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February 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Resin acids and Rosin acids, mixed esters with dipentaerythritol and 12-hydroxyoctadecanoic acid and stearic acid (INCI Name: Dipentaerythrityl Hexahydroxystearate/Hexastearate/Hexarosinate)

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 Full Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Full 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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FULL PUBLIC REPORT

Resin acids and Rosin acids, mixed esters with dipentaerythritol and 12-hydroxyoctadecanoic acid and stearic acid (INCI Name: Dipentaerythrityl Hexahydroxystearate/Hexastearate/Hexarosinate)

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Estée Lauder Pty Ltd (ABN 63 008 444 719)
21 Rosebery Avenue
ROSEBERY NSW 2018

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

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Density, Method of Determination, Vapour Pressure, Absorption/Desorption, Dissociation Constant, Auto-ignition Temperature, Explosive Properties, Reactivity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Cosmol 168 ARV
Salacos 168 ARV
Dipentaerythrityl Hexahydroxystearate/Hexastearate/Hexarosinate (INCI Name)

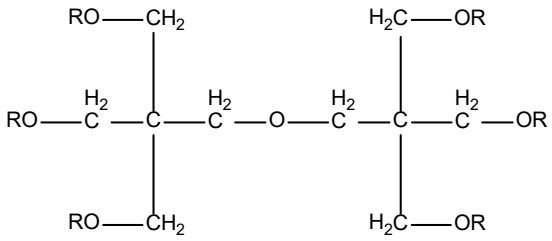
CAS NUMBER
208126-52-7

CHEMICAL NAME
Resin acids and Rosin acids, mixed esters with dipentaerythritol and 12-hydroxyoctadecanoic acid and stearic acid

OTHER NAME(S)
Rosin acids, mixed hexaesters with dipentaerythritol and 12-hydroxyoctadecanoic acid and octadecanoic acid
Dipentaerythrite Fatty Acid Ester

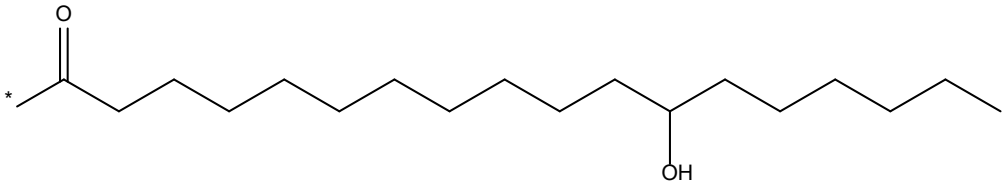
MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



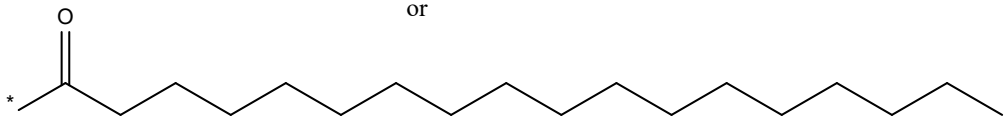
where R =

x =



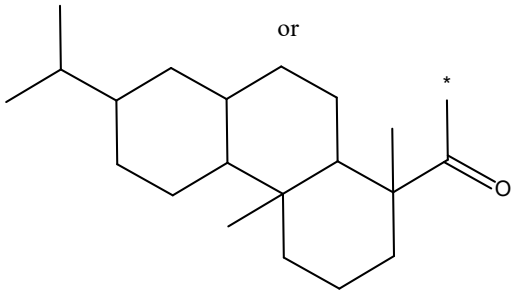
or

y =



or

z =



z = rosin or resin acids. The representative structure shown is for abietic acid.

Where the ratio of R groups (x : y : z) = 4.0 : 1.5 : 0.5

MOLECULAR WEIGHT
> 1800 Da.

