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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Pitera

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Director
Chemicals Notification and Assessment

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Procter & Gamble Australia Pty Ltd (ABN 91 008 396 245)
320 Victoria Road
Rydalmere NSW 2116

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Identity of chemical; and
Composition

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Adsorption/Desorption;
Partition coefficient;
Dissociation constant;
Flash point;
Flammability limits;
Autoignition temperature;
Explosive properties;
Acute dermal toxicity;
Acute inhalation toxicity;
Repeated dose toxicity;
Induction of germ cell damage;
Chromosome damage;
Fish, acute toxicity test;
Daphnia, acute immobilisation test and reproduction test;
Algal inhibition test;
Ready biodegradability; and
Bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
Early Introduction Permit (EIP) issued on 8 June 2004.

NOTIFICATION IN OTHER COUNTRIES
None known

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Pitera

METHODS OF DETECTION AND DETERMINATION

METHOD	Not provided
Remarks	A certificate of analysis was provided for the notified chemical, which indicates that the filtrate has moisture content of >95% and <5% solids. The major component of the solids

is sugars and proteins, with trace amounts of alcohol and electrolytes. A constituent of the solids component is assumed to be the active ingredient.

TEST FACILITY Japan Food Research Laboratories (2004)

3. COMPOSITION

DEGREE OF PURITY
>95%

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical, Pitera, will be imported as a component of finished cosmetic products. The MSDS describes the notified chemical as yeast fermented solution. No repackaging and reformulation of the imported products containing the notified chemical will take place in Australia.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.9	1.6	4.1	6.6	8

On a solids basis, the introduction volume will be a maximum of 80 kg per annum.

USE
The notified chemical will be used as a humectant in cosmetic skin applications, such as moisturisers and cleansers.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Not known

IDENTITY OF MANUFACTURER/RECIPIENTS
Procter & Gamble Australia Pty Ltd (ABN 91 008 396 245)
320 Victoria Road
Rydalmere NSW 2116

TRANSPORTATION AND PACKAGING
The cosmetic products containing the notified chemical will be imported as component of finished cosmetic products. The packaging sizes and shapes will depend on the type of cosmetic products, typical of consumer size containers and packaging.

5.2. Operation description

Following importation, the imported finished cosmetic products will be transported by road to the notifier's warehouse prior to distribution to selected retail outlets. Warehouse and transport workers will handle products containing the notified chemical while contained in their outer carton. The cosmetic products will be sold in a variety of small package sizes, typical of consumer size containers.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Waterside/transport	10	8	12 to 24
Warehouse	20 to 30	4	100
Retail workers at selected department stores	20 to 30	8	260

Exposure Details

Warehousing and transport of the notified chemical involves loading, unloading, moving and storing of packaged products. Worker exposure to the notified chemical may occur if the packaging is breached. Similarly, retail workers will handle the products in their retail packaging. Retail workers will unpack the cartons, place the cosmetic products onto the shelves and serve customers. The cosmetic product formulations will contain between 5 to <95% notified chemical.

Waterside, transport and warehouse workers will wear protective clothing and heavy duty gloves when handling packaged products.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Environmental release during importation and storage at the notifier's facility is not expected, except in the case of accident during transport, storage or container rupture. Environmental impact from accidents will be minimised by established spill response procedures. Any spills resulting from container rupture are likely to be limited due to the small container sizes.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be used as cosmetics and may be washed off to surface water (eg. during swimming) or washed off to sewer (eg. showering, facial washing). A lesser proportion will enter the landfill environment.

5.5. Disposal

After use, the notified chemical is expected to be washed off to sewer or wiped off from the skin using facial tissues, which will then be discarded as solid waste.

5.6. Public exposure

Public exposure during transport and storage is unlikely unless the packaging is accidentally opened or punctured. However, widespread and repeated exposure to the public may occur as a result of day-to-day usage of the cosmetic products containing between 5 to <95% notified chemical. Consumers will apply the product on the face twice daily as moisturisers and cleansers. The average quantity of the product (non-rinse) used per application is 0.8 g (SCCNFP, 2000). This is equivalent to 0.04 to 0.76 g notified chemical/application or 0.08 to 1.52 g notified chemical/day.

