File No: LTD/1577

February 2012

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Aladinate

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (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 Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Sustainability, Environment, Water, Population and Communities.

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:

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

Director
NICNAS

TABLE OF CONTENTS

SUMMARY 3
CONCLUSIONS AND REGULATORY OBLIGATIONS 3
ASSESSMENT DETAILS 5
1. APPLICANT AND NOTIFICATION DETAILS 5
2. IDENTITY OF CHEMICAL 5
3. COMPOSITION 5
4. PHYSICAL AND CHEMICAL PROPERTIES 5
5. INTRODUCTION AND USE INFORMATION 6
6. HUMAN HEALTH IMPLICATIONS 7
6.1. Exposure Assessment 7
6.1.1. Occupational Exposure 7
6.1.2. Public Exposure 7
6.2. Human Health Effects Assessment 8
6.3. Human Health Risk Characterisation 11
6.3.1. Occupational Health and Safety 11
6.3.2. Public Health 11
7. ENVIRONMENTAL IMPLICATIONS 11
7.1. Environmental Exposure & Fate Assessment 11
7.1.1. Environmental Exposure 11
7.1.2. Environmental Fate 12
7.1.3. Predicted Environmental Concentration (PEC) 12
7.2. Environmental Effects Assessment 13
7.2.1. Predicted No-Effect Concentration 13
7.3. Environmental Risk Assessment 14
APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES 15
APPENDIX B: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS 16
B.1. Ecotoxicological Investigations 16
B.1.1. Algal growth inhibition test 16
B.1.2. Algal growth inhibition test 16
BIBLIOGRAPHY 18

SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS SUBSTANCE	INTRODUCTION VOLUME	USE
LTD/1577	Firmenich Limited	Aladinate	Yes	< 1 tonne per annum	Component of cosmetic and household products

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the data provided the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] with the following risk phrase:

R38 Irritating to skin.

and

The classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2009) is presented below.

	Hazard category	***Hazard statement***
Skin Corrosion/Irritation	Category 2	Causes skin irritation
Aquatic Environment	Acute Category 1	Very toxic to aquatic life Not classified for long term hazard

Human health risk assessment
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, maximum import volume and the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following health hazard classification for the notified chemical:
  - Xi: R38 Irritating to skin

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc ≥ 20%: Xi; R38 Control Measures

Occupational Health and Safety

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the notified chemical when used in the proposed manner; however, these should be selected on the basis of all ingredients in the formulation.

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of to landfill. Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
  - the importation volume exceeds one tonne per annum notified chemical;
  - the concentration of the chemical exceeds or is intended to exceed 1.15% in fine fragrances, 2.5% in other cosmetic products and 5% in household cleaning products.

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of cosmetic and household cleaning products, or is likely to change 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.

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

ASSESSMENT DETAILS

The notifier has submitted with the application an assessment of the chemical by a notification and assessment scheme in an OECD country (Canada). The health and environment hazard assessment of the Canadian reports were provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment, including the recommendations on safe use of the notified chemical, were carried out by NICNAS.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Firmenich Limited (ABN: 86 002 964 794)
73 Kenneth Road
Balgowlah, NSW 2093

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, degree of purity, impurities and additives/adjuvants.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Dissociation constant and flammability

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
LVCR/85

NOTIFICATION IN OTHER COUNTRIES
Canada (2007), EU (2001), Japan (2006), Philippines (2005), Switzerland (2002), South Korea (2006), USA (2001).

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Aladinate

MOLECULAR WEIGHT
Mn < 500 Da

ANALYTICAL DATA
Reference NMR, IR, HPLC, GC, GPC, UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless Liquid

Property	Value	Data Source/Justification
Freezing Point	< –20°C	Measured (92/69/EEC A1)
Boiling Point	193 °C at 101.3 kPa	Measured (92/69/EEC A2, differential scanning calorimetry)

