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14 January 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

3,6,9-Trioxaundecanedioic acid

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

3,6,9-Trioxaundecanedioic acid

1. APPLICANT

Clariant (Australia) Pty Ltd of 675 Warrigal Road CHADSTONE VIC 3148 has submitted a limited notification statement in support of their application for an assessment certificate for 3,6,9-trioxaundecanedioic acid.

2. IDENTITY OF THE CHEMICAL

The purity of the notified chemical and the identity of its impurities have been exempted from publication in the Full Public Report and the Summary Report.

Chemical Name: 3,6,9-trioxaundecanedioic acid

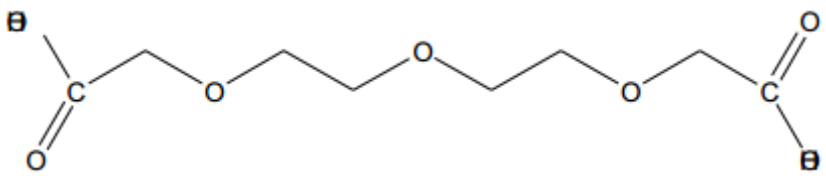
Chemical Abstracts Service (CAS) Registry No.: 13887-98-4

Other Names: 3,6,9-Diacid;
Tetraglycolic acid.

Marketing Name: 3,6,9-trioxaundecanedioic acid

Molecular Formula: $C_8H_{14}O_7$

Structural Formula:



Molecular Weight: 222.2

Method of Detection and Determination:	Ultraviolet/visible (UV/Vis), infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy
Spectral Data:	UV/Vis, IR and NMR spectra were provided for identification purposes

3. PHYSICAL AND CHEMICAL PROPERTIES

	Submission	**EPIWIN Model Data**
Appearance at 20°C and 101.3 kPa:	Colourless, odourless liquid	-
Melting Point:	liquid at 20°C	142.24°C
Boiling Point:	ND	373°C
Specific Gravity:	1.302	NE
Vapour Pressure:	ND	2.4 x 10^{-6} mm Hg at 25°C
Water Solubility:	Unlimited at 20°C	1 x 10^{6} mg/L
pH at 20°C:	1.8 (100 g/L water)	
Partition Co-efficient (n-octanol/water):	ND	Log P_{ow} = -2.56
Hydrolysis as a Function of pH:	ND	NE
Adsorption/Desorption:	ND	10 (log K_{oc} = 1)
Dissociation Constant:	ND	NE
Flash Point:	61 ℃, combustible liquid	NE
Flammability Limits:	No information available	
Autoignition Temperature:	No information available	
Explosive Properties:	No information available	
Viscosity:	8 945 m Pa.s at 20°C	NE
Reactivity/Stability:	Cannot be distilled without decomposition	

NE – not estimated. ND – not determined.

Comments on Physico-Chemical Properties

No test reports were provided. However, the notifier subsequently provided results from the model EPIWIN, version 3.01 (EPIWIN V 3.1, 1994-1999) for the physico-chemical parameters, some of which contrasted with the original data. For example, the model melting point is taken as incorrect as the notified chemical is a liquid at 20°C.

The notified chemical was tested for this assessment using the US EPA estimation model ASTER (US EPA, 1999). These results are presented below.

ASTER Model Results

Parameter	*Estimated Value*
Boiling point	289°C
Vapour pressure	3.76 X 10^{-4} mm of Hg
Water solubility	5.12 X 10^{6} mg/L
Hydrolysis	unlikely
Partition Coefficient, log P	-0.466 (P = 0.342)
Adsorption	12 (log K_{oc} =1.08)
Dissociation constant (pK_a)	3.37

The estimations obtained via the two models agree within allowable variation, except for the partition coefficient. The partition coefficients differ by two orders of magnitude but both indicate that the chemical is hydrophilic and therefore will remain dissolved in the water column. This is supported by the known high solubility of the chemical. The results for vapour pressure also differ by two orders of magnitude, but both indicate that the chemical is very slightly volatile. The K_{oc} indicates that the chemical will not adsorb to soil/sludge/suspended matter.

As indicated by the notifier, a chemical of this structure is unlikely to undergo hydrolysis.

