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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

SEFA Polybehenate

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Director
Chemicals Notification and Assessment

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SEFA Polybehenate

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT
Procter and Gamble Australia Pty Ltd (ABN 91 008 396 245)
99 Philip St
Parramatta NSW 2150

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:
Chemical name
Other names
CAS number
Molecular formula
Structural formula
Molecular weight
Spectral data

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Acute toxicity – oral
Acute toxicity – dermal
Acute toxicity – inhalation
Irritation – eye
A number of other toxicological and ecotoxicological studies on close analogues of the notified chemical or products containing the notified chemical were provided in place of studies on the notified chemical itself.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
Commercial Evaluation Permit: 2000

NOTIFICATION IN OTHER COUNTRIES
Previously notified in USA and Europe for use in personal care products.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
SEFA Polybehenate

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	Infrared (IR) spectroscopy
Remarks	A reference spectrum was supplied by the notifier.

3. COMPOSITION

DEGREE OF PURITY
99.7 %

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)
None

ADDITIVES/ADJUVANTS
None

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured or reformulated in Australia. It will be imported as a component of several finished cosmetic products under the trade name Olay.

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

Year	*1*	*5*
Kilograms	156	300

USE
The notified chemical will be used as an emollient and/or emulsifying agent in cosmetic products for facial cleaning. The notifier has indicated that, during year 1, around 12 % of the volume of notified chemical will be imported in facial cleansing milk and around 88 % in face cleaning cloths.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Storage and distribution:
Procter and Gamble Australia Pty Ltd
Arndell Park, NSW

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in finished cosmetic products, in small consumer packages, within cartons. The products will be imported by ship, and transported by road to the notifier's distribution warehouse. From there it will be sent to retail distribution warehouses and retail stores by road transport.

5.2. Operation Description

The unopened cartons will be distributed to the final retail store, where the individual consumer packages will be removed from the cartons and displayed for retail sale. During end use, a small amount of the products will be applied to the skin (face) and ultimately washed off. The facial cloth will be used to wipe and clean the face and skin and the used cloth discarded in domestic waste.

5.3. Release

RELEASE OF CHEMICAL AT SITE
Not applicable – not manufactured or reformulated in Australia.

RELEASE OF CHEMICAL FROM USE
The facial cloth will be used to wipe the face and then will be disposed of via domestic waste. The notifier has estimated that 50 % of the substance will be transferred to the face to be washed off in

the shower, and 50 % will remain in the cloth when it is disposed of to landfill. In year 5, approximately 130 kg will enter the sewer and another 130 kg of notified chemical will be disposed of in landfill.

The facial cleanser will be applied to the face and hands and then washed off. Approximately 12 %, equivalent to about 36 kg of the notified chemical in year 5, will enter the domestic sewer system during use of the cleanser, assuming 95 % of the substance is washed off after application. Approximately 5% of the contents will remain in the empty container, which will be disposed of via the general domestic garbage to landfill.

5.4. Disposal

The majority (approximately 55 %) of the total imported notified chemical will be disposed of via the sewer. The remainder (approximately 45 %) will go to landfill in the empty user containers or the used facial cloth.

6. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa	White waxy solid
MELTING POINT	72°C

Remarks No test reports were supplied by the notifier.

DENSITY	900 - 950 kg/m^3 at 72°C

Remarks No test reports were supplied by the notifier.

VAPOUR PRESSURE

Remarks Not expected to be volatile due to high molecular weight.

WATER SOLUBILITY	4.96 to 42.6 µg/L at 24°C

METHOD An in-house approved method was used to measure water solubility. The Protocol title was given in the test report as follows: Study plan for measuring the solubility of sucrose polyester (R.A. Jamieson, 12/3/79). Scintillation counting was used to determine the concentration of test substance in water following Addendum 2/11/80 of the Protocol (ITC Radiochemical Users Handbook, Analysis section).

Remarks The water solubility of ^{14}C-sucrose polyester was determined in both high quality water and in filtered influent sewage. The stock solution was prepared by adding the test substance to volumetric flasks containing dichloromethane and bringing them to the desired volume. The solvent was then evaporated under nitrogen. The test solutions were then made by adding the test media (water and sewage) to the test flasks containing measured aliquots of stock solution to give a saturated concentration of 10 ppm. The test solutions were shaken and centrifuged prior to removing aliquots for measurement of concentrations by scintillation counting. The tests were run over a maximum period of 14 days or until a concentration plateau was reached.

Two studies were performed to determine the solubility of sucrose polyester in water. In the first study, the solubility of the test substance was found to be 42.6 ± 24.8 µg/L after 14 days. In the second study, the solubility was found to be 4.96 ± 1.74 µg/L after 14 days. During the test, the pH of the water dropped from an initial value of 5.6 to a value of 5.2 after 12 days. It was concluded that the apparent water solubility of the test substance was in the range of 4.96 to 42.6 µg/L. While these results differ by a factor of ten, both values indicate the test substance is only slightly to very slightly water soluble.

The solubility of sucrose polyester in filtered influent sewage was found to be 89.3 ± 13.4 µg/L after 14 days. During the test, the pH of the effluent sewage dropped from an initial value of 7.8 to 6.3 after 12 days.

TEST FACILITY Procter & Gamble, Environmental Safety Department (1980a)

HYDROLYSIS AS A FUNCTION OF pH

Remarks The notified chemical contains ester groups which may hydrolyse under extreme pH conditions, but hydrolysis could not be measured due to the low water solubility.

PARTITION COEFFICIENT (n-octanol/water) log Pow at 20°C = 3.55 ± 0.16

METHOD The partition coefficient was determined for Sucrose Polyester using an in-house method: Partition coefficient on Sucrose Polyester (K Triebwasser, 29/10/79). Tests were conducted according to Standard Method VIII A-3, issue No. 2 Method B. The concentration of the test substance in octanol and water was determined by scintillation counting (ITC Radiochemical Users Handbook, Analysis section).

Remarks The determination involved partitioning 3 concentrations of test substance (25.7, 52.3 and 103 µg/L) in the deionized water saturated with distilled octanol. Due to the low solubility of the ^{14}C-radio-labelled test substance, the stock solution was initially prepared using an organic solvent and then evaporating the solvent prior to addition of the test substance.
Less than 100 disintegrations per minute were obtained on aliquots of the aqueous phase, but attempts at concentrating the analyte proved unsuccessful. Consequently, log P determinations are considered as "apparent" values according to test guidelines. The mean value for recovery was 102%, where recovery is the percentage of radioactive material originally added that was found in both n-octanol and water layers. The mean value for "apparent" log P was 3.55, indicating the test substance has some affinity to lipids.

TEST FACILITY Procter & Gamble, Environmental Safety Department (1980b)

SOIL MOBILITY TEST

METHOD In-house method. Testing was performed in accordance with the following experimental protocols: - Soil mobility test on X0356.01R, X0393.01R and P1636.02R, by Mr T.E. Ward, 9/4/86; and protocol addendum, Preparation of ^{14}C stock - X0393.01R, T Ward, 30/4/86.

Remarks A soil mobility test involving upward flow through a soil column was performed over a 66 day period to determine the mobility of sucrose polyester in sludge amended soil environments. Simulated groundwater (composition provided) was used as the transport phase and Borden Sand was used as the soil medium. No pH value or organic carbon content were provided for the soil. To simulate the transport mode under real field conditions, the test material was mixed with influent waste water from a domestic municipal treatment plant. Sucrose polyester was reconstituted in hexane prior to addition to the waste water according to protocol.
The validity of the test system was confirmed by comparing the mobility of the test substance to known mobile and immobile compounds, ie. stearic acid and polyacrylic acid. To test for uniformity of soil columns and recovery rates from each column, prior to testing, a highly mobile tracer comprising 1 g/L NaCl was added to each of 3 soil columns. To measure concentrations of test material in each phase, the leachate and representative slices of soil were collected from each soil column for analysis.
Results showed the immobile fractions of sucrose polyester accounted for 36.7 % of material, with the immobile fraction tending to remain in the first 2 cm of soil. The mobile fraction accounted for only 1.2 %, and was observed to leach rapidly through the soil column. The immobile fraction of stearic acid was uniformly distributed across the height of the soil column indicating adsorption to the soil. The immobile fraction of polyacrylic acid was concentrated at the inlet of the soil column indicating filtration of this material by the soil. These latter results confirm the validity of the filtering process.
A mass balance between the initial influent containing sucrose polyester and the final mobile and immobile phases was not attained, with 62 % of sucrose polyester unaccounted for. These results suggest significant degradation of the test material over the test period. Green algae was observed growing in the soil column during the test, hence degradation by the algae could account for some of the loss. However, these results should be treated with caution due to the irregularities observed during the test, and in light of the results of the biodegradability test (Section 8.1.1) which indicate no instability, but strong adsorption to sewage sludge.