Property	Value	Data Source/Justification
Density	900 kg/m^3 at 20ºC	Measured (92/69/EEC A3, Pycnometer method)
Vapour Pressure	0.115 kPa at 25 ºC	Measured (92/69/EEC A9)
Water Solubility	0.368 g/L at 20ºC	Measured (92/69/EEC A6, Flask method)
Hydrolysis as a Function of pH	≥ 60% at pH 2-12, 40ºC	Measured
Partition Coefficient (n-octanol/water)	log Pow = 3.17 at 20ºC	Measured (92/69/EEC A8, HPLC method)
Surface Tension	59.2 mN/m at 20ºC	Measured. The notified chemical is considered a surface-active material.
Adsorption/Desorption	Log Koc = 2.25	Measured (2001/59/EEC C19, HPLC screening method)
Dissociation Constant	Not determined	Does not contain dissociable functionality
Flash Point	66 ºC at 101.78 kPa	Classified as CI combustible liquid (NOHSC 2001)
Flammability	Not determined	Based on measured flashed point not classified as flammable (NTC 2007)
Autoignition Temperature	304 ºC	Measured
Explosive Properties	Predicted not to be explosive	Estimated

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use. Temperatures near or above the flash point should be avoided during transport and storage.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified chemical is 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 chemical.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia as a component (≤ 5%) of compounded fragrance preparations.

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 wharf or airport

IDENTITY OF MANUFACTURER/RECIPIENTS
Firmenich Ltd

TRANSPORTATION AND PACKAGING
The compounded fragrance preparations containing the notified chemical (at ≤ 5% concentration) will be imported in tightly closed lacquered drums, typically of 180 kg size, but also 100, 50, 25 10 or 5 kg. They will be transported by road from the wharf or airport of entry to the Firmenich Ltd warehouse for storage and then distributed to reformulation sites. The end-use products will be packaged in containers suitable for retail sale.

USE

The notified chemical will be used as a fragrance ingredient in a variety of cosmetic and household products, including fine fragrances (at ≤ 1.15% concentration), cosmetics (at ≤ 2.5%) and household cleaning products (at ≤ 5%).

OPERATION DESCRIPTION

The procedures for incorporating the imported compounded fragrance preparations (containing ≤ 5% notified chemical) into end-use products will likely vary depending on the nature of the cosmetic and household products formulated, and may involve both automated and manual transfer steps. However, in general, it is expected that the reformulation processes will involve blending operations that will be highly automated and occur in a fully enclosed environment, followed by automated filling of the reformulated products into containers of various sizes.

The final consumer products will be distributed to retailed outlets, displayed and sold to consumers and professionals such as hairdressers, workers in beauty salons or cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport workers	4	Unknown	Unknown
Mixer	5	4	2
Drum handler	5	4	2
Drum cleaner	8	4	2
Maintenance	5	4	2
Quality Control	1	0.5	1
Packaging	10	4	2
Salon workers	Unspecified	Unspecified	Unspecified
Cleaners	Unspecified	Unspecified	Unspecified

EXPOSURE DETAILS

Transport and storage workers may come into contact with the notified chemical, as a component of the imported compounded fragrance preparations or end-use products (at ≤ 5%), only in the event of accidental rupture of containers.

During formulation, dermal, ocular and perhaps inhalation exposure to the notified chemical (at ≤ 5% concentration) may occur during weighing and manual transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. Exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems and through the use of personal protective equipment (PPE) such as coveralls, safety glasses and impervious gloves.

Exposure to the notified chemical in end-use products (at ≤ 5% 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) or in the cleaning industry. Such professionals may use some personal protective equipment 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 through the use of fine fragrances (at ≤1.15%), cosmetics (at ≤2.5%) and household cleaning products (at ≤5%). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	moderately irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days	NOAEL > 1000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberration test in Human Lymphocyte cells	non genotoxic

Acute oral toxicity.
The acute oral toxicity of the notified chemical to Sprague-Dawley rats was determined in accordance with OECD Guideline for Testing of Chemicals 423. The notified chemical was administered undiluted by gastric gavage. Three female animals were dosed initially and observed to confirm survival and then three male animals were dosed in the same manner. Animals were dosed at 2000 mg/kg bw and were observed for 14 days. One male animal was found dead four days post-dose after showing clinical signs of decreased respiratory rate, gasping, laboured and noisy respiration, emaciation, dehydration and pallor of the extremities. Necropsy results of this animal indicated haemorrhagic lungs, dark liver, dark kidneys, and gaseous stomach and intestines. No speculation as to the cause of death of this animal was reported. No other animals died during the study and hunched posture was observed for all but one animal between ½ hour after dosing and 4 hours after dosing. The hunched posture was not observed in any animal one day after dosing. Ataxia was observed in one female, one hour after dosing but the animal recovered by the 2 hour observation. All surviving animals showed expected weight gains. No abnormalities were detected in any animals that completed the study. The acute oral LD50 for the notified chemical is > 2000 mg/kg bw and determined to be of low acute oral toxicity