6. PHYSICAL AND CHEMICAL PROPERTIES

The data below are for the ferment solution, which contains mostly water. Most properties cannot be described as the identity of the solid components is not known.

Appearance at 20ºC and 101.3 kPa Transparent to slightly yellow liquid

Boiling Point 100ºC

Remarks Test report not provided.

Density 1.000 to 1.015 kg/m^3

Remarks Test report not provided.

Vapour Pressure 0.13 kPa at 25^oC

Remarks Test report not provided.

Water Solubility Not determined

Remarks The notified substance is >95% water and the solids content are in solution as the MSDS describes it as a colourless to pale yellow, clear liquid.

Hydrolysis as a Function of pH Not determined

Remarks Based on the complexity of the aqueous solution, measurement of hydrolysis is not practicable.

Partition Coefficient (n-octanol/water) Not determined

Adsorption/Desorption Not determined

Dissociation Constant Not determined

Particle Size Not applicable.

Remarks The notified chemical is in liquid form.

Flash Point Not applicable.

Remarks The notified chemical is >95% water.

Flammability Limits Not flammable

Remarks The notified chemical is >95% water.

Autoignition Temperature Not determined.

Remarks The notified chemical is not expected to self-ignite.

Explosive Properties Not determined

Remarks The notified chemical is not expected to present an explosive hazard.

Reactivity

Remarks The notified chemical is stable under normal conditions of storage and handling. It does not contain any reactive groups that may cause spontaneous oxidation to combustible products.

7. TOXICOLOGICAL INVESTIGATIONS

The toxicity tests were carried out on the notified chemical and various finished product formulations containing 9 to >95% notified chemical.

Endpoint and Result	*Assessment Conclusion*
Mice, acute oral LD_{50} >48 g/kg bw	low toxicity
Rat, acute dermal	not conducted
Rat, acute inhalation	not conducted
Rabbit, skin irritation	non-irritating
Guinea pigs, 23 day cumulative skin irritation	non-irritating
Human, skin irritation	slightly irritating
Human, 21 day cumulative skin irritation	slightly irritating
Rabbit, eye irritation	non-irritating
Tissue equivalent - Eye irritation	non-irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Human, skin sensitisation	slightly irritating and limited evidence of sensitisation
Rat, repeat dose toxicity	not conducted
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro	not conducted
Genotoxicity – in vivo	not conducted
Human, photoallergy	no evidence of photosensitivity
Human, phototoxicity	no evidence of phototoxicity
Human, safety-in-use	considered safe under normal conditions of use

7.1. Acute toxicity – oral

TEST SUBSTANCE	Secret Key II Facial Treatment (SK II) (Product containing >90% notified chemical)
METHOD	Similar with OECD TG 401 Acute Oral Toxicity
Species/Strain	Mice/ddY
Vehicle	None
Remarks - Method	The test was conducted on mice instead of rats. The LD50 was calculated using the method described by Reed and Muench et al.

RESULTS

Group	*Number and Sex of Animals*	*Dose mL/kg bw*	*Mortality*
1	10/sex	>42 (M); >49 (F)	0
2	10/sex	>21 (M); >24 (F)	0
3	10/sex	>10 (M); >12 (F)	0
4	10/sex	>5 (M); >6 (F)	0
5 (control)	10/sex	0	0

LD50	Male: >42 mL/kg (>42000 mg/kg bw); Female: >48.8 mL/kg (>49000 mg/kg bw)
Signs of Toxicity	None.
Effects in Organs	None.
Remarks - Results	No effect on body weight gain was seen. There were no other observations described in the report.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Biochemical Laboratory (1980a)

7.2. Acute toxicity – dermal

Not conducted

7.3. Acute toxicity – inhalation

Not conducted

7.4. Irritation – skin

7.4.1. Skin irritation – rabbits

TEST SUBSTANCE	SK II (Product containing >90% notified chemical)
METHOD	Similar with OECD TG 404 Acute Dermal Irritation/Corrosion and EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	The test material was applied onto an abraded rather than intact skin. The observations and scoring were done at 24 and 72 hours after application.
RESULTS	
Remarks - Results	There were no irritation effects observed. All scores for erythema/eschar or oedema were zero.
CONCLUSION	The notified chemical is non-irritating to the skin under the conditions of the study.
TEST FACILITY	Biochemical Laboratory (1980b)