TEST FACILITY Roy F. Weston, Inc. (1987)

DISSOCIATION CONSTANT

Remarks No dissociable groups are present in the notified chemical.

PARTICLE SIZE

Remarks Not applicable as the notified chemical is a liquid and is not imported in pure form.

FLASH POINT 276.6°C at 101.3 kPa

Remarks No test reports were supplied by the notifier; value obtained from MSDS.

FLAMMABILITY LIMITS

Remarks The notified chemical is not flammable.

AUTOIGNITION TEMPERATURE

Remarks Not expected to autoignite below 400°C.

EXPLOSIVE PROPERTIES

Remarks Not expected to be explosive, based on structure.

REACTIVITY

Remarks Stable under normal environmental conditions and also at elevated temperatures.

7. TOXICOLOGICAL INVESTIGATIONS

7.1. Acute toxicity – oral

No reports on acute oral toxicity of the notified chemical were supplied by the notifier. The results of the repeat dose toxicity studies (see below) indicate that the acute oral LD50 must be greater than 15000 mg/kg bw in rats and 5500 mg/kg bw in dogs.

7.2. Acute toxicity - dermal

No reports on acute dermal toxicity of the notified chemical were supplied by the notifier. The low repeat dose oral toxicity and the low absorption of the notified chemical from the gastrointestinal tract indicate that skin absorption of the notified chemical is not likely to be a significant cause of toxicity.

7.3. Acute toxicity - inhalation

No reports on acute inhalation toxicity of the notified chemical were supplied by the notifier.

7.4. Irritation – skin

7.4.1 Skin irritation – human volunteers, 21 days

TEST SUBSTANCE	Four Oil of Olay Daily UV Protectant prototypes, three containing 0.5 % analogue chemical and one 1 % analogue chemical; the close analogue used was SEFA polycottonseedate, assessed by NICNAS as STD/1001.
METHOD	
Study Design	The products (0.2 g) were applied daily under occlusive conditions to the back for 24 hr. An existing formulation of the product, containing no analogue chemical, was also tested as a control. Skin reactions were evaluated at each patch application.
Study Group	34 subjects; 27 completed the study
Vehicle	None
Remarks - Method	Subjects not completing the study were excluded for poor compliance or for personal reasons.
RESULTS	
Remarks - Results	For the products containing the analogue chemical, the numbers of subjects showing irritation scores of ? (minimal or doubtful erythema) or + (definite erythema) were similar throughout the study. No higher scores were observed. Definite erythema was observed in a maximum of 4 subjects. For the control (then current product) the frequency of higher score increased through the study and up to 23 subjects showed definite erythema by the study conclusion. Numerical equivalents of 1 for ? and 2 for + were assigned and cumulative scores calculated. For the control (then current) formulation, a total score of 514 was obtained. For the formulation containing the analogue chemical at 1 %, the total score was 228 and for the formulations containing the analogue chemical at 0.5 %, the scores were 104, 87 and 196. Distilled water gave a score of 101 under the same conditions, while sodium lauryl sulphate gave a total score of 1424. Two formulations containing the analogue chemical were classified as "slightly irritating", however, based on the results of the then current formulation, it is probable that these results reflect the contribution of ingredients other than the analogue chemical.
CONCLUSION	A 21 day cumulative skin irritation patch study was conducted using

cosmetic products containing a close analogue chemical at 0.5 – 1 % under occlusive dressing. The test substance was slightly irritating under the conditions of the test.

TEST FACILITY TKL Research, Inc (1997a)

7.4.2 Skin irritation – human volunteers, 5 days

TEST SUBSTANCE Lotion squeezed from SC-14 composite high lipid cleansing cloths, which contain 3.18 % notified chemical and 12.73 % of the close analogue chemical SEFA polycottonseedate, assessed as STD/1001, using 50 mL water per sheet. The total sucrose polyester content of a single cleaning cloth is approximately 0.12 g.

METHOD

Study Design	The lotion at 100 %, 50 % and 20 % (v/v) were applied daily under both occlusive and semi-occlusive conditions to the back for 24 hr, four times. Skin reactions were evaluated at each patch application.
Study Group	11 subjects; all completed the study
Vehicle	Water

RESULTS

Remarks - Results	No signs of skin irritation were observed for any of the test solutions under any conditions; distilled water also produced no irritation under the same conditions, while sodium lauryl sulphate produced the expected irritation.

CONCLUSION A 5 day cumulative skin irritation patch study was conducted using a cosmetic product containing the notified chemical under both occlusive and semi-occlusive dressing. The test substance was non-irritating under the conditions of the test.

TEST FACILITY TKL Research, Inc (1999a)

7.4.3 Skin irritation – human product trial, 28 days

TEST SUBSTANCE Two facial cleansing cloth formulations, one containing 17.19 % analogue chemical and one 15.79 % analogue chemical; the close analogue used was SEFA polycottonseedate, assessed by NICNAS as STD/1001.

METHOD

Study Design	The products were used by the panellists twice per day for 4 weeks under uncontrolled conditions in a single-blind test. Dermatological and ophthalmological examinations were performed at the beginning and end of the study period.
Study Group	55 subjects per product; 49 using the 17.19 % cloths and 50 using the 15.79 % cloths completed the study.
Vehicle	None
Remarks - Method	Instructions for use of the product during the study and a diary for recording product use were supplied to the study participants. Three subjects discontinued the study due to adverse reactions. An initial phase of the trial was discontinued when an error in matching products to self-reported skin types was realised.

RESULTS

Remarks - Results	At the final dermatological examination, no subject showed dermal scores above 0.5 (minimal or doubtful erythema, or dry appearance

	without scaling). One panellist using the 17.19 % formulation discontinued on day 8 with mild erythema and dryness. At the final ophthalmologic examination, five panellists using products containing the notified chemical had conditions of greater than trace severity – mild to moderate conjunctival follicles, mild papillae, mild cysts. mild to moderate concretions, mild mucous lens deposits and severe blurred vision were variously recorded among these. Two panellists using the products containing the analogue chemical discontinued due to adverse effects. One showed severe itching, moderate erythema, papules, tightness, hives and skin dryness; three weeks later application to the arm produced similar symptoms after four days. The response in this case was considered to be definitely test product related. The other reported mild erythema, dryness, itching and tingling, with difficulty focussing and moderate conjunctival injection. Twelve days later, retesting on the arm caused no symptoms, but later facial application produced the same signs. The response was considered to be possibly elated to the test product. Diary entries showed that 18 of 50 panellists using the 17.19 % formulation and 12 of 50 panellists using the 15.79 % formulation reported some mild, transient skin or eye conditions, including dryness, redness, itching, stinging or burning, eye discomfort and blurred vision. Of the 30, 4 reported levels beyond "mild", though none were "severe". The formulations of the cleansing cloths were supplied, and the observed effects may be related to a number of constituents apart from the analogue chemical.
CONCLUSION	A 28 day product trial was conducted using two facial cleansing cloth formulations containing a close analogue chemical at 17.19 % and 15.79 %. One of one hundred panellists was considered to have definite reactions to the product used, while one other showed a possible reaction to the product used under the conditions of the test.
TEST FACILITY	TKL Research, Inc (2000a)

7.5. Irritation - eye

No reports directly addressing the eye irritation potential of the notified chemical were submitted by the notifier. The product study reported in Section 7.4.3 included ophthalmologic investigations (TKL Research, 2000a). While ocular exposure would be incidental in this study, the results indicate that normal facial use of the product does not result in excessive eye irritation. The eye irritation potential observed may be a result of other constituents of the product, such as surfactants.

The notifier also provided an in vitro study on a product containing the notified chemical using a cytosensor microphysiometer, which addressed the eye irritation potential of the product (Institute for In Vitro Sciences, 1998). However the validation studies (Botham et al, 1997; Bruner et al, 1991; Harbell et al, 1999) on the in vitro technique have addressed to relationship of the response from this system to the measured eye irritation for a number of surfactants, but not for chemicals with physico-chemical properties similar to the notified chemical, and the test must therefore be assumed to have been predominantly directed at identifying eye irritation resulting from the surfactants in the product.