Acute dermal toxicity.
The acute dermal toxicity of the notified chemical to Sprague-Dawley rats was determined in accordance with OECD Guideline for Testing of Chemicals 402. The notified chemical was administered to the back and flank area of five healthy male and five healthy female rats. All rats were dermally exposed to doses of 2000 mg/kg.bw undiluted notified chemical, which was corrected for density, and applied evenly to approximately 10% of the total body surface area for 24 hours under a gauze pad and semi-occlusive dressing. After 24 hours the dressing and pads were removed and residual test substance was removed by wiping with cotton wool moistened with distilled water. Dermal reactions were scored after patch removal and animals were observed for 14 days and then killed by cervical dislocation and necropsied. None of the animals died while on study and there were no signs of systemic toxicity. All animals showed expected body weight gains over the study period. No dermal irritation was reported and no abnormalities were noted at necropsy. The dermal acute LD50 for the notified chemical is > 2000 mg/kg bw and determined to be of low acute dermal toxicity.

Irritation.
a) The acute dermal irritation/corrosion of the notified chemical to New Zealand White rabbits was examined in accordance with OECD 404. Three male rabbits were dermally exposed to undiluted notified chemical. The notified chemical was introduced to shorn skin of the dorsal/flank region under a cotton gauze patch and semi-occlusive dressing. At the end of the 4-hour exposure period, dressing and patches were removed and residual notified chemical was removed by gentle swabbing with cotton wool soaked in 74% Industrial Methylated Spirits (IMS). Test sites were scored for erythema and edema by a numerical scale. Well-defined erythema and very slight oedema were noted at all treated skin sites one hour after patch removal which persisted in some animals to the 72-hour observation. Loss of skin elasticity and light brown discolouration of the epidermis was observed in at least one animal at the 72-hour observation and crust formation was noted in two animals at the 7-day observation. All treated sites were normal at the 14-day observation. Based on the results of this study the notified chemical is moderately irritating to skin under the conditions of the test.

b) The acute ocular irritation / corrosion of the notified chemical to New Zealand White rabbits was examined in accordance with OECD 405. Three male rabbits, one of which was a pilot animal, were subjected to ocular exposure with 0.1 mL undiluted notified chemical for a reported exposure of one second. One to two minutes

prior to dosing, both eyes of each animal were treated with one drop of local anaesthetic to minimize pain. Eyes were not washed after exposure to the notified chemical. All rabbits were examined for irritation at 1, 24, 48, and 72 hours post-dose and graded on a numerical scale. Minimal to moderate conjunctival irritation was noted in all treated eyes one hour and 24 hours after dosing. One animal was observed to have scattered or diffuse corneal opacity at the 24-hour observation and minimal conjunctival irritation was noted at the 48-hour observation. All treated eyes appeared normal at the 72-hour observation. Based on the results of this study the notified chemical is slightly irritating to the eyes under the conditions of the test.

Sensitisation.
Skin sensitisation of the notified chemical to guinea pigs was determined in accordance with OECD 406. For the purpose of establishing main study dose levels, range finding tests were conducted on two guinea pigs using doses of 1 and 5% v/v test substance in arachis oil for intradermal induction and 25, 50 and 75% v/v test substance in arachis oil and undiluted notified chemical for topical induction. The highest concentration that produced mild to moderate dermal irritation was selected for both of the induction phases of the main study (5% v/v test substance in arachis oil for intradermal induction, undiluted for topical induction), while the highest and second-highest (to confirm maximum non-irritant concentration) non-irritant concentrations were selected for the main study challenge (75% v/v test substance in arachis oil and notified chemical). The results for the intradermal induction phase of the main study indicated moderate and confluent erythema at 24 and 48 hours post-exposure to the notified chemical in all treated animals while discrete or patchy erythema was observed in all control animals at 24 hours post exposure to vehicle. Topical induction with the notified chemical resulted in discrete or patchy to moderate and confluent erythema in all treated animals at 1 hour post exposure and in discrete or patchy erythema in three test animals at 24 hours post-exposure. Control animals manifested no sign of erythema at either 1 or 24 hours post-exposure. Additionally, bleeding was observed in 6 treated animals and in 2 control animals at 1 hour post-exposure. Discrete or patchy erythema was observed in 5 treated animals at 24 hours post-exposure but not at 48 hours post-exposure. Control animals manifested no analogous reaction at either observation time point. These results indicate that under the test conditions, the notified chemical is considered to be a mild to moderate dermal irritant and not a skin sensitiser given the absence of response at 48 hours post challenge exposure to undiluted substance and the mild to moderate dermal reaction observed during the preliminary sighting experiments, the main study induction phases and at main study 24 hours post exposure.