7.4.2. Skin irritation – 23 Day Cumulative Skin Irritation Study in Guinea pigs

TEST SUBSTANCE	SK II (Product containing >90% notified chemical)
METHOD	Similar with OECD TG 404 Acute Dermal Irritation/Corrosion andEC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Guinea pig/Hartley
Number of Animals	10 females
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	The test material was applied once a day onto the back (fur was clipped off) of each animal for 23 days (except weekends), and the observations were done everyday for a total of 27 days (except Sundays). The observations and scoring were done at 24 and 72 hours after application.
RESULTS	
Remarks - Results	There were no irritation effects observed throughout the study.
CONCLUSION	The notified chemical did not cause cumulative skin irritation under the conditions of the study.
TEST FACILITY	Biochemical Laboratory (1980c)

7.4.3. Skin Irritation Human Irritation Patch Test (3-PAT)

TEST SUBSTANCE	FE0204.02 (Product containing >90% notified chemical) FE0259.01 (Product containing >85% notified chemical)
METHOD	The study was conducted in accordance with the Standard Operating Procedures of North Cliff Consultants, Inc.
Study Design	Human Irritation Patch Test
Study Group	Sixteen subjects completed the study (Ages 18 to 65 years old)
Vehicle	None
Remarks – Method	The study was conducted to evaluate the irritation potential of test substances using various concentrations, patch type, vehicle to established the appropriate conditions for longer term exposures. A maximum of 5 patches per arm (10 patches per subject) were applied. Arm patches were applied midway between the shoulder and elbow. The upper back patches were applied in the shoulder blade area and the lower back patches were applied between the waisteline and lower edge of the shoulder blade. Each patch was applied to the same site as the previous patch of a given test substance. Sites are marked with gentian violet so that the test site is visible at subsequent scoring/patching visits. Patches were applied three times, each for 24 hours, then the patch is removed. The sites were graded after patch removal except for the first patch, which was graded at 48 hours after patch removal.
RESULTS	
Remarks – Results	No skin irritation effects were seen in all of the subjects, except for one subject, who had mild skin irritation on Day 2 when tested with one of the test substances (FE0259.01).
CONCLUSION	The notified chemical was slightly irritating to the skin under the conditions of the test.
TEST FACILITY	North Cliff Consultants, Inc. (2000)

7.4.4. Skin Irritation 21-Day Cumulative Human Irritation Patch Test

TEST SUBSTANCE	FE0378.01 (Product containing <10% notified chemical)
METHOD	The study was conducted in accordance with the Standard Operating Procedures of North Cliff Consultants, Inc.
Study Design	Human Irritation Patch Test
Study Group	Twenty one subjects completed the study (Age 18 to 65 years old)
Vehicle	None
Remarks – Method	The test site is wiped with gauze pad saturated with 95% ethanol or 70% isopropyl alcohol prior to initial patch application. A maximum of 5 patches per arm (10 patches per subject) were applied. Arm patches were applied midway between the shoulder and elbow. The upper back patches were applied in the shoulder blade area and the lower back patches were applied between the waisteline and lower edge of the shoulder blade. All applications for individual samples were made on the same site unless reactions become so strong, which obscures the scoring. Sites are marked with gentian violet so that the test site is visible at subsequent scoring/patching visits. Patches were applied for 21 consecutive days, and the patch wearing time varied from <12 hours to >24 hours prior to patch removal. Upon removal of patches, the patch sites were rinsed with warm water to remove excess test substance. The sites were graded 20 to 40 minutes after patch removal.