This study involved the use of murine L929 fibroblast cells, and measured the metabolic rate by use of a silicon microsensor to measure the rate of formation of acidic metabolic products upon treatment with a range of concentrations of the test substance. The eye irritation potential is reported in terms of the MRD_{50} (the concentration of test substance required to reduce the acidification rate by 50 %). For the product containing the notified chemical, the MRD_{50} value was greater than 76 mg/mL, indicative of low irritation potential. The test substance was lotion squeezed from a cleansing cloth, which contained 3.18 % notified chemical and 12.73 % of the close analogue chemical SEFA polycottonseedate, assessed as STD/1001, using 50 mL water per sheet. The total sucrose polyester content of a single cleaning cloth is approximately 0.12 g. For comparison, sodium lauryl sulphate, measured at the same time, gave a MRD_{50} value of

approximately 0.08 mg/mL. These results indicate that, to the extent that the test system is sensitive to the notified chemical, it has low irritation potential.
The notified chemical is an unreactive oily hydrophobic substance similar to vegetable oils in physico-chemical properties. The eye irritation potential upon instillation of pure notified chemical would be expected to be similar to that for vegetable oils. Palm kernel oil has been tested in pure form, and was found to have low irritation potential (Cosmetic Ingredients Review, 2000). A related fatty acid ester compound, ascorbic acid dipalmitate, was also found to be non-irritant to eyes (Cosmetic Ingredients Review, 1999). Based on these results, it is not likely that the notified chemical would have eye irritant properties due to its physico-chemical properties.

7.6. Skin sensitisation

7.6.1 Skin sensitisation – human volunteers

TEST SUBSTANCE	Four Oil of Olay Daily UV Protectant prototypes, three containing 0.5 % analogue chemical and one 1 % analogue chemical; the close analogue used was SEFA polycottonseedate, assessed by NICNAS as STD/1001.
METHOD	
Study Design	Human Repeat Insult Patch Test.
Study Group	233 subjects (28 male, 205 female, age range 18 – 73); 200 completed the study. Of these, 102 were assessed as having "normal" skin and 98 as having "sensitive" skin.
Vehicle	None
Induction Procedure	The test substance was applied under occlusive conditions by patch to the skin of the back for 24 hours, at 72 hour intervals, for a total of nine applications. Evaluation occurred at each patch removal except those performed by the panellist at weekends, where evaluation was performed at the following patch application.
Rest Period	10 – 26 days
Challenge Procedure	Challenge patches were applied similarly to induction patches, to a site not previously treated. These were removed after 24 hours, and evaluation occurred 24 and 48 hours after patch removal..
Remarks - Method	A Monday holiday occurred during the test, and a 96 hour gap between patch applications was used on this occasion. Subjects discontinuing in the study did so for reasons unrelated to treatment with the analogue chemical.
RESULTS	
Remarks - Results	Scattered positive results were observed during induction with all formulations; at any observation, up to 8 panellists (for a given product) showed doubtful responses and up to 8 showed definite erythema (generally predominantly in the "sensitive skin" groups); at challenge a maximum of 2 doubtful responses and one response of definite erythema were observed for any product; the responses in all but one case were for a single panellist. The test did not provide evidence of sensitisation as the numbers of responses seen at challenge were no higher than those after the initial induction treatment for any product.
CONCLUSION	A Human Repeat Insult Patch Test was conducted using cosmetic products containing a close analogue chemical at 0.5 – 1 % under occlusive dressing. The analogue chemical was non-irritating and non-sensitising under the conditions of the test.
TEST FACILITY	TKL Research, Inc (1997b)

7.6.2 Skin sensitisation – human volunteers

TEST SUBSTANCE	Lotion squeezed from SC-14 composite high lipid cleansing cloths, which contain 3.18 % notified chemical and 12.73 % of the close analogue chemical SEFA polycottonseedate, assessed as STD/1001, using 50 mL water per sheet. The total sucrose polyester content of a single cleaning cloth is approximately 0.12 g.
METHOD	
Study Design	Human Repeat Insult Patch Test.
Study Group	113 subjects (24 male, 89 female, age range 19 – 70); 102 completed the study.
Vehicle	None
Induction Procedure	The test substance was applied under occlusive conditions by patch to the skin of the back for 24 hours, at 72 hour intervals, for a total of nine applications. Evaluation occurred at each patch removal except those performed by the panellist at weekends, where evaluation was performed at the following patch application.
Rest Period	10 – 14 days
Challenge Procedure	Challenge patches were applied similarly to induction patches, to a site not previously treated. These were removed after 24 hours, and evaluation occurred 24 and 48 hours after patch removal.
Remarks - Method	No significant variations from the above protocol.
RESULTS	
Remarks - Results	Scattered equivocal results were observed during induction (up to 26 panellists at a given observation time); definite erythema was observed for one panellist; at challenge 4 doubtful responses were recorded at 24 hours; no challenge responses were seen at 48 hours. The test did not provide evidence of sensitisation as the numbers of responses seen at challenge were generally lower than those seen after any single induction treatment, and only equivocal responses were observed.
CONCLUSION	A Human Repeat Insult Patch Test was conducted using a cosmetic product containing the notified chemical under occlusive dressing. The notified chemical was non-irritating and non-sensitising under the conditions of the test.
TEST FACILITY	TKL Research, Inc (1999b)

7.6.3 Skin sensitisation – human volunteers

TEST SUBSTANCE	Lotion squeezed from two facial cleansing cloth formulations, one containing one containing 17.19 % analogue chemical and one 15.79 % analogue chemical, using 50 mL water per sheet; the close analogue used was SEFA polycottonseedate, assessed by NICNAS as STD/1001. The total sucrose polyester content of a single cleaning cloth is approximately 0.12 g.
METHOD	
Study Design	Human Repeat Insult Patch Test.
Study Group	108 subjects (7 male, 101 female, age range 19 – 75); 107 completed the study.
Vehicle	None
Induction Procedure	The test substance was applied under occlusive conditions by patch to the skin of the back for 24 hours, at 72 hour intervals, for a total of nine applications. Evaluation occurred at each patch removal except those performed by the panellist at weekends, where evaluation was performed at the following patch application.

Rest Period	10 – 14 days
Challenge Procedure	Challenge patches were applied similarly to induction patches, to a site not previously treated. These were removed after 24 hours, and evaluation occurred 24 and 48 hours after patch removal.
Remarks - Method	No significant variations from the above protocol.

RESULTS

Remarks - Results	Scattered equivocal results were observed during induction (up to 4 panellists for one product at a given observation time); definite erythema was observed for a maximum of one panellist at any observation time for a given product; at challenge no responses were recorded for one product; for the other two responses of definite erythema and one equivocal response were seen at 24 hours, and one equivocal response at 48 hours. The test did not provide evidence of sensitisation as the numbers of responses seen at challenge were generally lower than those seen after any single induction treatment.

CONCLUSION	A Human Repeat Insult Patch Test was conducted using two cosmetic products containing a close analogue chemical under occlusive dressing. The analogue chemical was non-irritating and non-sensitising under the conditions of the test.
TEST FACILITY	TKL Research, Inc (2000b)

7.7. Repeat dose toxicity

7.7.1 Repeat dose toxicity – 28 and 91 days in rats

TEST SUBSTANCE	Sucrose polyester (SPE) prepared from completely and partially hydrogenated soybean oil
METHOD	The study, performed in 1972, predates development of guidelines for studies for regulatory purposes. The study design was similar to OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents. The study used soybean oil (SBO, a completely digestible lipid) and completely hydrogenated soybean oil (HSBO, an indigestible lipid) as controls.
Species/Strain	Rat/Sprague-Dawley
Route of Administration	Oral –diet
Exposure Information	Total exposure days: 28 or 91 days; Dose regimen: 7 days per week; Post-exposure observation period: None
Vehicle	Mixed in diet, with SBO added to give a total lipid content of 17 % (w/w)
Remarks - Method	The study predates GLP guidelines. In each group, 10 animals were sacrificed on day 28 and the remainder on day 91. Actual intakes of the notified chemical were not reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration Nominal (%)*	*Mortality*
I	20 male	0	0/20
II	20 male	4	0/20
III	20 male	8	0/20
IV	20 male	15	0/20
V	20 male	15 (HSBO)	0/20

Clinical Observations

No clinical signs of toxicity were observed. The animals receiving SPE showed greasy appearance of the hair near the anus, and differences in the appearance of the faeces were observed. These were softer for Group III, and unformed and pasty for Group IV during the first four weeks of the study; later they were pelleted but soft and light grey. Lower growth rates were recorded for Groups III and IV in a dose related manner; the growth rate for Group IV was similar to that for control Group V. Food consumption showed an inverse pattern, with the highest consumption rates for the groups receiving the highest dose of SPE. The calorific efficiency (gain in body weight per 100 kilocalories consumed) therefore decreased as the level of notified chemical increased.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

The study authors indicated that the measured triglyceride levels were unrealistic and apparently in error. No consistent significant differences in blood chemistry, haematological parameters or urine chemistry were observed between groups.