Repeated Dose Toxicity.
The repeated dose oral toxicity of the notified chemical to Sprague Dawley rats was examined in accordance with OECD Guideline for Testing of Chemicals 407. The notified chemical was administered in arachis oil by oral gavage to four groups of rats, for 28 consecutive days at dosage levels of 0, 15, 150, and 1000 mg/kg bw/day. These doses were chosen based on the results of a 14-day range-finding study.

No animal died while on test and clinical signs of increased salivation, hunched posture and tiptoe gait were considered to be of no toxicological importance. Animals in the 1000 mg/kg bw/day dose group were observed to have increased liver weights, which was considered to be an adaptive response as there was no histopathological evidence to support a toxicological effect on the liver. All animals showed normal body weight gains and there was no observed effect on food consumption. Haematological analysis revealed a statistically significant increase in the total white blood cell count (WBC) correlating with non-statistically significant increases in differential neutrophil and lymphocyte counts were observed in the high dose (1,000 mg/kg/day) males. A lack of dose response, gender specificity and failure of these treatment values (WBC, lymphocytes) to fall within the range of concurrent control values qualifies this change as one of toxicological uncertainty. Blood chemistry changes included statistically significant (males) and non-statistically significant (females) decreases in glucose levels in high dose animals. However these changes were deemed not to be toxicologically significant as no dose response was observed, observed changes fell within the historical range of values, but not within the range for concurrent controls, and correlations with other toxicity indicators, such as decreased body weight, were not observed. Additional changes included statistically significant decreases in serum cholesterol for females, which are considered to be toxicologically insignificant as they fell within the historical and concurrent control ranges of values.

No treatment-related adverse effects were observed in any dose group. The NOAEL for the notified chemical is > 1000 mg/kg bw/day.

Mutagenicity.
a) The *in vitro* genotoxicity of the notified chemical to *Salmonella typhimurium* strains was examined in accordance with OECD Guideline for Testing of Chemicals 471. Strains TA 1535, TA 1537, TA 98, TA 100 and TA 102 of *S. typhimurium* were treated with the notified chemical diluted in DMSO. A pre-experiment to assess

the toxicity of the test substance was conducted and indicated that a concentration of 5000 µg/plate should be the maximum recommended dose for the principle test.

The main study was conducted using the plate incorporation test involving two experiments which were identical in study design with one exception. Selected dose levels in both experiments were 15, 50, 150, 500, 1500 and 5000 µg/plate for each strain except for Experiment 2 in which the lowest dose level for TA100 and TA1537 was 50 µg/plate. The rationale for this difference in low dose selection was not provided, however it is assumed that the original lowest dose level of 15 µg/plate was dropped from the study design due to lack of observed toxicity at the highest dose (5000 µg/plate), which still allowed for compliance with the OECD guideline of 5 dose levels and was therefore considered not to have negatively impacted the outcome of the study. Results from Experiment 1 indicate that the high dose was not toxic to strains TA 102, TA 1537 or TA 98 in the absence or presence of metabolic activation. For both experiments, four non-toxic dose levels were plated and the positive and negative controls confirmed the activity of the S9 mixture and the sensitivity of the test strains. No significant increase in the frequency of revertants was recorded for any of the bacterial strains used, at any dose level, with or without metabolic activation. The notified chemical is not considered to be mutagenic to selected strains of *S. typhimurium* under test conditions.

b) The *in vitro* genotoxicity of the notified chemical to human lymphocytes was examined in accordance with OECD Guideline for Testing of Chemicals 473. Two experiments were conducted using the notified chemical diluted in DMSO. Doses tested in Experiment 1 were: 97.64, 195.29, 390.58, 781.15, and 1562.3 µg/mL both in the presence and absence of rat liver S9 metabolic activation. Doses tested in Experiment 2 were: 48.82, 97.64, 195.29, and 390.58 µg/mL followed by high doses of 585.86 and 781.15 µg/mL, and 781.15 and 1562.3 µg/mL, in the presence and absence of S9, respectively.