RESULTS

Remarks – Results	Mild skin irritation was observed in subjects.
CONCLUSION	The notified chemical was slightly irritating to the skin under the conditions of the test.
TEST FACILITY	North Cliff Consultants, Inc. (2003)

7.5. Irritation – eye

7.5.1. Eye irritation – Rabbits

TEST SUBSTANCE	SK II (Product containing >90% notified chemical)
METHOD	Similar with OECD TG 405 Acute Eye Irritation/Corrosion and EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	9
Observation Period	72 hours
Remarks - Method	Three groups consisting of 3 animals per group were used in the study. In Group 1, the treated eye remained unwashed while in Group 2, the treated eye was washed with lukewarm sterile distilled water 2 seconds after treatment. In group 3, the treated eye was washed with lukewarm sterile distilled water 4 seconds after treatment. Observations were done at 1, 24, 48 and 72 hours post instillation.

RESULTS

Remarks - Results	No abnormalities were observed in any of the animals tested. Scores for cornea, iris and conjunctiva were all zero.
CONCLUSION	The notified chemical is non-irritating to the eye.
TEST FACILITY	Biochemical Laboratory (1980d)

7.5.2. Eye irritation – Tissue Equivalent Assay

TEST SUBSTANCE	FE0344.01 (Product containing >20% notified chemical) FE0204.03 (Product containing >90% notified chemical)
METHOD	Tissue Equivalent Assay with Epiocular Cultures
Remarks - Method	Tissue equivalent assay is an in-vitro test using epiocular human cell construct to assess the potential ocular irritancy for the test material. The assay involves measurement of the rate of conversion of 3-[4,5-dimethylthiazol-2-yl] 2,5-diphenyltetrazolium bromide (MTT) by epiocular human cell constructs after exposure to the test substance. The duration of exposure resulting in a 50% decrease in MTT conversion for a test substance relative to control (T_{50}) is determined.

RESULTS

Remarks - Results	None of the test articles were observed to directly reduce MMT. The positive and negative controls gave the expected results indicating that the test system responded appropriately.
CONCLUSION	The test substance has a T_{50} of >24 hours and is therefore determined to be non-irritating to the eye.

TEST FACILITY	Institute for In Vitro Sciences, Inc (2003)

7.6. Skin sensitisation

7.6.1. Skin sensitisation – Guinea pig

TEST SUBSTANCE	SK II (Product containing >90% notified chemical)
METHOD	Similar to OECD TG 406 Skin Sensitisation – Adjuvant test and EC Directive 96/54/EC B.6 Skin Sensitisation – Adjuvant test.
Species/Strain	Guinea pig/Hartley
MAIN STUDY	
Number of Animals	Test Group: 10 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: >90%
Signs of Irritation	No signs of irritation in all animals.
CHALLENGE PHASE	
1st challenge	topical: >90%
Remarks – Method	Aqueous solution of sodium lauryl sulphate was applied a week prior to topical induction to provoke mild irritation.
RESULTS	
Remarks – Results	No irritation effects were observed at 24 and 48-hour observation in all animals. All scores were zero.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Biochemical Laboratory (1980e)

7.6.2. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical
METHOD	
Study Design	9 application repeat insult patch test
Study Group	100 volunteers (58 females and 42 males; age range not provided)
Vehicle	None
Induction Procedure	Induction Exposure: A series of 9 occlusive patches containing neat test substance were applied to the lateral surface of one upper arm (original site) for 24 hours. Each induction patch was applied to the same site, three times per week, for three consecutive weeks. Grading of test sites were conducted at 48 hours after patch applications (72 hours after weekend applications).
Challenge Procedure	An occlusive patch was applied 12-20 days after the last induction application, to both the original site and a similar site on the opposite side of the body for 24 hours. Grading of test sites were conducted at 48 and 96 hours after patch applications.
Remarks - Method	There were 112 (68 females and 44 males) subjects enrolled for the study but 12 subjects failed to complete the study due to reasons not related to the test administration. Deviations in the length of application and time for observations were reported. However, the authors indicated that such deviations did not affect the validity of the study.
RESULTS	
Remarks - Results	Mild erythema was observed during induction and 2 subjects have mild erythema at 48 hours after challenge exposure.
CONCLUSION	The test substance is slightly irritating and there was limited evidence of sensitisation reaction under the conditions of the test.