ANALYTICAL DATA
Reference IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY 100%

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: Pale yellow gel

Property	Value	Data Source/Justification
Melting Point	25-40°C	Measured
Boiling Point*	>350°C at 101.3 kPa	Estimated based on component chemical
Density*	~1000 kg/m^3	Estimated based on component chemical
Vapour Pressure*	<0.13 kPa at 25°C	Estimated based on component chemical
Water Solubility	0.3×10^{-3} g/L at 20°C	Measured
Hydrolysis as a Function of pH	Not determined	Hydrolysable functions present but they are expected to hydrolyse slowly at environmental pH (4 – 9)
Partition Coefficient (n-octanol/water)	Not determined	Expected to partition from water to n-octanol due to its predominantly hydrophobic chemical structure
Adsorption/Desorption	Not determined	Expected to partition to soil, sediment and sludge due to its predominantly hydrophobic chemical structure and high molecular weight
Dissociation Constant	Not determined	No readily dissociable functions
Particle Size	Not applicable	Gel at room temperature
Flash Point	306°C	Measured
Flammability	Not expected to be flammable	Based on flash point
Autoignition Temperature	306°C	Based on flash point
Explosive Properties	Not expected to be explosive	Estimated based on chemical structure

* Estimated based on a component chemical: Octadecanoic acid (CAS No. 57-11-4) (IPCS, 2005). Octadecanoic acid has a lower molecular weight than the notified chemical and does not contain all of the functional groups present in the notified chemical. However, some of the physical and chemical properties of the notified chemical can be approximated using octadecanoic acid. For example, it can provide upper or lower limits for the boiling point and vapour pressure.

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

Reactivity
The notified chemical is expected to be chemically stable and will not decompose under normal ambient conditions.

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 at ≤8% by sea in finished cosmetic products.

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

IDENTITY OF MANUFACTURER

Estée Lauder USA

TRANSPORTATION AND PACKAGING
Finished cosmetic products such as lipsticks and make-up preparations will be imported in small containers (such as 3 g or 6 g containers) packaged in cardboard cartons in cardboard shippers. Products will be transported from the wharf to the notifier's warehouse for storage and subsequent distribution to retail outlets.

USE
The notified chemical will be used as a viscosity increasing agent at up to 8% concentration in cosmetic products that mainly include lipsticks, but also make-up preparations, eyeliners, hair and skin care products.

OPERATION DESCRIPTION
The notified chemical will be imported in finished cosmetic products. The finished cosmetic products containing the notified chemical at up to 8% will be sold to consumers as well as health and beauty salons. Workers in hair and beauty salons will directly apply finished products containing the notified chemical at up to 8% concentration to clients.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and Storage	12	4	12
Packers	5	4	12
End Users	3×10^5	8	365

EXPOSURE DETAILS
Transport and Storage
Exposure to the notified chemical during transport and storage is not anticipated except in case of an accident resulting in release.

Use of finished personal care products
Occupational exposure is possible for workers in hair and beauty salons using products containing the notified chemical (up to 8%). Dermal exposure is expected to be extensive given that cosmetic, skin and hair care products containing the notified chemical will be applied directly to the skin and hair. Accidental ocular exposure and oral ingestion may also occur.

Although the level and route of exposure will vary depending on the method of application and work practices employed, extensive dermal exposure is expected in some occupational settings. This exposure is likely to be greater than that expected for the public (see below).

6.1.2. Public exposure
Public exposure to the notified chemical is expected to be widespread and frequent through daily use of cosmetic products containing the notified chemical at concentrations up to 8%. Exposure to the notified chemical will vary depending on individual use patterns. The principal route of exposure will be dermal, while ocular exposure and oral ingestion particularly from the use of eyeliner and lipstick products is also possible.

The estimated total daily systemic exposure resulting from the simultaneous use of various leave-on cosmetic products containing the notified chemical at up to 8% (with a default dermal absorption of 10%), is 0.3 mg/kg bw/day (SCCP, 2006).

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details of some of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 >5000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Human, repeat insult patch test	no evidence of sensitisation at 8% in lipstick
Rat, repeat dose oral toxicity – 28 days.	NOAEL = 50 mg/kg bw/day

Note: Information available on 12-Hydroxyoctadecanoic acid and the 'rosin esters category' (as reviewed by the US EPA, 2008) have been used to supplement the available toxicity data on the notified chemical. 12-Hydroxyoctadecanoic acid is a component of the notified chemical. It has a lower molecular weight than the notified chemical and does not contain all of the functional groups present in the notified chemical. Thus, data on 12-Hydroxyoctadecanoic acid would only provide an approximate indication of the notified chemical. The notified chemical is similar to some of the chemicals covered by the 'rosin esters category'. However, the 'rosin esters category' does not contain any chemical with fatty acid components such as those present in the notified chemical. Thus, the information available on the 'rosin esters category' only provides an approximate indication of the toxicity of the notified chemical.