In Experiment 1, cells were incubated in the presence of test substance for four hours, both in the absence and presence of 2% S9. After rinsing, a 20-hour expression period was used. The test material induced a small increase in the frequency of cells with aberrations in the absence of S9 at 390.58 µg/mL. This increase was within the historical range but was statistically significant compared to the negative controls. A 40% mitotic inhibition was achieved at 390.58 µg/mL and no metaphases were observed at and above 781.15 µg/mL.

In Experiment 2, cells were continuously exposed to test substance for 24 hours in the absence of S9, and cells were exposed to the test substance for four hours in the presence of S9, followed by a 20-hour expression period. The test material did not induce any statistically significant increases in the frequency of cells with aberrations in any dose group in the presence or absence of S9. At a dose of 390.58 µg/mL, mitotic inhibitions were 44% and 28% in the absence and presence of S9, respectively. No metaphases were observed at and above 781.15 µg/mL.

The small increase in the frequency of cells with aberrations in the first experiment was not reproducible in the second experiment. Therefore, the increase is not considered to be toxicologically significant and the notified chemical is not considered to be clastogenic under the conditions of the test.

Summary of health effects

Toxicokinetics
No toxicokinetic data on the notified chemical were submitted. Absorption of the notified chemical through the skin and gastrointestinal tract is expected based on the partition coefficient (3.17), water solubility (0.368 g/L) and low molecular weight (<500 Da).

Acute toxicity
The notified chemical expected to have a low acute oral and dermal toxicity based on studies conducted in rats (LD50 > 2000 mg/kg bw). No acute inhalation toxicity data on the notified chemical was provided.

Irritation and Sensitisation
The notified chemical is expected to be irritating to the skin and slightly irritating to the eyes based on studies conducted in rabbits. The notified chemical is not expected to be a sensitiser based on the results of a Guinea Pig Maximisation test.

Repeated Dose Toxicity
A NOAEL of > 1000 mg/kg bw/day was established for the notified chemical in a 28-day repeated dose oral toxicity test in rats based on no treatment-related adverse effects observed in any dose group.

Mutagenicity
The notified chemical tested was not mutagenic in the Ames test and not genotoxic in an *in vitro* mammalian chromosome aberration test.

Health hazard classification
Based on the data provided the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R38: Irritating to skin

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on available studies, the notified chemical is a skin irritant and is slightly irritating to the eye. It is expected to have low acute oral and dermal toxicity and low toxicity after repeated exposure. It is not a skin sensitiser and is not expected to be genotoxic.

Reformulation workers, cleaners and beauty care professionals may be exposed to the notified chemical at concentrations up to 5%. While the notified chemical was found to be irritating to the skin and slightly irritating to the eye, irritant effects are not expected at these concentrations, also based on the 20% cut-off for eye and skin irritants set by the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

Therefore, the risk to workers associated with the use of the notified chemical at ≤ 1.15% concentration in fine fragrances, ≤ 2.5% in cosmetics and ≤ 5% in household cleaning products, is not considered to be unreasonable.

6.3.2. Public Health
Members of the public may experience repeated dermal exposure to the notified chemical through the use of fine fragrances (≤ 1.15%), cosmetics (≤ 2.5%) and household cleaning products (≤ 5%). While the notified chemical was found to be irritating to the skin and slightly irritating to the eye, irritant effects are not expected at these proposed usage concentrations in end-use products. Hence the risk to public health from use of the notified chemical as proposed 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 a component of fragrance preparations for local reformulation into a variety of consumer products (cosmetics, household cleaning products, fine fragrances). Release during reformulation in Australia is expected to arise from spills (0.1%), formulation equipment cleaning (no release estimate as cleaning water is recycled) and residues in import containers (0.1%). Accidental spills during transport or reformulation are expected to be collected with inert material and disposed of to landfill. Import containers will either be recycled or disposed of through an approved waste management facility. Therefore, up to 0.2% of the import volume is estimated to be released to landfill as a result of reformulation in Australia.