Separate measurements were performed to determine the fat content of the faeces, and also the nitrogen content of faeces and urine. No significant differences in nitrogen absorption or excretion were observed. The fat content of the faeces indicated that the notified chemical was not significantly absorbed from the gastrointestinal tract (approximately 4 % of the dose level).

Effects in Organs

The only reported gross pathological difference between groups was in the nature of the contents of the gastrointestinal tract. A larger than usual amount of contents was found in the animals treated with the notified chemical, as a thick liquid anterior to the caecum, and pasty in the caecum and beyond. No test material related observations were reported from histopathological examinations.

The organ weights were not significantly different between groups except for the heart weight, which decreased in a dose-dependent fashion in the animals sacrificed at day 28. In the animals sacrificed at day 91, no similar effect was observed. The treatment with HSBO also led to decreased heart weights. Lipid levels in the liver, lungs, heart and kidney were also measured; no significant differences between groups were observed.

The liver lipids were further analysed, and showed slightly lower liver cholesterol for Groups IV (15 % SPE) and V (15 % HSBO), as well as lower liver triglycerides for the treated animals at day 28, although this was not seen for the animals sacrificed at day 91. The notified chemical was not identified as a component of the liver lipids in any group.

Remarks – Results

The attachments containing details of the individual animal pathology were not provided by the notifier. The results primarily reflected the difference in the absorbable fraction of the diet.

CONCLUSION

The No Observed Effect Level (NOEL) was established as 15 % in feed in this study, as all observed changes could be related to differences in the levels of absorbable lipids in the diet.

TEST FACILITY	Procter and Gamble Research and Development Department, Foods and Coffee Division (1973)

7.7.2 Repeat dose toxicity – 90 days in rats

TEST SUBSTANCE	Sucrose polyester (SPE) prepared from completely and partially hydrogenated soybean oil
METHOD	The study, performed in 1975, predates development of guidelines for studies for regulatory purposes. The study design was similar to OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents. The study used soybean oil (SBO, a completely digestible lipid) and completely hydrogenated soybean oil (HSBO, an indigestible lipid) as controls.
Species/Strain	Rat/Sprague-Dawley
Route of Administration	Oral –diet
Exposure Information	Total exposure days: 90 days; Dose regimen: 7 days per week;

	Post-exposure observation period: None
Vehicle	Mixed in diet, with SBO added to give a total lipid content of 16 % (w/w)
Remarks - Method	The study predates GLP guidelines. Sacrifice of the animals was performed over four days, commencing on day 95. Actual intakes of the notified chemical were not reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration Nominal (%)*	*Mortality*
I	10/sex	0	0/20
II	10/sex	4	0/20
III	10/sex	8	0/20
IV	10/sex	15	0/20
V	10/sex	15 (HSBO)	0/20

Clinical Observations

No clinical signs of toxicity were observed. Differences in growth rates were observed, with lower cumulative weight gains over the study period for Groups III and IV compared with Group II. Weight gains compared with controls receiving SBO only were not necessarily reduced due to changes in food consumption, however. Food consumption was highest for the groups receiving the highest dose of SPE, and for the group receiving HSBO. The calorific efficiency (gain in body weight per 100 kilocalories consumed) decreased as the level of notified chemical increased.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No significant differences in blood chemistry, haematological parameters or urine chemistry were observed between groups.

Separate measurements were performed to determine the fat content of the faeces, and also the nitrogen content of faeces and urine. No significant differences in nitrogen absorption or excretion were observed. The fat content of the faeces indicated that the notified chemical was not significantly absorbed from the gastrointestinal tract (between 0 and 13 % of the dose level).

Effects in Organs

No significant differences between groups were reported for organ weights, gross appearance or histopathology. Lipid levels in the liver, lungs, heart and kidney were also measured; no significant differences in levels or types of lipid present between groups were observed. The notified chemical was not identified as a component of the liver lipids in any group. Staining of other tissues, such as intestinal wall, did not indicate lipid accumulation.

Remarks – Results

Calculations based on raw weight and feed consumption data indicated that the dose consumed was approximately 15000 mg/kg bw/day for the females in Group IV. The results primarily reflected the difference in the absorbable fraction of the diet.

CONCLUSION

The No Observed Effect Level (NOEL) was established as 15 % in feed in this study, as all observed changes could be related to differences in the levels of absorbable lipids in the diet.

TEST FACILITY	Procter and Gamble Research and Development Department, Foods, Paper and Coffee Division (1975a)

7.7.3 Repeat dose toxicity – 28 days in dogs

TEST SUBSTANCE	Sucrose polyester (SPE) prepared from completely and partially hydrogenated soybean oil
METHOD	The study, performed in 1972, predates development of guidelines for studies for regulatory purposes. The study design was similar to that reported above for rats (Section 7.7.1).

	The study used soybean oil (SBO, a completely digestible lipid) and completely hydrogenated soybean oil (HSBO, an indigestible lipid) as controls.
Species/Strain	Dog/Beagle
Route of Administration	Oral –diet
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week; Post-exposure observation period: None
Vehicle	Mixed in diet, with SBO added to give a total lipid content of 17 % (w/w)
Remarks - Method	The study predates GLP guidelines. Two animals from each group were sacrificed on day 29 and two on day 30. Actual intakes of the notified chemical were not reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration Nominal (%)*	*Mortality*
I	4 male	0	0/4
II	4 male	4	0/4
III	4 male	15	0/4
IV	4 male	15 (HSBO)	0/4

Clinical Observations

No clinical signs of toxicity were observed. All animals maintained their weight throughout the study. Food consumption was highest for the groups receiving 15 % SPE or HSBO, but comparable for controls and 4 % SPE. For dogs fed 15 % SPE, faeces were lighter in colour than for the control or 4 % group, but were formed. No diarrhoea was observed.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No significant differences in haematological parameters or urine chemistry were observed between groups, except that the control group receiving HSBO showed slightly reduced haemoglobin. Lower blood cholesterol was seen for animals receiving SPE in a dose related manner, and to a lesser effect for the animals receiving HSBO. No other differences in blood chemistry were reported, and an independent measurement of blood cholesterol did not show any significant changes.

Separate measurements were performed to determine the nitrogen content of faeces and urine. No significant differences in nitrogen absorption or excretion were observed, except that the nitrogen percentage in the faeces of the dogs receiving SBO only was slightly higher, corresponding to the lower fat content of the faeces for these animals.

Effects in Organs

No significant differences between groups were reported for organ weights, gross appearance or histopathology. A larger quantity of material was present in the lower gastrointestinal tract for the animals of Groups III and IV. Lipid levels in the liver, lungs, heart and kidney were also measured. Increased heart lipids were observed for the treated animals, but not in a dose related fashion. Analysis of liver lipids showed an increase in liver cholesterol for the SPE treated animals. The notified chemical was not identified as a component of the liver lipids in any group. Staining of other tissues, such as intestinal wall, did not indicate lipid accumulation.

Remarks – Results

The study authors accepted the plasma cholesterol values showing significant differences between groups over the serum cholesterol values which showed similar results across the groups based on past experience with the laboratory which performed the former group of measurements. The results primarily reflected the difference in the absorbable fraction of the diet.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 15 % in feed in this study, due to uncertainty of the significance of the cholesterol measurements.