Toxicokinetics
The notified chemical has a high molecular weight (> 1000 Da.), low water solubility (~0.3 mg/L) and an estimated high log Pow value. Therefore, it is not expected to be absorbed significantly via the dermal or inhalation routes. Absorption across the gastrointestinal tract may occur to a limited extent by micellular solubilisation, given its highly lipophilic nature and low water solubility.

Acute toxicity
The notified chemical was found to be of low acute oral toxicity (LD50 > 5000 mg/kg bw) in rats (PRI, 1990).
No tests were conducted on the acute dermal or inhalation toxicity of the notified chemical. However, systemic toxicity is not expected via these routes of exposure given the unfavourable characteristics for absorption.

Irritation and Sensitisation
The notified chemical was found to be non-irritating to the skin of rabbits with no skin reactions evident at any observation time (RCC, 2007a). Slight reddening of the conjunctivae was observed in the eye of 2/3 rabbits 1 hour after instillation of the notified chemical. This had cleared within 24 hours indicating only mild eye irritation (RCC, 2007b).

A component of the notified chemical (Rosin, CAS No. 8050-09-7) is classified with 'R43: May cause sensitisation by skin contact' by Safe Work Australia (HSIS, 2010). However, a study conducted on a lipstick product containing the notified chemical at 8% in human volunteers reported that the product did not produce any signs of skin irritation or skin sensitisation (Consumer Product Testing Co., 2001). Therefore, the notified chemical is not considered to be a skin sensitiser at concentrations <8%.

Repeated Dose Toxicity
A 28-day repeat dose oral toxicity study conducted in rats at doses of 0, 50, 200 and 1000 mg/kg bw/day reported various effects. The no observed adverse effect level (NOAEL) is considered as 50 mg/kg bw/day (see Appendix B for details).

Mutagenicity
No data were available on the mutagenicity of the notified chemical. Rosin esters were found to be non-mutagenic in the presence and absence of metabolic activation (US EPA, 2008). 12-Hydroxyoctadecanoic acid was not mutagenic in *S. typhimurium* strains TA1535, TA100, TA1537, TA1538 and TA98. However, it was found to be mutagenic in the HS30 strain of *E. coli* (CIR, 1999). Another study found it was not mutagenic in the L5178Y TK+/- mouse lymphoma assay, with or without metabolic activation and it was also reported non-clastogenic in a chromosome aberration study in Chinese hamster ovary cells (CIR, 1999). Overall, based on the weight of evidence reported in studies on component chemicals, the notified chemical is not considered to be mutagenic or genotoxic.

Carcinogenicity
No data were available on the carcinogenicity of the notified chemical. An 18-month subcutaneous

carcinogenicity study on 12-Hydroxyoctadecanoic acid considered it may have the potential to be carcinogenic on the basis of subcutaneous sarcomas observed at the site of repeated sub-cutaneous injections in mice (CIR, 1999). However, the relevance of this to human health is uncertain. The CIR panel considered that the sarcomas may have been produced by a physical phenomenon unrelated to the test material and not relevant to use of the ingredient in cosmetics (CIR, 1999). A second study (4 weeks, intraperitoneal dose in mice) showed the frequency of lung tumours to be within the rate of spontaneous occurrence (CIR, 1999).

Toxicity for reproduction
No data were available on the reproductive toxicity of the notified chemical. However, Rosin esters are considered to be of low developmental and reproductive toxicity (US EPA, 2008). There were similar indications of the toxicity of 12-Hydroxyoctadecanoic acid (CIR, 1999).

Other effects
12-Hydroxyoctadecanoic acid was found to interfere with oxidative phosphorylation in rat liver mitochondria in an *in vitro* study (CIR, 1999).

Health hazard classification
Based on the data provided, the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Employees in hair and beauty salons will experience extensive dermal exposure during application of products containing the notified chemical (≤8%) by hand. If these employees use products containing the notified chemical for personal use as well as in a work setting their level of exposure would be higher than that of consumers.