RELEASE OF CHEMICAL FROM USE
The notified chemical is expected to be released to sewers in domestic situations across Australia as a result of its use in cosmetic and domestic products, which are either washed off the hair and skin of consumers, or disposed of following cleaning activities.

RELEASE OF CHEMICAL FROM DISPOSAL
It is estimated that a maximum of 3% of the consumer products containing the notified chemical will remain in end-use containers. These are likely to be disposed of through domestic garbage disposal and enter landfill or be

recycled.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to enter the sewer system. An estimated 82% of the notified chemical is predicted to removed during sewage treatment plant (STP) processes (SimpleTreat; European Commission, 2003), with 44% removal by degradation, 35% by volatilisation and a further 3% removed through partitioning to sludge, before discharge to surface waters on a nationwide basis. The provided study indicates that significant hydrolysis occurs at elevated temperatures in the environmental pH range, and the estimated half life at pH 7 and pH 8 (25ºC) is 231 and 23 days, respectively. In conjunction with its measured ready biodegradability (100% over 28 days, passed 10-day window criteria, OECD TG 301F) the notified chemical is not expected to persist in the aquatic environment. The notified chemical has low to moderate potential for bioaccumulation based on its partition coefficient (log Pow = 3.17). In the case of release to surface waters, the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

The notified chemical is moderately volatile (log H = 1.689 Pa/m^3/mol, SimpleTreat, European Commission, 2003) and may volatilise to air during use or sewage treatment. The half-life of the notified chemical in air is calculated to be ≤ 1.4 h and ≤0.64 h, based on reactions with hydroxyl radicals and ozone respectively (AOPWIN, v1.29, US EPA, 2009). Therefore, in the event of release to atmosphere, the notified chemical is not expected to persist in the air compartment.

A small proportion of notified chemical may be applied to land when treated sewage effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. Notified chemical residues in landfill, soil and sludge are expected to have medium mobility based on its soil adsorption coefficient (log Koc = 2.25), and are expected to degrade to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The following Predicted Environmental Concentrations (PEC) have been calculated assuming that all of the imported quantity of notified chemical will be released to sewer. Of this, an estimated 82% is predicted to be removed during sewage treatment plant (STP) processes (SimpleTreat, European Commission, 2003) before discharge to surface waters on a nationwide basis.

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	82%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River:	0.109	µg/L
PEC - Ocean:	0.011	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 0.182 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 chemical may approximate 0.001 mg/kg in applied soil. This assumes that degradation of the notified chemical occurs in the soil within 1 year from application. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated biosolids application, the concentration of notified chemical in the applied soil in 5 and 10 years may approximate 0.005 mg/kg and 0.01 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 chemical 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 0.109 µg/L may potentially result in a soil concentration of approximately 0.727 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 3.635 µg/kg and 7.270 µg/kg, respectively.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of the studies not assessed by Canada can be found in Appendix B.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity *Oncorhynchus mykiss*	96 h LC50 = 4.2 mg/L[1] (OECD TG 203 – Semi-static)	Toxic to fish
Daphnia Toxicity *Daphnia magna*	48 h EC50 = 6.9 mg/L[1] (OECD TG 202 – Static)	Toxic to aquatic invertebrates
Algal Toxicity *Scenedesmus subspicatus* *Scenedesmus subspicatus*	72 h E_rC50 = 1.91 mg/L 72 h E_rC50 = 0.54 mg/L	Very toxic to algae[2]
Bacterial Toxicity *Pseudomonas putida*	16 h NOEC = 80 mg/L (ISO 10712)	Not expected to be inhibitory to bacterial growth

[1] Endpoints based on the geometric mean of the measured results.
[2] Classification based on the lowest endpoint for *Scenedesmus subspicatus* (72 h E_rC50 = 0.54 mg/L).

Usually, where multiple data are available for a species, with the same endpoint and time period, the geometric mean value would be used in the effects assessment (EPHC, 2009). In this case, evaluation of the two study reports indicates that due to the instability of the notified chemical in the test system, the difference between the reported endpoints could in part be attributable to the limit of quantitation (LOQ) of the two analytical methods. The method LOQ affects the reported endpoints as ½ LOQ was used to calculate the measured concentrations of the notified chemical in the test solutions. Therefore, while both studies are considered to be reliable with restrictions, the result from the study with the lowest LOQ is most considered relevant, and is preferentially used in the effects assessment.