TEST FACILITY	Hill Top Research, Inc (1999)

7.7. Repeat dose toxicity

Not conducted

7.8. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	Similar with OECD TG 471 Bacterial Reverse Mutation Test and EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
	Pre incubation procedure
Species/Strain	*S. typhimurium*: TA100, TA1535, TA93, TA1537 and TA1538 *E. coli*: WP2uvrA$^-$
Metabolic Activation System	Kanecrol 500 activated S9 fraction
Concentration Range in Main Test	a) With metabolic activation: 10 to 10000 µg/plate b) Without metabolic activation: 10 to 10000 µg/plate
Vehicle	Distilled water
Remarks - Method	The study report did not include information whether a preliminary test was conducted. The report included a single test conducted in the presence and absence of metabolic activation.
RESULTS	
Remarks - Results	No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test material, either with or without metabolic activation.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Japan Food Research Laboratories (1980)

7.9. Genotoxicity – in vitro

Not conducted

7.10. Genotoxicity – in vivo

Not conducted

7.11. Human Photoallergy Study

TEST SUBSTANCE	FE0296.01 (Product containing >30% notified chemical)
METHOD	Human Photoallergy (Photosensitisation)
Study Design	The test substance was evaluated under occlusive patch conditions. A Xenon Arc Solar Simulator with a continuous emission spectrum in the UVA – UVB range (290 to 400nm) was used as a UV source. Minimal Erythemal Dose (MED) is defined as the time of light exposure required to produce a minimal erythema reaction 16 to 26 hours after irradiation using a standard UV source. Subjects used for this evaluation had Fitzpatrick skin types (burns easily to moderately upon exposure to UV, Category I, II and III).

	A preliminary test is conducted to determine the MED for each subject. An area (other than the study sites) on the subjects back was divided into 6 equal sites, irradiated and marked with a surgical marker. After 16 to 24 hours, the MED was determined by establishing the site which exhibited the least amount of perceptible erythema.
Study Group	28 subjects between the ages of 21 and 65
Vehicle	None
Induction Procedure	Induction Exposure: (Week 1, 2 and 3) The test substance was applied to two separate sites (irradiated site and non-irradiated site) on the subjects back under occlusive patch. The test substance was applied on each of the sites, twice weekly for a total of six applications (over a period of 3 weeks). After 24 hours of application, the patches were removed. One site is irradiated with three times the individual's MED. All sites were graded 24 hours after application of the test substance and 48 or 72 hours after irradiation.
Rest Period	Approximately 2 weeks
Challenge Procedure	Identical patches were applied to sites previously unexposed to the test substance. After 24 hours, one site was irradiated with ½ MED of UVB (290 to 320 nm) and 4 J/cm^2 of UVA (320 to 400nm). An additional site (irradiated control site) was also exposed to the same UV range. A non-irradiated site which received the test substance served as a non-irradiated control. All sites were graded 24 hours after application of the test substance and 24, 48 and 72 hours after irradiation.
Remarks - Method	30 subjects enrolled and 2 subjects discontinued due to reasons not related to the test substance being evaluated.
RESULTS	
Remarks - Results	No signs of skin reactions on the application sites were observed during the challenge exposure.
CONCLUSION	There was no evidence of photosensitivity to the test substance, under the conditions of the test.
TEST FACILITY	TKL Research, Inc (2001a)

7.12. Human Phototoxicity Study

TEST SUBSTANCE	FE0296.01 (Product containing >30% notified chemical)
METHOD	Human Phototoxicity
Study Design	The test substance was evaluated under occlusive patch conditions. A Xenon Arc Solar Simulator with a continuous emission spectrum in the UVA – UVB range (290 to 400 nm) was used as a UV source. Minimal Erythemal Dose (MED) is defined as the time of light exposure required to produce a minimal erythema reaction 16 to 26 hours after irradiation using a standard UV source. Subjects used for this evaluation had Fitzpatrick skin types (burns easily to moderately upon exposure to UV; Category I, II and III). A preliminary test is conducted to determine the MED for each subject. An area (other than the study sites) on the subjects back was divided into 6 equal sites, irradiated and marked with a surgical marker. After 16 to 24 hours, the MED was determined by establishing the site which exhibited the least amount of perceptible erythema.
Study Group	11 subjects between the ages of 22 and 58
Vehicle	None
Remarks - Method	The test substance was applied to two separate sites (irradiated site and non-irradiated site) on the subjects back under occlusive patch. After 24 hours of application, the patches were removed. One site was irradiated