TEST FACILITY	Procter and Gamble Research and Development Department, Foods and Coffee Division (1972)

7.7.4 Repeat dose toxicity – 30 days in dogs

TEST SUBSTANCE	Sucrose polyester (SPE) prepared from completely and partially hydrogenated soybean oil
METHOD	The study, performed in 1975, predates development of guidelines for studies for regulatory purposes. The study design was similar to that reported above for rats (Section 7.7.2). The study used soybean oil (SBO, a completely digestible lipid) and completely hydrogenated soybean oil (HSBO, an indigestible lipid) as controls.
Species/Strain	Dog/Beagle
Route of Administration	Oral –diet
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week; Post-exposure observation period: None
Vehicle	Mixed in diet, with SBO added to give a total lipid content of 17 % (w/w)
Remarks - Method	The study predates GLP guidelines. One animal per sex from each group were sacrificed per day, commencing on day 29. Actual intakes of the notified chemical were not reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration Nominal (%)*	*Mortality*
I	4/sex	0	0/8
II	4/sex	4	0/8
III	4/sex	15	0/8
IV	4/sex	15 (HSBO)	0/8

Clinical Observations
No clinical signs of toxicity were observed. Little change in body weight was observed throughout the study. Food consumption was generally higher for the groups treated with SPE or HSBO than for the SBO control.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
No significant differences in haematological parameters or urine chemistry were observed between groups. Decreases in blood cholesterol and phospholipids over the course of the study were seen for animals receiving SPE in a dose related manner. No similar changes were seen for the control (SBO) group. No change in triglyceride levels over the course of the study were reported.
Separate measurements were performed to determine the fat contents of faeces and the nitrogen content of faeces and urine. Fat balance measurements showed that the SPE was not absorbed from the diet within the limit of accuracy of the measurements. A small decrease in nitrogen absorption and increase in nitrogen excretion was observed for Group III. This group had higher protein intake than controls due to the higher food consumption.

Effects in Organs
No significant differences between groups were reported for organ weights, gross appearance or histopathology. Lipid levels in the liver, lungs, heart and kidney were also measured, and no differences between groups were observed. Analysis of liver lipids showed no difference in composition between the groups. The notified chemical was not identified as a component of the liver lipids in any group. Staining of other tissues did not indicate lipid accumulation.

Remarks – Results

Calculations based on raw weight and feed consumption data indicated that the dose consumed was approximately 5500 mg/kg bw/day for the females in Group III. The results primarily reflected the difference in the absorbable fraction of the diet.

CONCLUSION

The No Observed Effect Level (NOEL) was established as 15 % in feed in this study, as all observed changes could be related to differences in the levels of absorbable lipids in the diet.

TEST FACILITY Procter and Gamble Research and Development Department, Foods, Paper and Coffee Division (1975b)

7.7.5 Published absorption and repeat dose toxicity studies

A published study on absorption of sucrose polyesters reported using several radiolabelled sucrose polyesters administered to rats by oral gavage (Miller et al, 1995). The labelled material was administered after a 28 day acclimatisation period where unlabelled test substance was administered in feed. Animals were sacrificed 1, 3, 7 and 21 days after dosing. The majority of the radioactivity was recovered from the faeces, the gastrointestinal tract and contents, and solutions from washing the carcasses and cages. The percentage of absorbed radiolabel recovered from exhaled air, urine, tissues, carcass and blood maximised at around 7 days after dosing. For sucrose polyesters containing majority hepta- and octaesters, the absorbed radiolabel was always less than 0.1 % of the administered dose, while for sucrose polyester containing majority hexa- and pentaesters and below, up to 1.6 % of the administered dose was absorbed.

Two papers from published literature which address the repeat dose toxicity of a close analogue of the notified chemical have been provided by the notifier. Both papers used sucrose polyester derived from soybean oil.

One paper describes two 2-year feeding studies in Fischer 344 rats, using levels of 0, 0.99, 4.76 or 9.09 % in diet, and 0 and 9.09 % in diet respectively (Wood et al, 1991). In the first study, 75 animals per sex per dose level were used, with 15 per sex per dose level sacrificed at 12 months for toxicity testing and the remaining animals reserved for the carcinogenicity study; an additional 10 animals per sex per dose level were included for other studies. The second study had a similar design, with 50 males and 73 females per group, and 15 females per group sacrificed at 12 months; additional animals were also included.

In the first study at 12 months, the two higher dose groups showed a small increase in body weights; this was not observed at 24 months or in the second study, and was attributed to overcompensation for the reduced calorific content of the food. In the highest dose group, in the first study, there was increased mortality among the males compared with controls, but no similar effects were seen at other doses, in the females, or in the second study. Also the causes of death were not consistent within the group. No biologically significant differences were seen during ophthalmological examinations, or in haematology or urinalysis parameters, or in organ weights. Carcinogenicity investigations showed statistically significant differences in the incidence of some effects (particularly pituitary adenoma and mononuclear cell leukaemia in study 1), but these were not replicated in the other study, and were within normal historical limits.

It was concluded from these studies that the sucrose polyester did not show toxic or carcinogenic effects after 2 years feeding in rats at up to 9.09 % (equivalent to 4500 mg/kg bw/day).

The second paper reports a 20-month feeding study in beagle dogs, at dose levels of 0, 5 or 10 % of the diet (Miller et al, 1991). Five animals per sex were used for each dose level.

No treatment related mortalities were reported. No clinical, ophthalmological or neurological signs of toxicity were observed. Soft stools were occasionally observed among the treated

animals. A slight increase in food consumption was observed for the treated animals, along with a slight increase in body weights for the animals receiving 10 % SPE. Haematological, clinical chemistry and pathological studies showed no effects that were considered related to treatment.

It was concluded from these studies that the sucrose polyester did not show toxic effects after 20 months feeding in dogs at up to 10 % (equivalent to 3000 mg/kg bw/day).

7.8. Genotoxicity - bacteria

TEST SUBSTANCE	Sucrose polyester N0038.12
METHOD	In-house protocol (supplied) based on the method of Ames (1975) Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1538, TA1535, TA1537, TA98, TA100.
Metabolic Activation System	S9 fraction from the liver of rats induced with Aroclor 1254
Concentration Range in Main Test	a) With metabolic activation: 675 - 21600 µg/plate. b) Without metabolic activation: 675 - 21600 µg/plate.
Vehicle	Acetone
Remarks - Method	Testing was performed in triplicate. A single test was performed for each strain, with and without metabolic activation, except where confirmation of results was required.
RESULTS	
Remarks - Results	No signs of cytotoxicity were observed. Precipitation in the form of oil droplets was observed for higher concentrations of test substance (5400 µg/plate and above). No significant dose dependent increases in the numbers of revertants were recorded for any strain, either in the presence or absence of metabolic activation. One test was repeated because vehicle control values were outside the specified range. In another test, TA98 without metabolic activation, all treated plates showed revertant numbers three to four times above negative and vehicle controls, but without any indication of dose response. Retesting showed no increase in revertant numbers under these conditions. Appropriate positive controls were used and all resulted in large increases in revertant colonies, confirming the sensitivity of the test system.
CONCLUSION	The test substance was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	The Procter and Gamble Company, Human and Environmental Safety Division. (1983a)

7.9. Genotoxicity – in vitro

7.9.1 L5178Y TK+/- Mouse Lymphoma Assay

TEST SUBSTANCE	Sucrose polyester N0038.12
METHOD	L5178Y TK+/- Mouse Lymphoma Assay In-house protocol (supplied) based on the method of Clive (1975)
Cell Type/Cell Line	L5178Y Mouse Lymphoma Cells
Metabolic Activation System	S9 fraction from the liver of rats induced with Aroclor 1254
Vehicle	Acetone
Remarks - Method	

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Present	7860, 5890, 4420, 3310, 2480. 1860, 1400, 1040, 790, 590	4 hr	48 hr	10-12 days
Absent	7860, 5890, 4420, 3310, 2480. 1860, 1400, 1040, 790, 590	4 hr	48 hr	10-12 days

RESULTS

Remarks - Results: No cytotoxicity was observed in a preliminary test at up to 7860 µg/mL. No cytotoxicity was observed in the main test, and no significant differences in mutant frequencies relative to solvent controls were observed either in the presence or absence of metabolic activation.
Appropriate positive controls were used and all resulted in large increases in mutant frequencies, confirming the sensitivity of the test system.

CONCLUSION: The test substance was not mutagenic to L5178Y mouse lymphoma cells treated in vitro under the conditions of the test.

TEST FACILITY: Microbiological Associates (1983a)

7.9.2 Chromosome Aberration Study in CHO Cells

TEST SUBSTANCE: Sucrose polyester N0038.12

METHOD: In house protocol (supplied), similar to OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.