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is very toxic to algae and toxic to fish and aquatic invertebrates, and is formally classified as 'Acute Category 1: Very toxic to aquatic life'. The notified chemical is not formally classified for long-term hazard under the GHS on the basis of its acute toxicity to aquatic biota, its rapid degradability and partition coefficient (log Pow <4) in the absence of an experimentally derived BCF.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has been calculated from the lowest acute algal toxicity endpoint of the notified chemical and an assessment factor of 100, as measured acute endpoints are available for three trophic levels.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Alga).	0.54	mg/L
Assessment Factor	100	
PNEC:	5.4	µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.11	5.4	0.020
Q - Ocean	0.01	5.4	0.002

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations based on its annual importation quantity and the partial removal of the chemical from waste water by degradation, volatilisation and sorption to sewage sludge. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in surface waters, soil or air. Therefore, on the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic and domestic products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Surface Tension 59.2 mN/m at 22 °C

Method EC Council Regulation No 440/2008 A.5 Surface Tension.
Remarks Concentration: 0.263 g/L.
The notified chemical is considered to be surface active.
Test Facility SafePharm (2003a)

Hydrolysis as a Function of pH ≥ 60% after 28 days at 40ºC at pH 2-12

Method In-house

pH	*% hydrolysis after 8 days at 40ºC**	*% hydrolysis after 28 days at 40ºC**
2	~90	100
5	~25	~60
7	~20	~60
8.5	~50	~90
12	100	100

* Data points are approximated based on the provided graph

Remarks 200-300 ppm of notified chemical in buffer solutions (types A, C, D, F and I: Reference Handbook of Chemistry and Physics) with 1% non-ionic surfactant. GC-FID determination at day 1, 2, 5, 8, 16, 23 and 28.

The rate of hydrolysis was slowest under neutral conditions (pH 7) and increased under acidic and basic conditions. Hydrolysis was approximately 60% or more after 28 days at 40ºC across the tested pH range (2-12), indicating the notified chemical is likely to hydrolyse under environmental conditions.
Health Canada estimated hydrolysis half lives of $t_{½}$ = 23 d at pH 8 and 25ºC, and $t_{½}$ = 231 d at pH 7 and 25ºC (EPISuite, v3.11).

Test Facility Firmenich (undated)

Flash Point 66 °C at 101.78 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Remarks The determination was carried out using a Setaflash 13740-2 tester in closed cup flash-point apparatus.
Test Facility SafePharm (2001)

Autoignition Temperature 304°C

Method EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks
Test Facility SafePharm (2003b)

Explosive Properties Predicted not to be explosive

Method EC Directive 92/69/EEC Method A.14 Explosive Properties.
Remarks Calculation relating to structure.
Test Facility SafePharm (2003b)

APPENDIX B: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

B.1. Ecotoxicological Investigations

B.1.1. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test - Static EC Directive 92/69/EEC C.3 Algal Inhibition Test - Static
Species	*Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: Control, 1.0, 2.2, 4.6, 10, 22, 46 mg/L Actual: Control (not analysed), lowest concentration (not analysed, <NOEC), 0.41, 0.63, 0.81, 1.24, 1.91 mg/L (geometric mean).
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC/UV
Remarks - Method	After a range finding test, a definitive test was conducted in accordance with the guidelines above and in compliance with GLP standards and principles. No significant deviations to the test protocol were reported. As the test substance was determined to be a volatile substance, the test was performed in a closed system with additional sodium carbonate. Test conditions: 21-22ºC; pH 7.8-8.5.