The notified chemical was found to cause very slight irritation in the eye of rabbits. Such effects are not expected to be caused by use of products containing the notified chemical at ≤8%.

A component of the notified chemical is classified as a skin sensitiser. However, a study in human volunteers on a lipstick product containing the notified chemical at 8% reported no sensitisation effects. Therefore, exposure to cosmetic products containing the notified chemical at up to 8% is not expected to result in skin sensitisation.

The risk of toxicity following repeated exposure is not anticipated to be unacceptable based on the information available on components of the notified chemical and its high molecular weight, low water solubility, which indicate a low potential for absorption.

Overall, based on the available data, the notified chemical is not considered to pose an unacceptable risk to occupational health at concentrations up to 8% in cosmetic products.

6.3.2. Public health
Members of the public will experience widespread and frequent exposure to the notified chemical through daily use of cosmetic products (≤8%) which will be applied directly to the skin and hair.

The margin of exposure (MOE) was calculated using 50 mg/kg bw/day NOAEL, established in the repeat dose oral toxicity study conducted on the notified chemical and the total systemic exposure (0.3 mg/kg bw/day) as estimated in Section 6.1.2. The risk following repeated exposure is not anticipated to be unacceptable (MOE ~ 165). MOE values greater than or equal to 100 are considered acceptable to account for intra- and inter-species differences.

Based on the available toxicity data, the notified chemical is not considered to pose an unreasonable risk to public health at concentrations up to 8% in leave-on cosmetic products.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured or reformulated in Australia. It will be imported as a component of finished cosmetic products (e.g. lipsticks, make-up preparations, eyeliners, hair preparations and skin care preparations). There is unlikely to be any significant release of the notified chemical to the environment from storage and transport, except in the case of accidental spills. Accidental spills are expected to be contained and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical is a component in finished cosmetic products. The formulated product will be applied to the skin and will either be ingested, wiped off by tissues and disposed of to domestic garbage, or washed off the body and/or drink containers with ultimate release to the sewer.

RELEASE OF CHEMICAL FROM DISPOSAL

Expired waste and residue of the notified chemical in the empty containers (3%) is likely either to share the fate of the container and be disposed of to landfill, or to be washed to sewer when containers are rinsed before recycling.

7.1.2 Environmental fate

The notified chemical is expected to be disposed of to both the sewer and landfill. It is estimated that up to 90% of the notified chemical in influent is likely to adsorb to sediment and sludge in sewage treatment plants (Boethling and Nabholz, 1996), with the sludge eventually disposed of to landfill or re-used for soil remediation. In landfill or in soil, the notified chemical is expected to have low mobility, due to its low water solubility and anticipated high sorption to soil and sediment. It is not readily biodegradable but has the potential to degrade biotically and abiotically to form water and oxides of carbon. The notified chemical is not expected to bioaccumulate, based on its high molecular weight.

Refer to Appendix C for details of the environmental fate study.

7.1.3 Predicted Environmental Concentration (PEC)

A worst-case PEC for discharge of the notified chemical to surface waters has been calculated assuming that all of the imported quantity of the chemical is discharged to sewers nation wide and that no removal occurs in sewage treatment. The details of this worst case scenario are as follows:

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	200.0	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.65	µg/L
PEC - Ocean:	0.06	µg/L

The above calculation represents a conservative worst case as a significant fraction of the imported quantity of notified chemical is expected to end up as solid waste in landfill, in used containers and on tissues. The notified chemical is also likely to be removed from influent by up to 90% during sewage treatment processes. Therefore, significant release of the notified chemical to the aquatic compartment is not expected.

The notified chemical is expected to partition to sludge, and the removal of > 70% of the notified chemical from influent by STP processes is predicted, based on the estimated physico-chemical properties of the notified chemical (Simple Treat; European Commission, 2003). Partitioning to biosolids in STPs Australia-wide may

result in an average biosolids concentration of 4.661 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 31 µg/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 155 µg/kg and 310 µg/kg, respectively.

7.2. Environmental effects assessment

No ecotoxicity data were submitted. High molecular weight chemicals without significant ionic functionality are of low concern to the aquatic environment. Due to its low import volume, low solubility and likelihood for adsorption to sludge and sediment, the notified chemical is not expected to be present in water at concentrations that are hazardous to aquatic organisms. The notified chemical is not anticipated to cross biological membranes due to its high molecular weight and is therefore not expected to bioaccumulate.