4. PURITY OF THE CHEMICAL

Degree of Purity:	Very high
Non-hazardous Impurities (> 1% by weight):	Analogue of the notified chemical; present at <10%. Identity and exact concentration of substance is exempt information.
Additives/Adjuvants:	None

5. USE, VOLUME AND FORMULATION

The notified chemical is to be used as a component of cosmetic products for use by the general public.

The notified chemical will not be manufactured in Australia. It will be imported in 200 L polyethylene drums and transported from dockside to the notifiers warehouse for storage prior to being transported to two formulation sites. The notified chemical will be reformulated at these sites into cosmetic products at a concentration of less than 10% and packaged into 50 g glass jars or 30 mL plastic bottles. The production process at each of the sites is said to be the same. The resultant cosmetic product will be transported to consumer outlets for retail sale.

The estimated import volume of the notified substance will be up to one tonne per annum for the first five years.

6. OCCUPATIONAL EXPOSURE

Category of Worker	*Number*	*Exposure Duration - hours/year*
Storage Personnel	9	4
Chemical Dispensers	5	4
Formulators	5	12
Quality Assurance	8	4
Packaging Operators	46	26

Transport and Storage
The notified chemical will be imported in sealed 200 L drums and stored at the notifiers warehouse prior to delivery to two formulators sites. Occupational exposure is not expected during transport and storage except in the event of a spill.

Formulation Sites
Prior to production, quality assurance personnel take samples of less than 100 g from the import container and place them into sealed vials for quality control (QC) purposes. QC sampling also extends to aliquoting transfer vessel contents during production, and final product testing before packaging. Exposure during QC sampling is expected to be incidental and limited to dermal contact from drips or spills.

During cosmetic products production, the notified chemical is weighed for each batch of product by chemical dispensing personnel. Depending on the quantity of notified chemical to be dispensed, the notified chemical is either pumped into a batch pail in a dispensing room before transfer to mixing vessels or the measured quantity is pumped directly into a closed mixing vessel to which other raw materials are added. Formulators transfer chemical to mixing vessels and are also responsible for overseeing mixing vessel and associated pipeline cleaning (rinsing and steam cleaning) between batches. During these activities formulators may receive dermal and/or eye exposure from drips and spills as pump equipment is connected/disconnected and from rinse water during cleaning.

After mixing, the final product (containing less than 10% notified chemical) is pumped through a filling line for automatic filling of 50 g glass jars or 30 mL plastic bottles. Packaging operators supervise the filling and boxing process but do not directly contact the final product.

Control of Exposure
Protective clothing, respiratory protection, safety glasses and gloves are available to transport and storage workers in case of spillage. During formulation, workers use protective clothing, safety gloves and glasses as required. Weighing and dispensing are carried out under local exhaust ventilation. Mixing and packaging is carried out within closed systems.

Worker Education and Training
The notifier states that storage workers are trained and audited as required under ISO 9002 management system. At the formulator sites, workers receive specific instruction and training in the handling of all raw materials.

Adverse Effect Reporting
The notifier advised that throughout the period of laboratory and full scale synthesis of the notified chemical overseas, no health effects were reported from laboratory personnel or from shift workers. It was stated that these workers wore normal personal protective equipment, nevertheless contact with the substance could have occurred during tasks such as change of filters, handling incidents or product movement.

7. PUBLIC EXPOSURE

There is the potential for widespread public exposure to the notified chemical in cosmetic products, limited only by the commercial success of the products containing it.

Consumers will be exposed to the notified chemical in the cosmetic product via the dermal route, with the possibility of accidental ocular exposure. The notified chemical is a severe/corrosive eye irritant in rabbits, which is of concern as one of the cosmetic products listed in the submission is an eye cream. However, the hazards associated with eye irritation will be reduced by the low concentration (less than 10%) of the notified chemical in this and other cosmetic products.

To calculate systemic exposure from dermal application, assuming a maximum notified chemical concentration of 10% in cosmetic products, 100% absorption through skin (a worst case scenario, no data was given on dermal absorption) and a 60 kg bodyweight, a person applying 10g of a cosmetic product, once daily, would receive a systemic exposure of 1.7 mg/kg/day. A person who uses three cosmetic products containing the notified chemical daily, that is over a 24 hour period, would receive a systemic exposure of 5 mg/kg/day. The effects of this low level of systemic exposure are unknown, as a repeat dose toxicity study was not submitted.