	with ½ MED of UVB (290 to 320 nm) followed by 10 J/cm^2 of UVA (320 to 400nm). An additional site (irradiated control site) was also exposed to the UV ranges as above. The other site served as a non-irridiated control. A non-irradiated site, which received the test substance, served as an additional non-irradiated control. All sites were graded at 10 minutes after application of the test substance, and 10, 24 and 48 after irradiation.
RESULTS	
Remarks - Results	No adverse reactions reported.
CONCLUSION	There was no evidence of phototoxicity to the test substance, under the conditions of the test.
TEST FACILITY	TKL Research, Inc (2001b)

7.13. A 4-Week Randomised , Parallel Group, Double Blind, Safety-In-Use Study for Whitening Mask in Chinese Women

TEST SUBSTANCE	Mask Products (containing 30% notified chemical)
METHOD	
Study Design	On the first visit, the subjects had a baseline examination on criteria including dematological examination of face and ophthalmic examination. The subjects were randomly assigned to one of two whitening products containing the test substance (Code X and Code Y). The subjects were asked to apply the mask once a day, in place of their normal facial mask (if applicable) for 4 weeks. After 2 weeks of product usage, the subjects returned to the test site for checking the usage and to return the used product and to collect a new product for use for the rest of the test period. After 4 weeks product usage, subjects visited the test site for final dermatological/ophthalmologic examination.
Study Group	79 female subjects between the ages of 18- 55 years old
Remarks - Method	80 female subjects enrolled but 1 subject withdrew due to reasons not related to the test administration.
RESULTS	
Remarks - Results	There were 34 cases of adverse effects reported (13 subjects in Code X group and 11 subjects in Code Y group). From the 34 cases, 24 were skin related and could be related to the product tested. Skin related effects reported included irregular erythema on face but no pain and itching, dry and desquamation around the lips, tiny pimples, small papule on cheeks, mild erythema around eyes. These observations were considered as mild reactions by the investigators.
CONCLUSION	The test products are considered safe under normal use conditions as outlined in the study protocol.
TEST FACILITY	MDS Beijing Harris Clinical Research Co. Ltd (2001)

8. ENVIRONMENT

8.1. Environmental fate

No environmental fate data were submitted. Since the components are natural, the notified substance is likely to be biodegradable.

8.2. Ecotoxicological investigations

No ecotoxicity data were submitted.

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Following use, most of the notified substance will either be sent to landfill for disposal (ie. adhered to facial wipes, tissues, etc) or washed off to sewer, with a diffuse disposal pattern. Assuming all of the notified substance is disposed of to sewer (up to 8 tpa with <5% solids content or <400 kg/y) across a diffuse area of Australia, a predicted environmental concentration (PEC) for the substance in wastewater of ≤0.27 µg/L (on solids basis) has been derived. This value assumes no degradation during the sewage treatment process, and that a national population of 20.1 million people produces wastewater at a rate of 200 L/person/day. PEC values for inland river and oceanic receiving environments for discharged sewerage treatment plant effluent of 0.27 and 0.027 µg/L have been derived by division by safety factors of 1 and 10, respectively. As a worst case situation, these PECs may also apply where all of the notified substance applied to skin is washed off during water sports and swimming activities.

9.1.2. Environment – effects assessment

No ecotoxicity data were provided with which to assess the environmental hazard of the notified substance to aquatic organisms. The constituents of the notified substance are naturally occurring and water soluble and therefore unlikely to be of high toxicity to aquatic organisms.

9.1.3. Environment – risk characterisation

No ecotoxicity data were available with which to derive a predicted no effect concentration (PNEC). Although PEC values for the notified substance have been derived, biotic and abiotic reactions are likely to result in the degradation of the notified substance in aquatic environments and in landfill.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Transport, storage and warehouse workers will handle the finished products containing the notified chemical while contained in their outer carton. Retail workers will handle the products in their retail packaging. These workers are unlikely to be exposed to the notified chemical except when the containers are damaged or punctured. Similarly, exposure to the notified chemical during transport of the product is negligible expect in the event of transport accident.