RESULTS

Biomass		*Growth*	
E_bC50 *mg/L at 72 h*	*NOEC* *mg/L at 72 h*	*E_rC50* *mg/L at 72 h*	*NOEC* *mg/L at 72 h*
1.01 (95% confidence limit: 0.94-1.10)	0.63	1.91 (95% confidence limit: 1.79-2.07)	0.63

Remarks - Results	The validity criteria for the test were met. The measured concentration varied from 59-77% of the nominal concentration at the beginning of the test and decreased to below the limit of quantification (LOQ = 0.22 mg/L) for all test solutions after 72 hours. As the test system was closed, the observed decrease was considered to be predominantly caused by degradation of the test substance. Therefore, the reported results are based on the geometric mean of the measured concentrations, using ½ LOQ where the result was <LOQ. The EC50 endpoints were calculated using Probit Analysis and NOECs were determined by comparison to the control using Dunnett's test.
CONCLUSION	The notified chemical is toxic to algae
TEST FACILITY	RCC Ltd (2008)

B.1.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test - Static EC Directive 92/69/EEC C.3 Algal Inhibition Test - Static
Species	*Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: Control, 0.32, 1.0, 3.2, 10 and 32 mg/L Actual: <LOQ, 0.0276, 0.135, 0.277, 3.70 and 0.729 mg/L

	(geometric mean)
Auxiliary Solvent	None
Water Hardness	15 mg $CaCO_3$/L
Analytical Monitoring	GC/FID
Remarks - Method	After a range finding test, a definitive test was conducted in accordance with the guidelines above and in compliance with GLP standards and principles. No significant deviations to the test protocol were reported. As the test substance was determined to be a volatile substance, the test was performed in a closed system with additional sodium bicarbonate. Test conditions: 24±1ºC; pH 7.9-9.1.

RESULTS

Biomass		*Growth*	
E_bC50 mg/L at 72 h	*NOEC mg/L at 72 h*	*E_rC50 mg/L at 72 h*	*NOEC mg/L at 72 h*
0.37 (95% confidence limit: 0.33-0.41)	0.028	0.54 (95% confidence limit: could not be determined)	0.028

Remarks - Results	The validity criteria for the test were met. The measured concentration varied from 74-88% of the nominal concentration at the beginning of the test and decreased to below the limit of quantitation (LOQ = 0.0058 mg/L) to 2% of nominal after 72 hours. The test solution with measured concentrations <LOQ after 72 hours were the control and test solution at 0.32 mg/L (nominal). As the test system was closed, the observed decrease was predominantly caused by degradation of the test substance. Therefore, the reported results are based on the geometric mean of the measured concentrations using ½ LOQ where the result was <LOQ. The EC50 endpoints were calculated using Probit Analysis and NOECs were determined by comparison to the control using Dunnett's test. The results have not been corrected to account for purity of the test substance.
CONCLUSION	The notified chemical is very toxic to algae
TEST FACILITY	Safepharm (2004)

BIBLIOGRAPHY

EPHC (2009) Environmental Risk Assessment Guidance Manual for Industrial Chemicals. Environment Protection and Heritage Council, Australia, 109 pp, <http://www.ephc.gov.au/taxonomy/term/75>. Accessed 4 January 2011.

European Commission (2003) 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 - Parts II and III.

Firmenich (undated) Stability Test of Perfumery Raw Materials, Stability Test – Aladinate (undated). (Unpublished report submitted by the notifier).

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2001) National Code of Practice for the Storage and Handling of Workplace Dangerous Goods [NOHSC: 2017(2001)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edition [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

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

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 Ltd (2008) Aladinate Toxicity to *Scenedesmus subspicatus* in a 72-Hour Algal Growth Inhibition Test (Study number B50106, 1 April 2008). Itingen, Switzerland, RCC Ltd. (Unpublished report submitted by the notifier).

SafePharm (2001): (Notified Chemical): Determination of Flash point, Report No. 161/274, SafePharm, United Kingdom (Unpublished report submitted by the notifier).

SafePharm Laboratory (2003a): (Notified Chemical): Determination of General Physical-Chemical Properties (Surface Tension), Report No 0161/0398, SafePharm, United Kingdom (Unpublished report submitted by the notifier).

SafePharm (2003b): (Notified Chemical): Determination of Hazardous Physical-Chemical Properties (Auto-ignition Temperature, Explosive Properties), Report No 161/399, SafePharm, United Kingdom (Unpublished report submitted by the notifier).

Safepharm (2004) (Notified chemical): Algal Inhibition Test (Report No: 161/405, 15 March 2004). Derby, U.K., Safepharm Laboratories Limited. (Unpublished report submitted by the notifier).

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

US EPA (2009) Estimations Programs Interface Suite™ for Microsoft® Windows, v 4.00. United States Environmental Protection Agency. Washington, DC, USA.