Cell Type/Cell Line: Chinese hamster ovary (CHO) cells
Metabolic Activation System: 33 % S9 fraction from the liver of rats pretreated with Aroclor 1254
Vehicle: Acetone
Remarks - Method: No repeat assay was performed.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Present	1000*, 760*, 567*, 424, 316, 238, 179	4 hr	20 hr
Absent	1000*, 744*, 562*, 423, 318, 238*, 177	4 hr	20 hr

RESULTS

Remarks - Results: Cytotoxicity as indicated by reduced cloning efficiency (< 50 %) was observed for several of the lower doses in the absence of metabolic activation, although equivalent results were not seen in the preliminary cytotoxicity assay. The dose with the highest apparent cytotoxicity was analysed. No significant increases in the numbers of cells with chromosomal aberrations were seen either in the presence or absence of metabolic activation. Appropriate positive controls gave large increases in the numbers of cells with chromosomal aberrations, confirming the sensitivity of the test system.

CONCLUSION: The test substance was not clastogenic to CHO cells treated in vitro under the conditions of the test.

TEST FACILITY: Microbiological Associates, Inc (1983b)

7.9.3 Unscheduled DNA Synthesis Assay

TEST SUBSTANCE: Sucrose polyester N0038.12

METHOD: In-house protocol (supplied), based on the method of Williams (1977,

	1978)
Species/Strain	Rat/Sprague-Dawley
Cell Type/Cell Line	Hepatocytes
Metabolic Activation System	None
Vehicle	Acetone
Remarks - Method	Unscheduled DNA synthesis was monitored by incorporation of ^{3}H-thymidine

Test Substance Concentration (µg/mL)	*Exposure Period*
50, 75, 115, 170, 385, 580, 870, 1300, 1950	18-20 hr

RESULTS

Remarks - Results	No cytotoxicity was observed in a preliminary test at up to 7860 µg/mL. No cytotoxicity was observed in the main test, and no significant increases in ^{3}H thymidine incorporation relative to solvent controls were observed. An appropriate positive control was used and resulted in a large increase in ^{3}H thymidine incorporation, confirming the sensitivity of the test system.
CONCLUSION	The notified chemical was not clastogenic to rat hepatocytes treated in vitro under the conditions of the test.
TEST FACILITY	The Procter and Gamble Company, Biological Testing Facility (1983b)

7.10. Genotoxicity – in vivo

TEST SUBSTANCE	Unspecified sucrose polyester, previously heated to approximately 180^{o}C for 25 – 32 hours in air.
METHOD	Similar to OECD TG 475 Mammalian Bone Marrow Chromosomal Aberration Test.
Species/Strain	
Route of Administration	Oral – gavage.
Vehicle	None
Remarks - Method	A summary report of a preliminary test using the same doses but with a single administration was also provided (Microbiological Associates, 1992). The report for the subchronic study is in summary form, and states that the study was conducted using standard procedures for an in vivo rat bone marrow cytogenicity study. Doses were administered daily on 5 successive days; the sacrifice time below is from the time of the last dose.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I	10 per sex	500	6, 24
II	10 per sex	1700	6, 24
III	10 per sex	5000	6, 24
IV	10 per sex	20 (CP)	6, 24

CP=cyclophosphamide.

RESULTS

Doses Producing Toxicity	No signs of toxicity were reported.
Genotoxic Effects	No significant increases in the percentage of aberrant cells were seen.
Remarks - Results	A large increase in chromosomal aberrations was seen after treatment with the positive control, confirming the sensitivity of the test system.
CONCLUSION	The test substance was not clastogenic in this in vivo cytogenicity assay

under the conditions of the test.

TEST FACILITY Microbiological Associates, Inc (1993)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

Study 1

TEST SUBSTANCE Sucrose Polyester N0038.08, ^{14}C-SPE N0038.10

METHOD The fate of Sucrose Polyester (SPE) in Activated Sludge, D.E. Sullivan, 22/7/81, and addendum to study plan, 26/8/81

Inoculum: Activated sludge from WWTP

Exposure Period: 48 h

Auxiliary Solvent: 10 mg/L of AE_XS (alcohol ethoxylate surfactant)

Analytical Monitoring: A number of parameters were measured over the test period to determine concentrations and removal of ^{14}C-SPE. These included: total, soluble, solid radioactivity, sodium hydroxide traps, effluent, and CO_2 concentration (biometer).

Remarks - Method: Semi-continuous activated sludge units (SCAS) were used to determine the removal rates of sucrose polyester by biodegradation or adsorption onto biological solids. The test system comprised 8 reactors (2 × 4 replicates) containing a series of sodium hydroxide traps designed to remove atmospheric CO_2, and a barium hydroxide trap to indicate either inefficient removal by, or saturation of, the sodium hydroxide traps. The SCAS units each contained 2500 mg total suspended solids/L of activated sludge in 1500 mL volume, inserted in such a way that the effluent gas is directed through each of the trapping systems. Prior to testing, there was a 7 day period of acclimatisation, during which the test substances were incrementally fed into each pair of reactor vessels. During testing, test samples comprising a maximum concentration of either 0 (control), 4.5 mg/L, 9.5, or 14.5 mg/L of cold SPE, were added to test vessels which were sealed for a period of 2 days. In addition either 0 (control) or 0.5 mg/L of ^{14}C-SPE, and 10 mg/L of AE_XS, which was used to disperse SPE and ^{14}C-SPE, were also fed into the test reactor vessels.

RESULTS

Remarks - Results: Based on radioactivity analysis, removal of ^{14}C-SPE was > 95 % within 24 hours. The prime means of removal was adsorption onto activated sludge (ie > 90 %), and with less than 2 % of sucrose polyester biodegraded over the test period.

CONCLUSION The substance was not biodegradable under the test conditions.

TEST FACILITY Procter & Gamble, Environmental Safety Department (1981a)

Study 2:

TEST SUBSTANCE Sucrose polyester SPE – X0393.02; SPE – X0393.01R
Emulsified soybean oil – X0397.01

METHOD Protocol E86-008: Assessing the treatability and effects of SPE in secondary waste water treatment.

Inoculum: Activated sludge from municipal WWTP

Exposure Period	3-5 days
Auxiliary Solvent	Not reported
Remarks - Method	Two nominal concentrations of test material were used (60 and 1000 μg/L) to determine removal in a model Continuous Activated Sludge (CAS) system. From the information provided, it could not be determined if a reference substance was used.

RESULTS

Remarks - Results	The overall removal was determined to be 84 % at 60 μg/L and 84.9 % at 1000 μg/L. The percentage partitioning into liquid and on solids was also determined. In the effluent this was found to be 27.4 % in the liquid and 74.3 % on the solids for 60 μg/L, while for 1000 μg/L it was 24.1 % in liquid and 72.8 % on solids. This separation was observed to change in the aeration basin where at 60 μg/L, 0.4% was in liquid and 98.7 % on the solids, and at 1000 μg/L, 0.2 % was in the liquid and 95.5 % on solids.
CONCLUSION	The results show that the chemical is removed via physical means rather than through biological activity.
TEST FACILITY	Procter & Gamble, Environmental Safety Department (1986)

8.1.2. Bioaccumulation

TEST SUBSTANCE	Sucrose polyester radiolabelled ^{14}C (ESD Number: N0038.10)
METHOD	Fish Bioconcentration Continuous Flow Test (In house method contained in laboratory book No. ZE 1102 and MP 8043, p.35-43)
Species	Bluegill Fish (*Lepomis macrochirus*)
Exposure Period	Exposure: 28 days Depuration: 14 days
Auxiliary Solvent	ESD laboratory blended water
Concentration Range	
Nominal	30 μg/L
Actual	25.3±8.8 μg /L
Analytical Monitoring	Liquid Scintillation Counting
Remarks - Method	Type of study – continuous flow. Four fish were sampled for SPE content at each sampling period.