It is expected that during transport, reformulation and storage, exposure of the general public to the notified chemical will be minimal, except in the event of an accidental spill. The procedures for spill clean up provided in the notifiers Material Safety Data Sheet (MSDS) should enable clean up operators to prevent widespread contamination and notified chemical

from entering watercourses and drains.

8. ENVIRONMENTAL EXPOSURE

Release

Release of the chemical will be during manufacture and end use of the cosmetic products.

The notifier has not indicated what proportions of the import volumes will be handled at each formulation site. So it has been assumed that each will handle 50% of the import volumes, that is 500 kg each.

Formulation Site 1:

The notifier did not provide any information regarding spills, it is assumed that annually up to 1% (a maximum of 5 kg) of the notified chemical is lost in this way.

The empty import drums are washed on-site and collected by drum recyclers. The washwater will go to the on-site effluent treatment plant. The notifier claims that less than 3% of the final product will be left in the process equipment. All washwater from equipment and drum washing will go to the on-site treatment plant. This is estimated at up to 15 kg per year of notified chemical.

Formulation Site 2:

The notified chemical will be stored in a bunded area. Effluent from spill clean up will enter the on-site settling tank. Washwater from process equipment and drum washing will be recycled to the process or go to the on-site settling tank. The effluent in the settling tank will be aerated and allowed to settle. The supernatant will then go to a mixing tank for pH adjustment. It will then be released to sewer. A licensed waste disposal contractor will remove the sludge from the settling tank.

It is estimated that up to 1.1% of the final product volume will remain in the process equipment. This equates to a maximum of 5.5 kg of waste notified chemical.

The notifier did not indicate the amount of notified chemical lost via either spills or drums residues. This assessment has estimated that 1% is lost via both spills and drum residues, i.e. a maximum of 5 kg per annum each.

End Use

Small quantities of the cosmetic products will be applied to skin. Any excess will be wiped or washed off. Ultimately, all of the cosmetic product will be washed from the skin and thus enter the sewer. This represents approximately 86.4% of the notified chemical (a maximum of 864 kg).

The notifier has estimated that up to 5 g of product may remain in the retail container (50 g jar or 30 mL plastic bottle) before being discarded. Annually this equates to 10% of the imported volume of notified chemical, a maximum of 100 kg. It is likely that discarded containers including the residual notified chemical will go to landfill.

Fate

A summary of the maximum amounts of waste notified chemical generated in the reformulation process is:

Event	*Formulation Site 1*	*Formulation Site 2*	*Waste system*
Spills	5 kg (1%)	5 kg	treatment plant
Equipment washwater and drum washing	15 kg (3%)	10.5 kg	treatment plant/sewer

Thus the total amount of waste notified chemical generated during manufacture is 35.5 kg (3.6% of the imported volume).

The waste notified chemical from either reformulation process will either end up in sludge which is taken to landfill, or in supernatant that is released to sewer. The estimates for partition coefficient (including ASTER model and Mackay Level 1 environmental partitioning at 25 ^{o}C of 99.99% into water), high water solubility and K_{oc} indicate that the chemical will not end up in the sludge but will remain in the supernatant.

In the home, it is likely that the majority of the chemical will ultimately be washed into the sewer, while the empty container and residues will be disposed of in the general domestic garbage and go to landfill. It is likely that the chemical will be leached out, but at very low concentrations and in a very diffuse manner.

The MSDS provided by the notifier gives a greater than 95% elimination value of 13 days using the OECD Inherent Biodegradation method 302B. This test is a simple static method for the evaluation of ultimate biodegradation of organic chemicals in water by micro-organisms in an aerobic environment.

The ASTER model biodegradation half-life is 3 to 12 days. The EPIWIN model ultimate biodegradation is 3.4 days. These values indicate that the chemical will degrade quickly.

The bioconcentration factor (BCF) generated by the ASTER model was 1, while the EPIWIN BCF estimation was 3.162. These values indicate that the chemical is not likely to bioconcentrate.

9. EVALUATION OF TOXICOLOGICAL DATA

In support of their application for an assessment certificate the notifier provided the following toxicity studies using 3,6,9-Trioxaundecanedioic acid.