7.2.1 Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) was not calculated since no ecotoxicity data were available for the notified chemical and low aquatic exposure is expected.

7.3. Environmental risk assessment

The potential for exposure of the notified chemical to the aquatic environment is low due to the relatively low import volume and the significant proportion of cosmetics containing the notified chemical that are expected to be disposed to landfill through disposal of tissues containing used cosmetics to domestic garbage. The risk for harm to aquatic organisms due to release to the sewer is mitigated by the insolubility of the notified chemical and expected propensity to adsorb to sludge and sediment. Taking into account the mitigation of exposure to aquatic organisms, the notified chemical is therefore not expected to pose an unacceptable risk to the environment based on its proposed use pattern.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the data provided, the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unacceptable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unacceptable risk to public health.

Environmental risk assessment
On the basis of the reported use pattern, the notified chemical is not expected to pose a risk to the environment.

Recommendations
CONTROL MEASURES

- 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.

  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.

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;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from an ingredient in leave-on cosmetic products at ≤8%, 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 and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 25-40ºC

Method	Unknown
Remarks	Test report not cited
Test Facility	Estée Lauder USA

Water Solubility 0.3×10^{-3} g/L at 20ºC

Method	OECD TG 105: Water Solubility
Remarks	In a preliminary test the solubility was found to be < 10^{-2} g/L but the column elution method could not be performed due to the pasty consistency of the of the test substance. The definitive test was conducted by the shake flask method as follows. Approximately 0.1 g of test substance was weighed into each of 6 flasks with 100 mL water. The flasks were shaken at about 30ºC for 24, 48 and 72 hours respectively. The flasks were then equilibrated for 24 hours at 20ºC. The supernatant solutions were filtered and analysed for total organic carbon by a TOC analyser. The 48 hour data was not used due to sample contamination. The 24 and 72 hour TOC data differed by about 22% which is higher than the 15% limit required for a valid test. However, the test is considered reliable.
Test Facility	RCC (1998a)

Flash Point 306ºC

Method	Unknown
Test Facility	Estée Lauder USA (2004)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – eye

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 2004/73/EC B.5 Acute Toxicity (Eye Irritation).

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 (2 Females/1 Male)
Observation Period	72 hours
Remarks - Method	No significant protocol deviation

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0	1	<24 hrs	0
Conjunctiva: chemosis	0	0	-	0
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

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

Remarks - Results: A slight reddening of the conjunctivae was observed in 2 females 1 hour after instillation.

CONCLUSION: The notified chemical is slightly irritating to the eye.

TEST FACILITY: RCC (2007b)

B.2. Skin sensitisation – human volunteers

TEST SUBSTANCE: MAC Lustre Lipstick containing the notified chemical at 8%

METHOD:

Induction Procedure:
Approximately, 0.2 g of the test substance was applied to a 1 inch x 1 inch absorbent pad of a clear semi-occlusive patch and applied to an area between the scapulae on the upper back of the volunteers. The patches were applied to the same area (which was marked) 3 times a week for a total of 9 applications. The patches were removed 24 hours after application with the first removal supervised and the subsequent removal performed individually at home. The site was re-evaluated for signs of irritation or sensitisation immediately prior to the next test substance application.

If a moderate (level 2) reaction was observed (with the exception of the first evaluation) during the induction phase, application was moved to an adjacent site. If another moderate reaction was observed at the adjacent site, or a level 3 or 4 reaction was observed, the volunteer was removed from the study.

Rest Period: 1 or 2 days

Challenge Procedure:
Approximately 2 weeks after the final induction application, a challenge patch was applied to an area adjacent to the induction site in the same way described above for induction. The patch was removed and the site scored at 24 and 72 hours after application.

Study Group: 101 volunteers completed the study (out of 118 who started. None of the

	volunteers withdrew from the study due to reactions to the application of the test substance).
Vehicle	None
Remarks - Method	None

RESULTS

Remarks - Results	No skin reactions indicative of irritation or sensitisation were reported among any of the volunteers who participated in the study.

CONCLUSION	A human repeated insult patch test was conducted using MAC Lustre Lipstick containing the notified chemical at ≤8% under a semi-occlusive dressing. The notified chemical was non-irritating and non-sensitising under the conditions of the test.
TEST FACILITY	Consumer Product Testing Co. (2001)

B.3. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
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	
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period:
Vehicle	Corn oil
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 M/5 F	0	0
low dose	5 M/5 F	50	0
mid dose	5 M/5 F	200	0
high dose	5 M/5 F	1000	2

Mortality and Time to Death

Two animals died spontaneously during the study. A male treated with 1000 mg/kg bw/day was found dead on Day 7 and a female also treated with 1000 mg/kg bw/day was found dead on Day 23. A cause of death was not established for either animal. The male decedent displayed dark red discolouration, autolysis, pelvic dilation of the right kidney, reduced size of prostate and seminal vesicles. The female showed dark red discolouration and incompletely collapsed lungs and a reddish discolouration of the thymus.

Clinical Observations

Females treated with 1000 mg/kg bw/day showed statistically significant increased body weight gain at Day 28. However, the mean body weights of the high dose females were comparable to those in the control group and this was not considered to be an adverse effect.

Males from the high dose group were found to have a statistically significant increase in the mean locomotor activity values (0-10 minutes) compared to controls. However, this was reported as a transient effect limited to male animals and unrelated to treatment.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

A statistically significant reduction in the mean absolute neutrophils count was noted in females in the low dose group. In males in the low dose group, a statistically significant reduction in total bilirubin was observed. However, in the absence of any significant decreases in the higher dose groups, these effects were considered to be unrelated to treatment.

Effects in Organs

Statistically significant reductions in the mean absolute and relative thymus weights of males in all treated groups were observed. In addition, males in the mid dose group were found to have a statistically significant reduction in mean absolute kidney weights and kidney to body weight ratios.

Macroscopic examination showed incidental findings in some animals such as reddish foci in the stomach, thymus and pelvic dilation of the kidneys. In the absence of a dose-response, these findings were not considered adverse.

Microscopic examination showed a slight increase in incidence of thymus atrophy and involution in males from the low and high dose groups. There was a difference in the incidence of these findings between the low and high dose groups and the control group. However, there was no dose-response relationship (the incidence in the mid dose group was identical to the incidence in the control group) and the findings were considered likely to be adverse but not related to treatment with the notified chemical.

Remarks – Results

The mortalities and adverse effects observed during the study were not considered to be caused by the notified chemical.

The study author's concluded that the NOAEL was 1000 mg/kg bw/day. This was unable to be confirmed in the absence of the full study report.

CONCLUSION

Considering the increased locomotor activity (statistically significant) in males and the 2 mortalities reported at 1000 mg/kg bw/day as well as the statistically significant reductions in thymus weights of males at 50, 200 and 1000 mg/kg bw/day with thymus atrophy reported in males at 50 and 1000 mg/kg bw/day, NICNAS considered the No Observed Adverse Effect Level (NOAEL) as 50 mg/kg bw/day.

TEST FACILITY RCC (2008)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge from a domestic wastewater treatment plant
Exposure Period	28 days
Auxiliary Solvent	None reported
Analytical Monitoring	Pressure decrease measured by electrode type manometer
Remarks - Method	The test substance was transferred into two test flasks at nominal loading levels of 108 and 92 mg/L. Ultrasound dispersion was used for 15 minutes to emulsify the test substance. The test vessels were incubated in the dark at 22ºC and the pH in the flasks at the end of the test ranged from 7.4 to 8.0. The chemical oxygen demand for the test substance (COD) was calculated as 257 mg O_2 / 100 mg.

RESULTS

Test substance		*Sodium Benzoate*	
Day	*% Degradation**	*Day*	*% Degradation**
1	0.5	1	23.5
7	9.0	7	78.5
14	21.0	14	82.0
28	35.5	28	83.0

* Mean of two replicates

Remarks - Results	The reference substance was degraded > 60% by the 10th day, indicating a suitable aerobic activated sludge inoculum was used. In the toxicity control containing sodium benzoate and the test substance, no inhibitory effect on the activated sludge was observed. All validity criteria for the test were satisfied. The test substance did not reach the pass level of 60% degradation for this test and therefore cannot be classified as readily biodegradable. However, the test substance can be considered inherently biodegradable.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	RCC (1998b)

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