9.2.2. Public health – exposure assessment

Cosmetics containing the notified chemical will be sold in the public domain, consequently there is potential for widespread and repeated public exposure. Exposure will be principally via dermal route. During use, 0.08 to 1.52 g/day of the notified chemical is expected to be applied by dermal route. Assuming 100% of the notified chemical is absorbed by the skin, the consumer would be exposed to a maximum of 1520 mg/day notified chemical, which is equivalent to a systemic exposure of 24 mg/kg/bw for a 60 kg female.

It is expected that during import, transport and storage of products containing the notified chemical, exposure of the general public will be limited except in the event of an accidental spill.

Exposure to the notified chemical is considered low due to the low frequency of use (maximum twice/day) and the expected low systemic exposure of the notified chemical when used as a facial moisturiser or cleanser.

9.2.3. Human health – effects assessment

The notified chemical was of low acute oral toxicity. It is assumed that the notified chemical will

also have low acute dermal toxicity since the notified chemical consists primarily of water. In rabbits, the notified chemical is non-irritating to the eye or skin. The notified chemical is not a skin sensitiser in an adjuvant study in guinea pigs. It is not mutagenic in bacteriological testing.

Available human studies conducted on various concentrations of the notified chemical (between 30 to <95%), suggests that the notified chemical may cause slight skin irritation as shown in the irritation and cumulative irritation patch test. An in vitro eye irritation test using epiocular human cell construct did not produce any irritation effects when tested with the notified chemical. Slight skin irritation but a limited evidence of sensitisation was observed in a human repeat insult patch test. Furthermore, there was no evidence of skin reactions when tested for photosensitivity and phototoxicity. In a 4-week randomised, parallel group, double blind, safety-in-use study, there was no serious adverse skin reactions observed during the study and the test substance containing 30% notified chemical was considered safe when used as specified in the submission.

Based on the available data there is insufficient information to classify the notified chemical as a hazardous substance under the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical will be imported as a component of finished cosmetic products. There is no manufacture, reformulation and packaging of the products containing the notified chemical in Australia. Worker exposure to the notified chemical is expected to be low since warehouse, retail and transport workers will handle the finished products containing the notified chemical while contained in their outer packaging.

Due to the low hazard of the notified chemical and the low potential for exposure, the risk posed by the notified chemical to occupational health and safety is low.

9.2.5. Public health – risk characterisation

Members of the public will make dermal contact with the cosmetic products containing the notified chemical. Assuming 100% dermal absorption, systemic exposure would be 2.4 mg/kg/bw for a 60 kg female, which is much lower compared with the acute oral LD50 in female rats (>49 mg/kg bw), and would provide an adequate margin of safety. Although slight skin irritation is possible when using the products containing the notified chemical, it considered that these products are safe for their intended use based on a safety in use study conducted on products containing 30% notified chemical.

Given the expected low toxicological hazard and the low exposure during use as cosmetics, the risk to public health is considered low.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data there is insufficient information to classify the notified chemical as a hazardous substance under the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

and

There is insufficient information available to classify the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003). This system is not mandated in Australia and carries no legal status but is presented for information purposes.

10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its low level of

importation and reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is No Significant Concern to public health when used as a humectant in cosmetic skin applications.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for the notified chemical and products containing the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

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 itself, 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 NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Environment

Disposal

- The notified chemical should be disposed of to landfill, sewer or incinerator in accordance with local waste disposal regulations.

Emergency procedures

- Spills/release of the notified chemical should be handled by containing the spill by absorption on suitable absorbent material (eg. sand, earth, vermiculite, tissue, cloth) for disposal.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- new information on animal and human health toxicity studies becomes available;
- significant new information on adverse environmental effects becomes available;
- the notified chemical is introduced as a solid concentrate.
- import levels reach ≥1 tonne per annum on a solids basis, provision of aquatic ecotoxicity data (fish, daphnia, algae) will be required.

(2) Under Section 64(2) of the Act:
- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

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