9.1 Acute Toxicity Summary of the acute toxicity of 3,6,9-Trioxaundecanedioic acid

Test	*Species*	*Outcome*	*Reference*
Acute oral toxicity	Rat	LD_{50} > 2 000 mg/kg	(Pharma Research Toxicology and Pathology, 1990c)
Skin irritation	Rabbit	Non irritating	(Pharma Research Toxicology and Pathology, 1990e)
Eye irritation	Rabbit	Severe irritant	(Pharma Research Toxicology and Pathology, 1990b)

9.1.1 Oral Toxicity (Pharma Research Toxicology and Pathology, 1990c)

Species/strain:	Rat/Wistar
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Oral gavage of aqueous solution
Test method:	OECD TG 401
Clinical observations:	None
Mortality:	None
Morphological findings:	None
LD_{50}:	> 2 000 mg/kg
Result:	The notified chemical was of very low acute oral toxicity in rats

9.1.2 Skin Irritation (Pharma Research Toxicology and Pathology, 1990e)

Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	72 hours
Method of administration:	0.5 mL of the test substance under semi-occlusive dressing for 4-hours, then rinsed with warm water
Draize scores:	All individual scores were zero
Test method:	OECD TG 404
Result:	The notified chemical was not irritating to the skin of rabbits

9.1.3.1 Eye Irritation (Pharma Research Toxicology and Pathology, 1990b)

Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	72 hours
Method of administration:	0.1 mL of the test substance into the conjunctival sac of the left eye of each rabbit
Test method:	OECD TG 405

Draize scores of unirrigated eyes:

	Time after instillation											
Animal	***1 hour***			***1 days***			***2 days***			***3 days***		
Cornea	***o***		***a***	***o***		***a***	***o***		***a***	***o***		***a***
1	3		3	4		2	4		2	3		4
2	3		2	4		1	3		2	3		3
3	4		1	4		3	4		2	4		2
Iris												
1		0			1			1			1	
2		0			1			1			1	
3		0			1			1			1	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	3	3	3	3	4	2	3	4	3	3	4	2
2	3	3	2	3	3	2	3	3	2	3	3	2
3	3	3	2	3	4	2	3	4	2	3	4	2

[1] see Attachment 1 for Draize scales
o = opacity a = area r = redness c = chemosis d = discharge

Ocular response: From one hour up to 72 hours post application, the conjunctivae of all animals showed a diffuse, deep red colouring and a swelling with half to totally closed eye lids. The cornea showed nacreous to opaque opacity areas. After 24 hours all animals had reddened irises. Additionally, a clear, colourless or white-mucous discharge was observed. Conjunctivae and nictitating membranes changed to a white colouring during the observation period. Furthermore bleeding and detaching of parts of the conjunctiva and nictitating membrane could be seen. Animals were euthanised at 72 hours for humane reasons.

Result: The notified chemical was severely irritating to the eyes of rabbits

9.1.3.2 Eye Irritation – *In Vitro* Models

Eyetex, irritection and CAMVA assays were conducted on a product containing less than 6% notified chemical, with a pH of 3.84. The Eyetex assay used 100 μL of product and produced a Draize equivalent score of 22.9, predicting mild to moderate ocular irritation. The irritection assay used 125 μL of product and produced a Draize equivalent score of 16.9, predicting mild to moderate ocular irritation. The CAMVA assay produced an RC_{50} of 13% (95% confidence limits; 7.1-24.0), with a result of greater than 3% being classified as non-irritant to the eyes. Epiocular and CAMVA assays were conducted on two cosmetic products containing less than 6% notified chemical with a

pH of 3.71. The Epiocular test on 100 μL of product gave a score of greater than 60, consequently ocular irritation was predicted to none/minimal. The CAMVA assay produced an RC_{50} of 27% (95% confidence limits; 17-41), and was therefore concluded as non irritant to the eyes. Epiocular and CAMVA assays were conducted on a third cosmetic product containing less than 6% notified chemical, with a pH of 3.79. The Epiocular result was the same as the previous test on two other cosmetic products; the RC_{50} for the CAMVA assay was greater than 100% and was concluded as non-irritant to the eyes. An irritection assay using 125 μL of less than 6% TDA, pH of 3.73, produced a Draize Equivalent score of 14.0, predicting mild ocular irritation.