RESULTS

Bioconcentration Factor	< 50 (based on the detection limit in fish).
Remarks - Results	No mortalities were observed throughout the study. At 28 days no SPE was detected in the fish. The uptake and elimination rate constants could not be determined.
CONCLUSION	Concentrations of SPE in the test fish at 28 days of exposure was not detectable, therefore, uptake and elimination rate constants were not determined. The BCF is estimated to be < 50 based on the detection limit in fish, suggesting the chemical is unlikely to bioaccumulate.
TEST FACILITY	Procter & Gamble, Environmental Safety Department (1981b)

8.2. Environmental Effects

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Sucrose polyester – SPE – N00389.08,
METHOD	Freshwater Fish Toxicity – Static
Species	Bluegill sunfish (*Lepomis macrochirus*)
Exposure Period	96 h
Auxiliary Solvent	None
Water Hardness	48 mg $CaCO_3$/L
Analytical Monitoring	None
Remarks – Method	Only a summary test report was provided in the notification dossier. The test substance was sonicated in distilled water before dilution to test solutions. All test solutions were continuously mixed throughout the test period. All test concentrations initially had undissolved material on the surface and were cloudy in appearance. At 96 hours, the materials at the lowest test concentrations (220 and 130 mg/L) were no longer on the surface but had adhered to the glass walls and tubing.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1h*	*24h*	*48h*	*72h*	*96h*
1000		10	0	0	0	0	0

LC50	>1000 mg/L at 96 hours.
NOEC (or LOEC)	1000 mg/L at 96 hours.
Remarks – Results	
CONCLUSION	These results indicate that the chemical is not toxic to Bluegill sunfish (*Lepomis macrochirus*).
TEST FACILITY	EG&G-Bionomics (1980a)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Sucrose polyester – SPE
METHOD	Methods for acute toxicity tests with fish, macro-invertebrates, and amphibians, US EPA, 1975 and in-house protocol, static acute freshwater invertebrate toxicity study of N0038.08, 12/21/82
Species	*Daphnia magna* (<25 hours old)
Exposure Period	48 hours
Auxiliary Solvent	Dilution water (fortified well water)
Water Hardness	160±20 mg $CaCO_3$/L
Analytical Monitoring	None
Remarks - Method	A measured weight of test substance was added directly to test beakers containing dilution water. Because some of the test material adhered to weighing dishes, these were left in the test vessels throughout the study. The test beakers were sonicated for 20 minutes. All solutions of sucrose polyester were cloudy and contained undissolved material on the solution surface and on the weighing dishes throughout the exposure period. Hence, all test results are based on nominal concentrations.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0		15 (5 daphnia and 3 replicates)	0	0
79		15 (5 daphnia and 3 replicates)	0	3
130		15 (5 daphnia and 3 replicates)	2	4
220		15 (5 daphnia and 3 replicates)	2	4
360		15 (5 daphnia and 3 replicates)	2	2
600		15 (5 daphnia and 3 replicates)	2	7
1000		15 (5 daphnia and 3 replicates)	1	7

LC50	1800 mg/L at 48 hours
NOEC (or LOEC)	Not given
Remarks - Results	Water fleas exposed to the test solutions became entrapped on the undissolved sucrose polyester. The observed mortalities appeared to be due to the physical entrapment rather than to the direct toxicity of the test substance. A satisfactory dose-response curve could not be obtained from the data, and an accurate estimate of the 48-hour LC50 could not be made. The 48 h LC_{50} was estimated by probit analysis (C.I. 470 - ∞).
CONCLUSION	The results obtained from probit analysis indicate that sucrose polyester is not toxic to daphnia.
TEST FACILITY	EG&G-Bionomics, Aquatic Toxicity Laboratory (1980b)

8.2.3. Algal growth inhibition test

Study 1

TEST SUBSTANCE	Sucrose polyester (N0038.08), 98.3% active ingredient
METHOD	Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians, US EPA, 1975 and an in-house protocol, static acute freshwater invertebrate toxicity study of N0038.08, 12/21/82. Procter & Gamble protocol, Toxicity of N0038.08 to algae, 21/12/82, by V.T. Wee, based on A Method For Measuring Algal Toxicity And Its Application To The Safety Assessment Of New Chemicals, by Payne and Hall and US EPA, 1978.
Species	Freshwater diatom *(Navicula seminulum)*
Exposure Period	120 hours (5 day)
Concentration Range	
Nominal	100 and 1000 mg/L
Actual	Not given
Auxiliary Solvent	Algal growth medium
Water Hardness	Not given
Analytical Monitoring	*In vivo* chlorophyll *a* (relative fluorescent units) and cell counts (hemacytometer).
Remarks - Method	Measured amounts of the test material were placed in 125 mL flasks to which 50 mL of algal growth medium was added to give nominal concentrations of 0 (control), 100 and 1000 mg/L of test material. The flasks were sonicated in a water bath to disperse the material, after which time the flasks were inoculated with the *Navicula*. Cell counts were made with a hemacytometer over a 5 day period. Chlorophyll fluorescence was determined each day over the 5 day test period. Undissolved test material was observed in the test medium.
RESULTS	
Remarks - Results	After 5 days of exposure, cell counts decreased by 9 % in cultures exposed to 100 mg/L and 58 % in those exposed to 1000 mg/L compared to the control. *In vivo* chlorophyll *a* studies indicated the same

findings as the cell counts. Visual observations revealed the algae to be adhering to the undissolved test material, and apparently still growing well on the surface of the test substance. It was thought that the decrease in growth was due to the algal cells sticking and clumping together rather than to a direct toxic effect of the test substance because the algae appeared to be growing well when in direct contact with the material. As such, the 5 day algistatic concentration was determined to be >1000 mg/L.

CONCLUSION: These results suggest that the sucrose polyester is not toxic to the freshwater diatom, *Navicula seminulum*.

TEST FACILITY: EG &G-Bionomics, Marine Research Laboratory (1983a)

Study 2

TEST SUBSTANCE: Sucrose polyester (N0038.08)

METHOD: Methods for acute toxicity tests with fish, macro-invertebrates, and amphibians, US EPA, 1975 and in-house protocol, static acute freshwater invertebrate toxicity study of N0038.08, 12/21/82. Procter & Gamble protocol, Toxicity of N0038.08 to algae, 21/12/82, by V.T. Wee, based on A Method For Measuring Algal Toxicity And Its Application To The Safety Assessment Of New Chemicals, by Payne and Hall and US EPA, 1978.

Species	*Selenastrum capricornutum*
Exposure Period	120 hours (5 day)
Concentration Range Nominal	100 and 1000 mg/L
Concentration Range Actual	Not given
Auxiliary Solvent	Algal growth medium
Water Hardness	Not given
Analytical Monitoring	*In vivo* chlorophyll *a* (relative fluorescent units) and cell counts (hemacytometer).
Remarks - Method	Measured amounts of the test material were placed in 125 mL flasks, and to these were added 50 mL of algal growth medium to give nominal concentrations of 0 (control), 100 and 1000 mg/L of test substance. The flasks were then sonicated in a water bath to disperse the material, after which the flask was inoculated with the algae. Cell counts were made with a hemacytometer over a 5 day period. Chlorophyll fluorescence was determined each day over the 5 day test period. Undissolved material was observed to remain in the test medium.

RESULTS

Remarks - Results: After 5 days of exposure, cell counts decreased by 11 % in cultures exposed to 100 mg/L and 88 % in those exposed to 1000 mg/L. *In vivo* chlorophyll *a* studies indicated the same findings as the cell counts. Visual observations revealed the algae to be adhering to the undissolved test material, and apparently still growing well on the surface of the test substance. It was thought that the decrease in growth was due to the algal cells sticking and clumping together rather than to a direct toxic effect of the test substance because the algae appeared to be growing well when in direct contact with the material. As such, the 5 day algistatic concentration was determined to be >1000 mg/L.

CONCLUSION: These results indicate that the sucrose polyester is not toxic *Selenastrum capricornutum*.

TEST FACILITY: EG &G-Bionomics, Marine Research Laboratory (1983b)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Usage patterns indicate that, ultimately, up to 60 % of the notified chemical will be released into the aquatic environment at end use via sewage treatment facilities. The notified chemical is only very slightly water soluble and hence, in sewage treatment plants, is expected to partition mainly into the sediment. The substance is not biodegradable. In the biodegradation test, up to 90 % of the substance was lost due to adsorption onto sewage.

