Rat (Study No. B27494, December, 2007). Füllinsdorf, Switzerland, RCC Ltd (Unpublished report submitted by the notifier).

RCC-CCR (2006) Salmonella typhimurium and Escherichia coli Reverse Mutation Assay with GR-86-7554 (Study No. 917502, January, 2006). Rossdorf, Germany, RCC Cytotest Cell Research GmbH (RCC-CCR) (Unpublished report submitted by the notifier).

RCC-CCR (2007) In Vitro Chromosome Aberration Test in Chinese Hamster V79 Cells with GR-86-7554 (Study No. 1082500, October, 2007). Rossdorf, Germany, RCC Cytotest Cell Research GmbH (RCC-CCR) (Unpublished report submitted by the notifier).

RIVM (2010) Observations on the Methodology for Quantitative Risk Assessment of Dermal Allergens, Report 320015003/2010, National Institute for Public Health and the Environment.

SAES (2007a) Ready biodegradability Test of GR-86-7554 with Closed Bottle Test Method (Study No. S-011-2007, June, 2007). Shanghai, P. R. China, Shanghai Academy of Environmental Sciences (Unpublished report submitted by the notifier).

SAES (2007b) Acute Toxicity Test of GR-86-7554 on fish (Study No. S-006-2007, June, 2007). Shanghai, P. R. China, Shanghai Academy of Environmental Sciences (Unpublished report submitted by the notifier).

SCCS (2010) Notes of Guidance for testing of Cosmetic Ingredients and Their Safety Evaluation (7th revision) European Commission - Scientific Committee on Consumer Safety.

SDA (2005) Exposure and Risk Screening Methods for Consumer Product Ingredients. Washington DC USA, The Soap and Detergent Association.

Supervision and Test Center (2008) Bioaccumulation test of GR-86-7554 in zebra fish (Semi-Static Method) (Study No. G0744J0010, May, 2008). Shenyang, P.R. China, Supervision and Test Center for Pesticide Safety Evaluation and Qualitv Control (Unpublished report submitted by the notifier).

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/managing-risks-of-hazardous-chemicals-in-the-workplace.

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 >.

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 >.

US EPA (2010) Estimations Program Interface Suite™ for Microsoft® Windows, v 4.10. United States Environmental Protection Agency. Washington, DC, USA.