9.1.4 Human Repeat Insult Patch Test (Consumer Product Testing Co., 1997)

Test substance:	Cosmetic product containing < 6% notified chemical.
No of Subjects:	107 volunteers, male and female, ranging in age from 18 to 74 years.
Test method:	Federal Register, Vol 46, No 17, Tuesday Jan 27, 1981.
Induction procedure:	Ten 24-hour occlusive patches to the same skin site on the back over a three week period followed by a 2 week rest period.
Challenge procedure:	Following the 2 week rest period, the test substance was applied under occlusive dressing to the original skin site and to a virgin site on the volar forearm and observations made 24 and 48 hours after patch application.
Dermal reactions:	Induction: Scattered, transient, mild non-specific patch test responses were observed with 3 subjects during the induction phase. These responses were judged not to be clinically significant. One subject (#85) exhibited moderate erythema at the second induction patch reading; application was discontinued for the remainder of the induction phase. Challenge: No skin reactions observed, except for subject (#85). Rechallenge: Subject #85 was further investigated. Under occlusive patch conditions mild to marked erythema and mild to moderate oedema was observed during the 96 hour observation period. Under semi occlusive conditions mild erythema was observed. No dermal reactions were observed under open patch conditions. The observed dermal reactions were considered evidence of pre existing hypersensitivity to one or more components of the test formulation, since the subjects reactivity occurred early in the induction phase.

Result:	Formulations containing the notified chemical at <10% did not exhibit clear evidence of skin sensitisation in humans.

9.1.5 Photocontact Allergy Test (Ivy Laboratories Inc, 1998d)

Test substance:	Three different products each containing < 6% notified chemical
Test method:	Kaidbey KH, Kligman AM, *Contact Dermatitis,* 6:161-169, 1980.
Number of subjects:	27 volunteers, 14 males and 13 females, ranging in age from 18 to 46 years.
Induction procedure:	Day 1 Pre-treatment: one side of the midback was exposed to 3 minimal erythema doses (MED) from a xenon arc solar simulator; Treatment: 40 mg of the test substance (tested as supplied) applied to the lower back under occlusive dressing for 24 hours; Day 2 Skin sites were exposed to 3 MED followed by a 48 hour rest period; Day 4 A further patch was applied; after 24 hours the sites were reexposed to 3 MED, followed by a 48 hour rest; This sequence was continued twice weekly for a total of 6 exposures
Challenge procedure:	Day 21 Occlusive patches were applied to duplicate new skin sites on the opposite side of the lower back for 24 hours; one set of patches received 4 J/cm^2 UVA while the UVB was filtered out.
Comment:	No side-effects or unexpected reactions of any kind were observed. Following challenge, no reactions suggestive of photocontact allergy were seen in any of the volunteers at either 48 or 72 hours post exposure.
Result:	None of the test substances possessed phototcontact sensitising potential

9.1.6 Contact Sensitisation Potential – Maximisation Test (Ivy Laboratories Inc, 1998c), (Ivy Laboratories Inc, 1998a), (Ivy Laboratories Inc, 1998b)

Test substance:	Three different products each containing <6% notified chemical.
Test methods:	Kligman AM, *Journal of Investigative Dermatology* 47(5):393-409, 1966; Kligman AM, Epstein W, *Contact Dermatitis*, 1:231-239, 1975.
Number of subjects:	26, 25 and 25 volunteers respectively for the above products
Induction procedure:	Approximately 0.1 mL of aqueous sodium lauryl sulphate (SLS) (0.25%) under occlusive dressing for 24 hours; the test substance was applied to the same site under occlusive dressing for 48 hours or 72 hours if placed over a weekend; if no irritation was present, a further SLS patch was applied to the same site followed by a new induction patch; the sequence was repeated for 5 induction exposures; if irritation developed at any time point during the induction phase, the SLS treatment was eliminated and only the test material was reapplied to the same site after a 24-hour rest period
Challenge procedure:	After a ten-day rest period following the last induction patch, subjects were challenged with a single application of the test substance to a new skin site; pre-treatment with approximately 0.1 mL of a 5% SLS aqueous solution under occlusive patch for 1 hour was followed by treatment with the test substance for 48 hours.
Comment:	No instances of contact allergy recorded at either 48 or 72 hours after the application of the challenge patches
Result:	The products tested were not skin sensitisers in humans.