A worst case scenario daily PEC for the aquatic environment resulting from release at end use of products containing the notified chemical is provided. In calculating the PEC, we have assumed that release of the notified chemical to sewage systems occurs on a nationwide basis, is continuous throughout the year with no removal by adsorption. While it is recognised that larger releases of the chemical are likely to occur in higher population areas where usage rates would be higher, it was not considered practical to determine such releases for end use. Thus, a worst case nationwide Predicted Environmental Concentration (PEC) can be estimated as follows:

Maximum amount released	0.5 tonnes
Number of days	365days
Population	18 million
Amount of water used per person	150 L
Daily water usage	$18000000 \times 150 = 2700$ ML
Nationwide daily PEC	$500/(365 \times 2700) = 5 \times 10^{-4}$ mg/L

The physico-chemical properties and results of the biodegradation test indicate that a significant portion of the notified chemical will be removed from sewage treatment facilities due to adsorption either on sediments or sludge, which would reduce the PEC significantly.

9.1.2. Environment – effects assessment

The results of the ecotoxicological data indicate the notified chemical was not toxic to aquatic organisms. The LC50 for all the fish, daphnia, and algae tested were greater than 1000 mg/L.

A predicted no effects concentration (PNEC) can be determined when at least one acute LC50 for each of the three trophic levels is available (ie. fish, daphnia, algae). The PNEC is calculated by taking the LC50 value of the most sensitive species, and dividing this value by an assessment safety factor of 100 (OECD). Since the LC50 for these species was >1000 mg/L, using a worst case scenario safety factor of 100, the PNEC(aquatic) is 10 mg/L.

9.1.3. Environment – risk characterisation

The toxicity tests on a sucrose polyester indicate that it is not toxic to fish, daphnia or algae. However, the substance did have adverse effects on daphnia and algae resulting from the organisms physically adhering to undissolved test substance in the test media. This is unlikely to occur in the natural environment, however, because the concentration of the chemical encountered by organisms in the aquatic environment will be low when taking into account the very high dilution rates involved in the release processes. The calculated PEC values are many orders of magnitude lower than the lowest concentrations found to have adverse affects on daphnia and algae, and showing no adverse effects on fish.

The PEC/PNEC ratio for the local aquatic environment, assuming nationwide use and no removal by adsorption, is 5×10^{-5}. This value is significantly less than 1, indicating no immediate concern to the aquatic compartment.

The high partition coefficient and results of the biodegradability tests indicate that up to 90 % of the notified chemical could enter the soil environment via disposal of sewage sludge or residual wastes containing the substance. In soil environments, the notified chemical is expected to be largely immobile. While the substance is not biodegradable, in soil environments, it is expected to undergo slow degradation through biotic and abiotic processes.

While the partition coefficient is relatively high, due to its large molecular size, the notified chemical is not expected to cross biological membranes and bioaccumulate (Connell, 1990). This is supported by the BCF < 50, indicating a low potential to bioaccumulate.

Given the above considerations, the notified chemical is not expected to pose any significant hazard to the environment. The anticipated nationwide use of the product indicates that the levels of release of the chemical to the environment will be low, and significantly lower than the levels of exposure having adverse effects on algae and daphnia.

9.2. Human health

9.2.1. Occupational health and safety

9.2.1.1 OCCUPATIONAL EXPOSURE ASSESSMENT

The notifier indicated that 6 – 12 transport workers (4 hr/day, 50 days/year), 8 – 12 warehouse workers (2 hr/day, daily) and of the order of 10000 retail workers (1 hr/day, daily) will handle the products containing the notified chemical. The work will involve handling of the products in their retail packaging only, and in the case of workers apart from retail workers, in outer cartons as well. Retail workers will unpack cartons and handle individual containers. Even in the case of an accident, little exposure is expected due to the small package sizes.

9.2.2. Public health

Exposure of the general public as a result of transport and disposal of products containing the notified chemical is assessed as being negligible. Public exposure to the notified chemical will occur as a result of dermal application of cosmetic products. The skin area exposed to the notified chemical would normally be restricted to the face. Exposure is expected to occur up to several times per day and the amounts of the notified chemical to which individuals will be exposed is expected to vary considerably depending upon individual use patterns. However it may be approximately 8 mg/day or more. The duration of exposure to the notified chemical is expected to be minimal since products are designed to be washed off soon after application.

9.2.3. Human health - effects assessment

9.2.3.1 SUMMARY OF TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50	test not conducted
Rat, acute dermal LD50	test not conducted
Rat, acute inhalation LC50	test not conducted
Human, skin irritation	non-irritating
Rabbit, eye irritation	test not conducted
Human, skin sensitisation	no evidence of sensitisation.
Rat, Oral Repeat Dose Toxicity	
28 and 91 days	NOEL = 15 % in feed
90 days	NOEL = 15 % in feed (~15000 mg/kg bw/day)
2 years.	NOEL = 4500 mg/kg bw/day
Dog, Oral Repeat Dose Toxicity	
28 days	NOEL = 15 % in feed
30 days	NOEL = 15 % in feed
20 months.	NOEL = 3000 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	Non mutagenic
Genotoxicity – in vitro:	
L5178Y TK+/- mouse lymphoma assay	Non genotoxic
Chromosome aberration study in CHO cells	Non genotoxic
Unscheduled DNA synthesis assay	Non genotoxic
Genotoxicity – in vivo cytogenicity assay	Non genotoxic
Pharmacokinetic/Toxicokinetic Studies	Not absorbed from the gastrointestinal tract
Carcinogenicity	not carcinogenic

9.2.3.2 DISCUSSION

The toxicity studies on the notified chemical or close analogues demonstrate that they are not absorbed from the gastrointestinal tract. A study on absorption of close analogues showed that sucrose polyesters containing mostly hepta- and octaesters, as is the case for the notified chemical, are not significantly absorbed after oral administration. Based on these results, and on the physico-chemical properties of the notified chemical (high molecular weight, unreactive and hydrophobic), it is unlikely that significant absorption across biological membranes will occur.

No results for the acute toxicity of the notified chemical were provided by the notifier. However, based on the very high doses of close analogue chemical tested in repeat dose studies without toxic effects and the low probability of absorption across biological membranes, it can be concluded that the acute oral LD50 is greater than 15000 mg/kg in rats, and that there is little likelihood of systemic toxicity by any other exposure route.

Human patch testing using products containing the notified chemical or a close analogue showed at most slight irritation, and comparison with products containing similar ingredients but excluding the notified chemical indicated that the observed results are not likely to be due to the notified chemical. Eye irritation testing was not carried out, but product testing in a human panel showed no indications of a product containing a close analogue chemical being hazardous to the eye. materials of similar physico-chemical properties to the notified chemical have been tested as being non-irritant to the eye. Human patch testing of products containing the notified chemical did not provide evidence of sensitising properties.

A close analogue of the notified chemical has been extensively tested in repeat dose and chronic feeding studies in dogs and rats, and no significant indications of toxicity have been found even at very large doses or over extended periods (eg treatment of rats with 4500 mg/kg bw/day in feed for 2 years). No indications of carcinogenicity of the analogue chemical were found in the 2 year study in rats.

Additional in vitro and in vivo genotoxicity studies showed no indications of genotoxic effects from close analogue of the notified chemicals. Additionally, testing of previously heated sucrose polyester showed no indication of genotoxicity in a number of tests, nor of subchronic toxicity in a 91 day feeding study in rats (Williams et al, 1996).

Long term repeated exposure of humans in the USA to high levels of the notified chemical or a close analogue in consumer products, both by skin application and ingestion, have not resulted in indications of toxicity in humans.

9.2.4. Human health – risk characterisation

9.2.4.1 OCCUPATIONAL HEALTH AND SAFETY

The notified chemical is not expected to pose a significant risk to occupational health and safety due to the low occupational exposure and also to the low toxicity of the notified chemical.

9.2.4.2 PUBLIC HEALTH

Exposure of the general public as a result of transport and disposal of products containing the notified chemical is assessed as being negligible. Although members of the public will make frequent dermal contact with products containing the notified chemical, the risk to public health is considered to be minimal since the notified chemical is not expected to cross biological membranes, it is expected to be of low toxicological hazard and the duration of exposure to the notified chemical is expected to be short since products containing it are designed to be washed off soon after application to the skin.

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

10.1. Environment

On the basis of the PEC/PNEC ratio:

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.2. Health hazard

Based on the available data the notified chemical is not classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

10.3. Human health

10.3.1. Human health – Occupational health and safety

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

10.3.2. Human health – public

There is Negligible Concern to public health when used in cosmetic products as described in the notification.

11. RECOMMENDATIONS

11.1. Control measures

Occupational Health and Safety

- 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.

11.2. 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 Subsection 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.

No additional secondary notification conditions are stipulated.

12. 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.

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