9.2 Genotoxicity

9.2.1 *Salmonella typhimurium* Reverse Mutation Assay (Pharma Research Toxicology and Pathology, 1990a)

Strains:	TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration range:	0, 4, 20, 100, 500, 2 500, 10 000 μg/plate
Test method:	OECD TG 471
Comment:	The mutagenicity was tested in the absence or presence of metabolic activation provided by Aroclor 1254-induced SD rat liver S9 fraction; appropriate positive controls demonstrated the sensitivity of the test and the negative controls were within historical limits
Result:	The notified chemical was not mutagenic in bacteria

9.3 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity in rats (LD_{50} > 2 000 mg/kg) and was not a skin irritant in rabbits. It was a severe eye irritant in rabbits. *In vitro* assays used as models for ocular irritation gave results ranging from non-irritant to moderate irritation for different formulations containing <6% notified chemical at pH 3.7 to 3.8. Cosmetic products containing the notified chemical at <6% were not allergenic or photoallergenic in humans. The notified chemical was not mutagenic in bacteria.

The notified chemical is determined to be a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) because of the potential to induce serious eye damage and warrants the risk phrase R41: Risk of serious damage to eyes.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

In support of their application for an assessment certificate the notifier has provided the following ecotoxicological data.

Test Organism	*Result*	*Reference*
Zebra fish	96 hr LC_{50} >500 mg/L	(Pharma Research Toxicology and Pathology, 1990d)
Effluent bacteria	24 hr EC_{50} = 2 500 mg/L	(Hoeschst AG, 1987)

10.1 Acute Toxicity in Fish

The fish test appears to have been carried out according to OECD Test Methods and EEC Guidelines.

Ten fish were assigned to each test group. The test was carried out in 10 L glass tanks filled with oxygen saturated distilled water. The nominal concentrations used were 0 and 500 mg/L with the initial pH being 8.3 and the temperature maintained at 22^{o}C. During the test the tanks were not aerated but a day/night light cycle of 12 hours was followed. Over the 96 hour trial period no deaths or changes of behaviour were observed in either concentration. Therefore the LC_{50} was greater than 500 mg/L.

10.2 Bacterial Toxicity

The effluent bacterial study was a fermentation tube test. However, a full test report in English was not supplied, so the method and test details can not be confirmed.

Results indicate that the chemical is practically non-toxic to fish and sewerage micro-organisms.

Calculated toxicological data retrieved by ASTER is given in the following tables.

Acute Toxicity

Test Organism	*Method*	*Endpoint*	*Concentration, mg/L*
Water Flea (*Daphnia Magna*)	Static 48 hours	LC_{50} (mortality)	13 147
Bluegill (*Lepomis macrochirus*)	Flow through 96 hours	LC_{50} (mortality)	23 477
Fathead minnow (*Pimephales promelas*)	Flow through 96 hours	LC_{50} (mortality)	34 230
Channel catfish (*Ictalurus punctatus*)	Flow through 96 hours	LC_{50} (mortality)	14 662
Rainbow trout (*Oncorhynchus mykiss*)	Flow through 96 hours	LC_{50} (mortality)	18 919

Chronic Toxicity

Test Organism	*Method*	*Endpoint*	*Concentration, mg/L*
Fathead minnow (*Pimephales promelas*)	Flow through 32 days	MATC	3 485

These results support the values given in the MSDS and indicate that the chemical is practically non-toxic to fish and daphnia.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Most of the notified chemical will eventually reach the aquatic compartment. The following is a Predicted Environmental Concentration (PEC) for normal use of the cosmetic products and assumes that ultimately all of the applied cosmetic product is washed off into the sewer.

Maximum amount of chemical entering the sewer	864 kg
National Population	18 million
Volume of water used person	150 L
Number of days used	365
Dilution receiving waters	1:10
Receiving water PEC	0.00009 mg/L (0.09 ppb)

A worst case scenario would be if some of the import containers lost their entire contents to sewer. A PEC is calculated below for the situation where 3 of the 200 L drums rupture:

Amount of notified chemical entering sewer	30 kg (approximately)
Volume of water handled by STP	250 ML
Dilution in receiving waters	1:10
Receiving water PEC	0.012 mg/L (12 ppb)

Both these PECs are orders of magnitude less than the toxicity values derived from the tests or ASTER, indicating a very low aquatic hazard.

Any notified chemical that ends up in a landfill is likely to leach out due to its high solubility and its K_{oc}. However, this should not pose a hazard because it will be occurring at very low concentrations and in a very diffuse manner.

The overall environmental hazard posed by this chemical is very low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical was of very low acute oral toxicity in rats (LD_{50} > 2 000 mg/kg) and was not a skin irritant in rabbits. It was a severe eye irritant in rabbits. *In vitro* assays used as models for ocular irritation gave results ranging from non-irritant to moderate irritation for different formulations containing less than 6% notified chemical at pH 3.7 to 3.8. Products containing the notified chemical at less than 6% were not allergenic or photoallergenic in humans. The notified chemical was not mutagenic in bacteria. Acute lethal dermal and inhalation studies and a repeated dose toxicity study were not provided.

The notifier claims that no injuries or diseases related to exposure to the notified chemical are known from its use overseas.

Based on the observed severe eye irritation, the notified chemical is classified as a hazardous substance under the NOHSC *Approved Criteria for Classifying Hazardous Substances Classifying Hazardous Substances*. The overall hazard classification, is Irritant (Xi) with risk phrase R41 - Risk of serious damage to eyes, assigned. In the absence of repeat dose testing no determination can be made of effects arising from chronic exposure.

Occupational Health and Safety
Based on the toxicological data submitted, severe eye irritation is the critical effect for the notified chemical in the workplace.

It is anticipated that dockside, transport and storage workers would have negligible health risk when handling the notified chemical except in the event of an accidental spill. Exposure after a spill would be controlled by use of the recommended practices for spillage clean up given in the MSDS supplied by the notifier.

Formulation and packaging of the cosmetic products is carried out in enclosed, automated systems and extensive occupational exposure is not expected under normal conditions. Nevertheless, incidental dermal and possibly ocular exposure may occur to drips and spills during quality control sampling, weighing and transfer operations, pump line connection/disconnection, and during equipment cleaning. Exposure during these activities is expected to be infrequent and minimal, as these activities will occur infrequently (4 to 30 hours per year) and workers are provided with personal protective equipment, namely gloves, goggles and protective clothing. In addition, where notified chemical is handled in neat form local exhaust ventilation is present which will control the accumulation of irritant aerosols in the workplace atmosphere. Given the engineering controls and personal protective equipment the risk of adverse health effects arising from exposure of workers to the notified chemical or products that contain it is low. It is critical that workers wear eye protection when handling imported compound and the formulated product.

Public Health
Based on the eye irritation, the National Drugs and Poisoning Scheduling Committee (NDPSC) in November 1999 agreed upon labelling requirements for consumer products that contain the notified chemical. The notified chemical will appear in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) with the following entry:

Schedule 5

3,6,9-TRIOXAUDECANEDIOIC ACID **except** in preparations containing 5 per cent or less of 3,6,9-trioxoaudecanedioic acid, the pH of which is 3.5 or greater.

Appendix F, Part 3

3,6,9-trioxoaudecanedioic acid

Warning Statement 5

Safety Direction 1

13. RECOMMENDATIONS

To minimise occupational exposure to the notified chemical the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);
- Industrial clothing should conform to the specifications detailed in AS 3765.1 (Standards Australia, 1990);
- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia, 1998);
- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994c);
- Where respiratory protection is required it should conform to AS 1715 (Standards Australia/Standards New Zealand, 1994a), and AS 1716 (Standards Australia/Standards New Zealand, 1994b);
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

The notified chemical may be recommended to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC *List of Designated Hazardous Substances*;

Consumer products containing the notified chemical, where appropriate, be labelled in accordance with the SUSDP.

If the conditions of use are varied, such as the concentration of the notified chemical in products increases, then greater exposure of the public may occur. In such circumstances, further information may be required to assess the hazards to public health

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

Under Section 64(1) of the Act, should the notified chemical be introduced or likely to be introduced at a volume greater than 1 000 kg per annum, the Director is to be advised within 28 days and an algal toxicity will need to be submitted for assessment.

16. REFERENCES

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema 0 Very slight erythema (barely	
perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	3 severe	Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe