File No: LTD/1334

September 2008

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

2,6-Naphthalenedicarboxylic acid, 2, 6-bis (2-ethylhexyl) ester (Diethylhexyl 2,6-Naphthalate)

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

This Full Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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FULL PUBLIC REPORT

2,6-Naphthalenedicarboxylic acid, 2, 6-bis (2-ethylhexyl) ester (Diethylhexyl 2,6-Naphthalate)

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Symrise Pty Ltd (ABN 67 000 88 09 46)
168 South Creek Rd
Dee Why NSW 2099

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: Identity of Manufacturer, Introduction volume

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Hydrolysis as a function of pH, Explosive properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2002)

STATUS UNDER OTHER AUSTRALIAN AGENCIES
Contained on list of Substances That May Be Used in Listed Medicines in Australia

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
2,6-Naphthalenedicarboxylic acid, 2,6-bis (2-ethylhexyl) ester

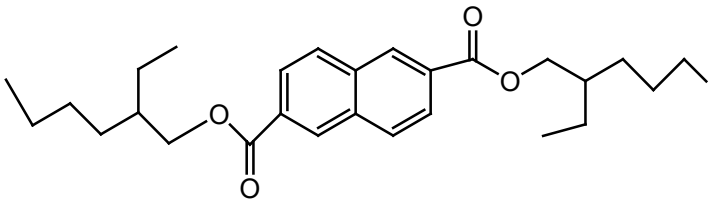
MARKETING NAME(S)
Corapan TQ

OTHER NAME(S)
2,6-Naphthalenedicarboxylic acid, bis(2-ethylhexyl) ester,
Bis (2-ethylhexyl) naphthalene-2, 6-dicarboxylate (IUPAC Name),
Diethylhexyl 2,6-Naphthalate (INCI Name)

CAS NUMBER
127474-91-3

MOLECULAR FORMULA
$C_{28}H_{40}O_4$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
440.6

ANALYTICAL DATA
Reference FTIR, UV and GC spectra were provided.
Major and minor components were also identified by Karl Fischer and HPLC.

3. COMPOSITION

DEGREE OF PURITY 97.6%

IMPURITIES/RESIDUAL MONOMERS

Chemical Name 2,6-naphthalenedicarboxylic acid-2-(2-ethylhexyl)-6-methylester
CAS No. *Weight %* 1.8%

Chemical Name Unknown impurities (6 components)
CAS No. *Weight %* 0.6%

Chemical Name Water
CAS No. *Weight %* 0.02%

DEGRADATION PRODUCTS
Not determined.

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Liquid

Property	Value	Data Source/Justification
Melting Point	6°C	Measured
Boiling Point	362°C	Measured
Density	1022.3 kg/m^3 at 20°C	Measured
Vapour Pressure	1.6 x 10^{-4} kPa	Measured
Water Solubility	<1.0 x10^{-4} g/L at 20°C	Measured
Hydrolysis as a Function of pH	Not Determined	Not expected to hydrolyse within the environmental pH range of 4-9.
Partition Coefficient (n-octanol/water)	log Pow > 6.2 at 20°C	Measured
Adsorption/Desorption	Log Koc > 5.6	Measured
Dissociation Constant	Not Determined	The notified chemical does not contain dissociable groups.
Particle Size	The notified chemical is a liquid at room temperature.	N/A
Flash Point	235°C	Measured
Autoignition Temperature	415°C	Measured
Explosive Properties	Not expected to be explosive.	Estimated
Photostability	Photostable	Measured

DISCUSSION OF PROPERTIES

For full details of tests on physical and chemical properties, please refer to Appendix A.
Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Dangerous Goods classification
Based on the available data the notified chemical is not classified as a Dangerous Good according to the Australian Dangerous Goods Code (FORS, 1998).

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Corapan TQ will be imported into Australia in 20 Kg steel drums by sea.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 1	< 1	< 1	< 1	< 1

PORT OF ENTRY
SYDNEY

IDENTITY OF MANUFACTURER/RECIPIENTS
The notified chemical will not be manufactured in Australia. However, formulation and packaging of cosmetics containing the notified chemical will occur in Australia at different sites.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in 20 kg steel drums by sea and will be initially stored at notifier's warehouse for further distribution to other companies for formulation and packaging of cosmetics containing the notified chemical.

USE
Photostabiliser and emollient in skin products at up to 5%

OPERATION DESCRIPTION
The notified chemical will not be manufactured in Australia. However, formulation and packaging of cosmetics containing the notified chemical will occur in Australia.

Blending of cosmetics at formulation sites is stated to be generally carried out in automated processes. The consumer packages of cosmetics are usually packed by means of automated and enclosed filling systems into various size and container types. However, at some sites, less automated processes may be used. The maximum concentration of the notified chemical in cosmetics is expected to be 5%. The packaged cosmetics will be distributed to retail outlets. They may also be used in beauty salons.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport	0	0	0
Warehouse	1	0	0
Production	2	0.5	4
Beauticians & retail workers	100	0.5	100
QC	-	0.5	4

EXPOSURE DETAILS

Transport and distribution workers are not expected to be exposed to the notified chemical except in the unlikely event of an accident and breakage of the packaging of the consumer products containing up to 5% of the notified chemical. Accidental exposure of transport and distribution workers is also unlikely in the case of import and distribution of neat notified chemical. In case of such accidental exposure, main routes of exposure would be dermal and ocular. However, the likelihood of such an accidental exposure is minimal.

In case of neat notified chemical for reformulation into consumer products, dermal and ocular exposure of workers involved in reformulation may occur during transfer of the notified chemical (100% purity) from the drums into the mixing vessel. However, this exposure is expected to be low due to the likely automated process during blending and packaging of cosmetics containing the notified chemical and the use of PPE by workers. In the initial mixing stage, the use of chemical resistant gloves (PVC) is recommended to minimise any dermal exposure to workers. The mixing sites should be equipped with industrial safety equipment such as eye-wash and exhaust controls.

Dermal and ocular exposure to the notified chemical in the neat form and in formulated products is possible for workers involved in quality control during sampling and testing of finished products. This exposure is also likely to be low as these workers are expected to wear laboratory coats, safety glasses and rubber gloves.

Sales workers and beauticians may experience frequent dermal and ocular exposure to the notified chemical if involved in the demonstration or application of products containing the notified chemical to the consumers. The extent of this exposure is likely to be comparable to the exposure of the consumers that would use the same products.

Overall, the exposure of formulators and transport workers to the notified chemical is expected to be low. However, sales workers and beauticians may have frequent dermal contact with cosmetic products containing the notified chemical at up to 5% when applying creams and moisturizers on consumers.

6.1.2. Public exposure

Exposure of the public to the notified chemical is expected to be widespread and frequent through a daily use of personal care products containing the notified chemical typically at the maximum concentrations of 5%.

The principal route of exposure is dermal, with deliberate application over the skin. Accidental eye exposure is also possible during the use and application of the face and body skin products. Oral exposure through the use cosmetic consumer products is unlikely and only possible in case of accidental ingestion.

Potential systemic exposure to the notified chemical through typical consumer use of body lotions containing sunscreens and moisturizing body lotions are calculated below:

Based on body lotion use:

Use Level	8 g per use x 1 applications/day	8 g/day
Dermal Exposure	8 g/day x 5% (conc. of chemical)	0.4 g/day
Absorption[a]	10%	0.04 g/day
Systemic exposure	(0.04 g/day) / 60 kg bw	0.67 mg/kg bw/day

^Based on sunscreen lotion use:

Use Level	estimated as	18 g/day
Dermal Exposure	18 g/day x 5% (conc. of chemical)	0.9 g/day
Absorption[b]	5%	0.045 g/day
Systemic exposure	(0.045 g/day) / 60 kg bw	0.75 mg/kg bw/day

[a] and [b] vary as absorption of the notified chemical in the context of cosmetic formulation varies. The absorption of the notified chemical for moisturizing lotions is likely to be higher from that for the sunscreen lotions as they are formulated to moisturize and enhance absorption into the skin, while the sunscreen lotions are formulated to retain the UV filters on the surface of the skin for maximal protection. This approach is consistent with the Notes of Guidance by the SCCNFP (2003) for the testing of cosmetic ingredients and their safety evaluation which states that when considering dermal absorption it is important to know whether the formulation can affect the bioavailability of one of its compounds (discussed in more detail in sections 6.2 and 6.3.2). Based on the results of an in vitro percutaneous absorption study and a high log Kow, a maximum of 10% absorption has been used for the calculation.

^ Secondary sunscreens that meet the NICNAS Cosmetic Standard are regulated as cosmetics..

6.2. Human health effects assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	oral LD50 > 5000 mg/kg bw, low toxicity
Rabbit, acute dermal toxicity	LD50 > 2000 mg/kg bw, low toxicity
Rabbit, skin irritation (15% in corn oil)	slightly irritating
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation (15% in corn oil)	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test.	inadequate evidence of sensitisation
Skin sensitisation – human volunteers (RIPT)	not sensitising
Rat, repeat dose oral toxicity – 28 days.	NOAEL 300 mg/kg bw/day
Mutagenicity – bacterial reverse mutation (2 studies)	negative
Genotoxicity – in vitro chromosome aberration	positive
Genotoxicity – in vivo micronucleus	negative
Phototoxicity – human volunteers	negative
Photosensitisation – human volunteers	negative
Percutaneous Absorption In Vitro (an emulsion with 8% concentration)	does not result in percutaneous penetration through *ex vivo* pig skin

Toxicokinetics, metabolism and distribution.
An in vitro skin penetration study report in summary form was provided for the notified chemical. Using an *ex vivo* pig skin system, significant transdermal permeation did not occur, and the majority of the material recovered was found on the surface of the skin or in the stratum corneum. None of the chemical was detected in the receptor fluid. No other toxicokinetic data was available on the notified chemical. Based on its structure, it may be expected to hydrolyse or be metabolised to 2,6-naphthalenedicarboxylic acid and ethylhexanol and these chemicals may have a different skin penetration potential.

Acute toxicity.
Based on animal studies the notified chemical is of low oral and dermal toxicity.

Irritation and Sensitisation.
Based on two dermal and two ocular studies in rabbits the notified chemical is a slight eye and skin irritant, however it is noted that erythema in dermal studies and conjunctival redness in ocular studies persist for some time. In one dermal study slight erythema was present 14 days after treatment in one animal and in one ocular study conjunctival redness was seen for up to 18 days after dosing. It is also noted that the protocol for some of these studies does not clearly state the concentration tested, and the chemical may have irritation potential at levels such as 10% and 15%. Mild skin responses in some subjects after repeated application in a human repeat insult test (RIPT) are likely to be related to the irritation potential of the notified chemical.

The notified chemical did not show evidence of sensitisation in a guinea pig adjuvant test or in a human repeat dose insult test. A number of subjects did not complete the human study, however this was stated to be due to reasons unrelated to the effects of the chemical.

Phototoxicity and photosensitisation studies on a 20% solution of the notified chemical in human volunteers using UVA/UVB irradiation were negative.

Repeated Dose Toxicity
In a 28-day oral gavage study in rats, histological findings were seen in the liver at the two highest doses, 600 and 1000 mg/kg bw/day. Intercellular vacuolisation occurred in a dose-dependent manner, while cell degeneration was observed at the highest dose only. The effects were less evident in the recovery test group, suggesting that some reversal was occurring. No other substance-related effects were seen in the study and the NOAEL was determined to be 600 mg/kg bw/day on the basis of the cell degeneration observed at the high dose level.

Mutagenicity.
The notified chemical was not mutagenic in two bacterial reverse mutation studies (only one of which included E. coli.) It elicited positive genotoxic results at the highest dose levels in an *in vitro* chromosome aberration study, where significant cytotoxicity also occurred. An *in vivo* mouse micronucleus test indicated no evidence of genotoxicity. As the ratio of immature to total erythrocytes did not change significantly, it cannot be confirmed that the notified chemical reached the bone marrow.

Toxicity for reproduction.
No studies were provided for this endpoint. Macroscopic and microscopic examination of reproductive organs was carried out as part of the 28-day repeated dose study on rats, and no anomalies were found. The expected metabolite ethylhexanol can be oxidised to ethylhexanoic acid, which is classified as a Class 3 reproductive toxicant with risk phrase R63 (Posssible risk of harm to the unborn child).

The notified chemical has some structural similarity to diethylhexylphthalate, that is known to have reproductive effects, however, the reproductive effects observed with DEHP in rats occurred only at relatively high dose levels, namely, 590 mg/kg bw/day (NTP, 2006).

Observations on Human Exposure.
The notifier advised that no adverse effects on workers have been noted from use of the chemical.

The chemical is contained in the list of "Substances that may be used in Listed Medicines in Australia" and therefore may be used in products regulated by TGA in Australia. It is allowed at levels up to 10% in products, with a warning regarding eye irritation required.

Classification

Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human health risk characterisation

6.3.1. Occupational health and safety

Based on the available data, the notified chemical is a slight eye and skin irritant and is not a skin sensitiser.
Transport workers may be exposed to the notified chemical in case of accident when raw material containing the notified chemical (100% purity) is imported and transported in Australia. In such a case there will be a risk of slight skin and eye irritation that is expected to be low due to employment of standard hygiene practices to minimise skin contact, including the use of appropriate gloves and protective clothing and eye protection. The Material Safety Data Sheet (MSDS) should inform workers about the potential hazards of the notified chemical. The likelihood of accidental exposure to the notified chemical during transport and storage is considered to be low and thus the corresponding risk is considered low.

In case of import of the notified chemical as raw material, dermal, ocular and inhalation exposure to high concentrations of the notified chemical is also possible for workers involved in formulation and quality control testing of consumer products. However, worker exposure is expected to be minimal if standard industrial hygiene practices are undertaken and the recommended PPE are used. . Under these circumstances, the risk of adverse effects for formulators and workers involved in quality control testing is considered to be acceptable.

Workers involved in packaging of the finished consumer products may encounter dermal and ocular exposure to the notified chemical at significantly lower concentrations. Considering the limited opportunity for direct contact with the notified chemical and the use of PPE such as safety glasses and gloves for skin protection, the risk is low.

The highest potential exposure to products containing the notified chemical at up to 5% is for sales workers and beauticians. Sales workers can have frequent dermal exposure to the notified chemical if involved in the demonstration of products containing the notified chemical. Similarly beauticians may have repeated dermal exposure when applying products to customers. Incidental ocular exposure may also occur. The level of exposure and the risk of adverse effects for this category of workers are likely to be comparable to that of consumers using the same products. While there are indications that dermal absorption is low, it cannot be ruled out. The products of hydrolysis or metabolism also have potential for dermal absorption.

Overall, the exposure of most categories of workers to the notified chemical is expected to be low. Formulators and workers involved in handling the notified chemical as introduced and during formulation should have skin and eye protection.

The risk for sales workers and beauticians is expected to be similar to that of the public, discussed in the following section.

6.3.2. Public health

Members of the public will have widespread and frequent exposure to the notified chemical through daily use of skin products containing it. The principal route of exposure is dermal, with deliberate application over the skin. Accidental eye exposure is also possible during the use and application of the face and body skin products. Potential health risks associated with this pattern of use of the notified chemical are mainly skin and eye irritation and sensitisation. Systemic effects are also possible if there is significant dermal penetration or accidental oral ingestion.

The notified chemical is considered to be a slight eye irritant although the potential risk of eye irritation during use of the finished products is reduced as a result of the low concentration of the notified chemical (5%) in the products. In the available studies, the effects on the eye were mild but long lasting and appeared to occur even when diluted solutions of the chemical were tested. . A warning statement regarding possible eye irritation may be appropriate.

The notified chemical is also considered to be a slight skin irritant, and skin irritation may occur based on the expected exposure pattern. However, the potential risk is reduced as a result of the low concentration of the notified chemical in the finished products (< 5%). A warning statement advising consumers to discontinue use if skin irritation reactions occur may be appropriate.

The notified chemical is not regarded as a skin sensitiser based on the available data.

On the basis of studies in human volunteers, the notified chemical is not expected to be phototoxic or photosensitising.

While the notified chemical was non-mutagenic in reverse mutation assays bacteria, it gave positive results in an in vitro chromosome aberration test. However, its ability to cause chromosome damage in vivo could not be demonstrated in a mouse micronucleus assay. It could not be confirmed in this assay that the test substance had reached the bone marrow, however, the dose level used was considerably higher than the anticipated exposure to the notified chemical. Overall, the chemical is not considered genotoxic based on available data.

The potential systemic exposure to the notified chemical through typical consumer use of products for dermal application containing up to 5% of the notified chemical is conservatively estimated to be 0.67 mg/kg bw/day and 0.75 mg/kg bw/day for body and sunscreen lotion, respectively (see section 6.1.2.), based on an absorption rate of 10%. The margin of exposure (MOE) compared to the NOEL of 600 mg/kg bw/day determined for the notified chemical in the 28-day subchronic study is therefore >100 in both exposure scenarios. Therefore, the risk of systemic effects due to repeated exposure to the notified chemical is considered low.

It is also noted that the potential metabolite of this notified chemical, namely ethylhexanoic acid, has been associated with adverse reproductive effects in animal studies. The notified chemical also has some structural similarity to diethylhexyl phthalate, which is also known to produce adverse reproductive effects in animal studies. In both cases, effects were observed at dose levels at least two orders of magnitude higher than the anticipated systemic exposure to the notified chemical.

Overall, based on the available data, the use of the notified chemical at concentrations up to 5% in cosmetic products is not considered to pose an unreasonable public health risk.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical will be reformulated into cosmetic products in Australia. Residues in empty import containers are expected to account for 0.1% of the import volume. The cleaning of formulation equipment may release up to 1% notified chemical to the aquatic environment through onsite treatment facilities.

RELEASE OF CHEMICAL FROM USE
The formulated product will be applied to skin. Therefore, the majority of the notified chemical is expected to be washed off and enter the sewer, with the remainder disposed of in landfill as residues in product containers. Sludge containing the chemical will be disposed of to landfill.

Residues from empty cosmetic containers are expected to contain on an average of 0.1% of the notified chemical most of which will go to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL
The notified chemical would be disposed of to landfill as residues in empty containers or from spills.

7.1.2 Environmental fate

The notified chemical contains groups that might hydrolyse under severe conditions, but is expected to be stable under normal environmental conditions. Due to its low water solubility, the notified chemical in solid wastes is expected to remain bound within the soils and sediments of landfills. Although the chemical is not readily biodegradable it is anticipated that in soil it would eventually degrade through biotic and abiotic processes. If spilt on land, the notified chemical is expected to bind to soil and become immobilised in the soil layer. If spilt to water, it is not expected to dissolve but rather disperse or settle to sediment. Incineration of the notified chemical will result in the formation of water vapour and oxides of carbon.

For the details of the environmental fate studies please refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

Since most of the chemical will be washed into the sewer, under a worst case scenario, with no removal of the notified chemical in the sewage treatment plant, the resultant Predicted Environmental Concentration (PEC) in sewage effluent on a nationwide basis, Predicted No-Effect Concentration (PNEC) and Risk Assessment (Q) are estimated as follows:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment

Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100.000%	
Annual quantity of chemical released to sewer	1,000.000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	

Daily effluent production:	4,232	ML
Dilution Factor – River	1.0	
Dilution Factor – Ocean	10.0	
PEC – River:	0.65	µg/L
PEC – Ocean:	0.06	µg/L

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish).	1.00	mg/L
Assessment Factor	100.00	
Mitigation Factor	1.00	
PNEC:	10.00	µg/L

7.2. Environmental effects assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	EC50 ≥ 1 mg/L	The notified chemical is not toxic to *Danio rerio* up to the limit of its water solubility.
Daphnia Toxicity	EC50 ≥ 1 mg/L	The notified chemical is not toxic to *Daphnia magna* up to the limit of its water solubility
Algal Toxicity	EC50 ≥ 1 mg/L	The notified chemical is not toxic to Algae up to the limit of its water solubility.
Inhibition of Bacterial Respiration	EC50 > 10000 mg/L	The notified chemical is not toxic to Bacteria
Ready Biodegradability	Biodegradation after 28 days: 4%	The notified chemical is not readily biodegradable

All results are indicative of low risk. Full test reports were provided for all studies. The biodegradation tests indicate only partial degradation.

7.3. Environmental risk assessment

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q – River:	0.65	10	0.065
Q – Ocean:	0.06	10	0.006

As the PEC/PNEC ratio is considerably less than 1, there should be a low risk to aquatic organisms.

The products containing the notified chemical are likely to be used throughout Australia. Based on the proposed use pattern, the release of the notified chemical to the aquatic environment is expected to be low and dispersed. Adsorption to sludge, soil and sediment as well as degradation and dilution in receiving waters should further reduce environmental concentrations.

Given the above, environmental exposure and the overall environmental risk are expected to be low.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

And

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Environment	Category 4	May cause long lasting harmful effects to aquatic life.

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

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

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the reported use pattern, the notified chemical is not considered to pose a risk to the environment.

Recommendations

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced and as diluted for use, formulated into consumer products:
  - Avoid contact with skin and eyes

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced and as diluted for use, formulated into consumer products:
  - Protective gloves
  - Eye goggles
  - Overalls

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

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

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

Public health

Formulators of products containing the notified chemical should consider whether the following label warnings are warranted:

- Discontinue use if skin irritation occurs
- Avoid contact with eyes

Disposal

- Where possible recycling is preferred to disposal or incineration. If recycling is not possible dispose of waste to landfill.

Storage

- Keep the container tightly closed in dry and well ventilated place.

Emergency procedures

- Avoid subsoil penetration.
- Spills should be wiped with absorbent material, and dispose of to landfill.

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if

- the importation volume exceeds one tonne per annum notified chemical; or

or

(2) Under Section 64(2) of the Act; if

- the function or use of the chemical has changed from photostabiliser and emollient in skin products at up to 5%, or is likely to change significantly;
- the chemical is proposed for use in products to be used in eye make-up or treatment;
- the chemical is proposed for use in products specifically for use on children or babies;
- if the chemical has begun to be manufactured in Australia;
- additional toxicological information on the notified chemical becomes available, in particular, information on genotoxicity or reproductive toxicity
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

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

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point 6°C

Method	EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	An endothermic signal was recognisable in the range of 5-10 °C. The evaluation of the endothermic signal results in a melting point of the test item of 6°C (onset temperature).
Test Facility	Kesla Forschung & Service KG (2001a)

Boiling Point 362°C at 101.3 kPa

Method	EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	The measurement was carried out using a Differential Scanning Calorimeter (DSC) that operates according to the power compensated temperature null principle. An endothermic signal was recognisable with a maximum at approximately 400 °C. The evaluation of the endothermic signal results in a boiling point of the test item of 362°C (onset temperature).
Test Facility	Kesla Forschung & Service KG (2001b)

Density 1022.3 ± 0.25 kg/m^3 at 20°C

Method	EC Directive 92/69/EEC A.3 Relative Density.
Remarks	Determined using the pycnometer method. The test temperature was 20°C. The relative density of liquid test item was 1.0211 on average. The absolute density is as stated above.
Test Facility	Kesla Forschung & Service KG (2001c)

Vapour Pressure 1.6×10^{-10} kPa at 20°C

Method	OECD TG 104 Vapour Pressure. EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks	Determined using a commercially available vapour pressure equipment.
Test Facility	Sicherheitstechnik (2001)

Water Solubility $<1.0 \times 10^{-4}$ g/L at 20°C

Method	EC Directive 92/69/EEC A.6 Water Solubility.
Remarks	Column Elution Method was used. The notified chemical was not detected in water fractions from the column.
Test Facility	Kesla Forschung & Service KG (2001d)

Hydrolysis as a Function of pH Not Determined

Remarks	The notified chemical contains structure which could hydrolyse but is not expected to occur under the environmental pH range of 4-9.

Partition Coefficient (n-octanol/water) log Pow > 6.2.at 20°C

Method	OECD TG 117 Partition Coefficient (n-octanol/water). EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks	HPLC Method/Flask Method. The test material eluted well after the reference substances. A value for the partition coefficient was estimated to be 12.2 by extrapolation.
Test Facility	Kesla Forschung & Service KG (2001g)

Adsorption/Desorption log Koc > 5.6
– screening test

Method	HPLC method.
Remarks	HPLC Method/Flask Method The test material eluted well after the reference substances. A value for the adsorption coefficient was estimated to be 6.8 by extrapolation.
Test Facility	Kesla Forschung & Service KG (2001f)

Flash Point 235°C at 99.88 kPa

Method	EC Directive 92/69/EEC A.9 Flash Point.
Remarks	Determined by non-equilibration method with a Pensky-Martens flash point tester.
Test Facility	Kesla Forschung & Service KG (2001f)

Autoignition Temperature 415°C

Method	EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	Measured using an autoignition temperature apparatus.
Test Facility	Noack Laboratorium fur Angewandte Biologie (2001)

Photostability Photostable

Method	30 mg of emulsion were spread onto a glassplate (microscope slide) with an area of ca. 10 cm^2 (4 samples for each interval), slides were immersed in 25 mL of ethanol and samples were dissolved ultrasonically. Light source used was Suntest CPS Heraeus, Xenonlamp and doses under cooling (temperature 25°C) were 28.4 J/cm^2 (120 min) and 56.7 J/cm^2 (240 min). Irradiance was 40W/m^2 calibrated by UV-sensor (280-400nm) before irradiance. Above solutions were analysed both UV-spectrophotometrically and chromatographically (HPLC).
Remarks	Loss of extinction of concentration was less than 5%.
Test Facility	Symrise

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	Method analogous to OECD TG 401 Acute Oral Toxicity – Limit Test.
Species/Strain	Rat/Wistar-strain albino
Vehicle	15% w/v corn oil
Remarks – Method	No significant variations from the protocol.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5000	0

LD50	> 5000 mg/kg bw
REMARKS – RESULTS	No adverse clinical signs were noted and weight gain was normal.
Conclusion	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Consumer Product Testing Co. (1999a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	Method analogous to OECD TG 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rabbits/New Zealand white
Vehicle	15% w/v corn oil
Type of dressing	Occlusive.
Remarks – Method	No significant variations from the protocol. Weight was measured before dosing and at 7 d and 14 d.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2000	0

LD50	> 2000 mg/kg bw
Remarks – Results	Draize scores at 24 h showed very slight to well-defined erythema in all animals, very slight oedema in 9/10 animals and moderate oedema in 1 animal. At necropsy (day 14) 2/10 animals had slight reddening of the skin. Reporting of weight units was inconsistent, however 9/10 animals showed slight weight gains, 1/10 slight weight loss.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Consumer Product Testing Co. (1999a)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical at 15% in vehicle
METHOD	Method analogous to OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 M, 3 F
Vehicle	Corn oil
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks – Method	Initial observations were performed 4.5 hours after application of the test substance.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	1.1	2	> 14 days	1
Oedema	0	0	-	0

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

Remarks – Results	Slight erythema was still apparent at the end of the observation period in one animal. One male showed well-defined erythema and other 5 animals showed very slight erythema 4.5 hours after termination of exposure. 6 animals showed very slight erythema 24 and 48 hours after termination of exposure One male showed well-defined erythema and other 5 animals showed very slight erythema 72 hours after termination of exposure. Two males and two females showed very slight erythema 7 days after termination of exposure.
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	Consumer Product Testing Co. (1999a)

B.4. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/SPF albino
Number of Animals	4 F
Vehicle	Diethylphthalat/Ethanol 1:1
Observation Period	14 days
Type of Dressing	Occlusive.
Remarks – Method	6 concentrations were used in the test, including the vehicle control. Based on consistency of effects *vs* concentration, the coding for the sites in the table of original scores and in the description appears to be incorrect. It should read as AL: Anterior left test field = 100%, ML: Middle left test field = 25%, PL: Posterior left test field =1%, AR: Anterior right test field = 50%, MR: Middle right test field = 10% and PR: Posterior right test field = 0% (vehicle). The summary table is consistent with the expected order of effects. However the inconsistencies do not affect the results of the testing with 100% concentration.

RESULTS

Lesion	*Concentration (%)*	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	*0*	0	0	-	0
	1	0	0	-	0
	10	0.7	2	> 72 hours	0
	25	1.1	2	> 72 hours	0
	50	1.5	2	> 72 hours	0
	100	1.8	2	> 72 hours	0
Oedema	*0*	0	0	-	0
	1	0	0	-	0
	10	0.2	1	> 72 hours	0
	25	0.3	1	> 72 hours	0
	50	0.8	2	> 72 hours	0
	100	1.3	2	> 72 hours	0

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

Remarks – Results: Because of the possible confusion of coding it is not possible to make comments on the results for all concentrations. No reactions were seen at the control (vehicle) site. The 100% material elicited mild to well defined erythema and oedema at 24, 48 and 72 h after treatment. At 7 days after treatment, scaling was seen at some sites but there were no other effects reported. All animals were free of any signs of skin irritation 14 days after termination of exposure.

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

TEST FACILITY: Frey-Tox Germany (2001a)

B.5. Irritation – eye

TEST SUBSTANCE: Notified chemical at 15% in vehicle

METHOD: Method analogous to OECD TG 405 Acute Eye Irritation/Corrosion.

Species/Strain: Rabbit/New Zealand White

Number of Animals: 3M, 3F

Vehicle: Corn oil

Observation Period: 21 days

Remarks – Method: No significant variations from the protocol. From the method description, it seems that the eye was dosed with 0.1 mL of the notified chemical, however this is not clear and 0.1 mL of the 15% solution may have been administered. A fluoroscein test was performed prior to dosing.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	1.3	2	> 14 days	0
Conjunctiva: chemosis	0.17	1	> 24 hours	0
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

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

Remarks – Results: Conjunctivae effects were noted that resolved within 7 to 18 days after termination of exposure in all animals.

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

TEST FACILITY Consumer Product Testing Co. (1999a)

B.6. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain Rabbit/ SPF albino
Number of Animals 4 F
Observation Period 7 days
Remarks – Method No significant variations from the protocol. An examination with fluoroscein was carried out 24 h after treatment.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	1	2	72 hours	0
Conjunctiva: chemosis	0.75	1	72 hours	0
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

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

Remarks – Results Signs of irritation ranging from slight to well-defined were observed on the treated eyes. All animals were free of any signs of eye irritation 7 Days after the application of the test article.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Frey-Tox Germany (2001b)

B.7. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation - <Magnusson and Kligman>.
EC Directive 96/54/EC B.6 Skin Sensitisation - <Magnusson and Kligman>.

Species/Strain Guinea pig/female SPF albino
PRELIMINARY STUDY Maximum Non-irritating Concentration: 50%
intradermal: 0.6, 1.3, 2.5, 5.0% v/v in peanut oil
topical: 25, 50, 75, 100% v/v in Ethanol/Diethylphthalat 1:1
MAIN STUDY
Number of Animals Test Group: 10 Control Group: 5
INDUCTION PHASE Induction Concentration:
intradermal: 0.6% v/v in peanut oil
topical: 25% v/v in Ethanol/Diethylphthalat 1:1
Signs of Irritation Intradermal injections of Freund's complete adjuvant mixed with the notified chemical or vehicle elicited erythema and oedema. Slight erythema were observed during the dermal induction phase.
CHALLENGE PHASE
1st challenge topical: 25% v/v in Ethanol/Diethylphthalat 1:1
2nd challenge topical: 10% v/v in Ethanol/Diethylphthalat 1:1
Remarks – Method No significant variations from the protocol. A periodic testing of the positive control hexylcinnamaldehyde was carried out by the test laboratory, to ensure the reliability of the method.

RESULTS

Animal	*Challenge Concentration*		*Number of Animals Showing Skin Reactions after:*			
	1st challenge	*2nd challenge*	*1st challenge*		*2nd challenge*	
			24 h	*48 h*	*24 h*	*48 h*
Control Group (Left anterior)	25% v/v	10% v/v	1/5	0/5	0/5	0/5
(Left posterior- vehicle)	25% v/v	10% v/v	0/5	0/5	0/5	0/5
Test Group (Left anterior)	25% v/v	10% v/v	3/10	0/10	0/10	0/10
(Left posterior – vehicle)	25% v/v	10% v/v	0/10	0/10	0/10	0/10

Remarks – Results

One animal of the control group showed a slight, discrete erythema on the anterior left test field 24 hours after the challenge application. In the test group 3 out 10 animals showed a slight, discrete erythema on the anterior left test field 24 hours after the challenge application. These observations of slight skin reactions in both groups could indicate other reasons than sensitisation. To further clarify the results of the challenge a rechallenge was performed. The negative response of the animals to the rechallenge treatment both in the control group and in the test group supported this interpretation.
The animals showed no signs of illness. The animals had a normal weight gain during the study period.

CONCLUSION

The notified chemical did not cause skin sensitisation under the conditions of the test.

TEST FACILITY

Frey-Tox Germany (2001c)

B.8. Skin sensitisation – human volunteers

TEST SUBSTANCE

Notified chemical

METHOD

Repeated insult patch test

Study Design

Induction Procedure: Patches with approximately 0.2 mL of the test material were applied 3 times per week (e.g., Monday, Wednesday, and Friday) for a total of 9 applications.
Rest Period: 24 hours following each Tuesday and Thursday removal, and 48 hours following each Saturday removal
Challenge Procedure: Approximately 2 weeks after the final induction patch application, a challenge patch was applied to a virgin test site adjacent to the original induction patch site, following the same procedure for induction. The patch was removed and the site scored at the clinic 24 and 72 hours post-application.

Study Group

47 F, 10 M; age range 16-77

Vehicle

None

Remarks – Method

Semi-occluded.

RESULTS

Remarks – Results

Six of the fifty seven subjects discontinued participation in the trial for reasons unrelated to the application of the test material. Mild erythema and skin dryness was observed in one subject (male, age 31) at the last two induction applications. Barely perceptible or spotty erythema was noted in two other subjects (females aged 52 and 74) during the induction phase, after some of the applications. None of these subjects showed any response at challenge.
One subject (female, aged 50) exhibited a barely perceptible (+) to marked (3-level) response during the induction phase which required the discontinuation of the final application. However, she too exhibited no adverse reactions during the challenge phase. This subject presented

	responses to numerous test substances on this shared panel, suggestive of a hyper-reactive individual. Therefore the study authors did not consider her data in the final test results. No other reactions were seen during the induction or challenge stages of the study.
CONCLUSION	The test substance did not indicate a clinically significant potential for dermal irritation or allergic contact sensitisation under the conditions of this study. The skin responses during induction may be indicative of irritation after repeated exposure.
TEST FACILITY	Consumer Product Testing Co. (1999c)

B.9. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).
Species/Strain	Rats/Wistar Crl:WI BR strain
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	None
Remarks – Method	No significant variations from the protocol.

RESULTS

Dose mg/kg bw/day	*Number and Sex of Animals*	*Mortality*
0	10 per sex	0
300	5 per sex	0
600	5 per sex	0
1000	10 per sex	0

Mortality and Time to Death

None of the animals died during the course of investigation.

Clinical Observations

Soft faeces were observed in single animals on some days. Because this symptom was only observed once in the animals of the control group but nine times in the high dose group it could be assumed that it was caused by the administration of the test substance.

None of the animals showed further alterations of their general state of well-being and behaviour.

The examination of sensory response, grip strength or motor activity did not show any alterations prior to the administration of the test substance or at the end of the study.

Neither the body weights nor the body weight gain of the animals were influenced by the administration of the test substance. One high weight gain in the third week by a male in the 300 mg/kg bw/day group was considered to be incidental

The food consumption of the animals was not influenced by the administration of the test substance. Higher food consumption by one male in the high dose recovery group occurred in the first week, but was within historical controls.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

None of the haematological parameters investigated was affected by the administration of the test substance.

Only two significant differences were noted (erythrocytes, females, 300 mg/kg bw/day group; platelet count, males, 300 mg/kg bw/day group). These seemed to be incidental, because the values were in the confidence range of the historical control data in the testing facility.

The parameter of the leucocyte differential count was all in the normal range for the strain used.

None of the coagulation parameters investigated was affected by the administration of the test substance.

The creatinine level was statistically decreased in the female animals in all dose groups, as a result of an unusually high value of the control group. This was confirmed through measurements of the creatinine levels in control and test recovery groups, where no statistically significant differences were found between the two

groups.
None of the other clinical-biochemical parameters investigated were considered to be affected by the administration of the test substance. The noted single statistically significant differences (AST, males, 1000 mg/kg bw/day group; Urea, females, 600 mg/kg bw/day group; Sodium, females, 1000 mg/kg bw/day group and Potassium, males, 600 mg/kg bw/day group) were deemed to be incidental, because the values were in the confidence range of the historical control data in the testing facility for the strain used.

Effects in Organs
None of the absolute or relative organ weights investigated was affected by the administration of the test substance. Only one significant difference was noted (1000 mg/kg bw/day group, males, adrenal left [absolute weight]).
It was deemed to be in incidental because the differences were not confirmed by the right organs and by the relative weights and the value was in the range of the historical control data in the testing facility for the strain used.
No abnormalities were found in any animal in macroscopic pathological findings.
In histological findings, the incidence and the area of findings of intracellular vacuoles in the liver were strongly increased in the 1000 mg/kg bw/day group compared to the control group. Therefore the livers of all other animals were also examined microscopically.
The incidence and dimension of these liver effects increased with dose, indicating that it was caused by the administration of the test substance. There was little difference between the control and 300 mg/kg bw/day groups with minor vacuolisation seen in 1 or 2 animals in each group. At 600 mg/kg bw/day a higher number of animals in each group showed vacuolisation, over a larger area. At 1000 mg/kg bw/day almost all animals showed diffuse vacuolisation. At this dose level, cell degeneration was also observed in the liver of most animals. In one female, necrosis was also noted.
These intracellular vacuoles were also found in some animals of the 1000 mg/kg bw/day group of the satellite groups (recovery groups), but the incidence and dimension of area of finding were decreased compared to the animals of the 1000 mg/kg bw/day main group. The cell degeneration observed at the 1000 mg/kg bw/day dose level was absent in the recovery group but there was some evidence of cellular repair occurring. The findings in the recovery group of "focus (approx. 100 µm) with polymorphonuclear leucocytes" and "partly occurrence of the leucocytes and histiocytes" were considered to be indications of repair processes occurring during the recovery period.
Other histological findings (lung, kidney, urinary bladder and thymus) were considered to be incidental. They are in the physiological range of the animals used and the effects in the lungs are likely to be caused by the euthanasia or by the ether anaesthesia for blood sampling.

Remarks – Results
The daily oral administration of the notified chemical at doses of 300, 600 and 1000 mg/kg bw to rats for a period of 28 days was tolerated without any marked effects on physical condition.
The body weight, the food consumption, the haematological, coagulation and clinical-biochemical parameters were not influenced by administration of the test substance. No substance-dependent pathological macroscopic findings were observed, and the organ weights were not affected.

The major effect noted in the study was a dose-related increase in intracellular vacuoles in the liver, connected with a degeneration of liver cells in the animals of the 1000 mg/kg bw/day group. Based on the results in the 1000 mg/kg bw/day recovery group, the effects may be reversible, but did not reverse completely in the 14 days recovery period. Soft faeces in some animals in different groups may be dose related and caused by test substance administration.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 600 mg/kg bw/day in this study, based on the increased incidence of cell degeneration in the livers of animals at higher dose levels. .

TEST FACILITY Kesla Forschung & Service KG (12002)

B.10. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD	Consumer Product Testing Co. # 55-B, similar to OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA (pKM101)
Metabolic Activation System	Aroclor 1254 induced rat liver microsomes
Concentration Range in Main Test	a) With metabolic activation: 0, 100, 500,1000, 5000,10000 µg/plate b) Without metabolic activation: 0, 100, 500,1000, 5000,10000 µg/plate
Vehicle	DMSO
Remarks – Method	Triplicate plates were used at each concentration.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity in the Test	*Precipitation*	*Mutagenic Effect*
Absent			
Test	> 10000	> 10000	negative
Present			
Test	> 10000	> 10000	negative

Remarks – Results	Strains TA98 and TA100 were used in the preliminary toxicity test at concentration levels of 0.5, 1, 5, 10, 50, 100, 500, 1,000, 5,000, 10,000 µg/plate. The results showed turbidity at all concentration levels (ie, no evidence of toxicity). Therefore concentrations of 100, 500, 1,000, 5,000 and 10,000 µg/plate were chosen in the main test. The results showed that the test strains are sensitive to the positive control mutagens and had a spontaneous reversion rate well with the accepted values of each strain, indicating that under the test conditions, the strains were sensitive to the detection of potentially genotoxic agents. Using the same test conditions, there was no significant increase in the number of revertants in the treated plates compared to the control plates, either in the presence or absence of the S9 enzyme activation, at the following concentrations: 10,000, 5,000, 1,000, 500 and 100 µg/plate.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Consumer Product Testing Co. (1999b)

B.11. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	Method analogous to OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	Liver homogenate (S9) from Aroclor 1254 pretreated male rats
Concentration Range in Main Test	a) With metabolic activation: 0, 50, 150, 500, 1500, 5000 µg/plate b) Without metabolic activation: 0, 50, 150, 500, 1500, 5000 µg/plate
Vehicle	Ethanol
Remarks – Method	No preliminary test was performed. Plates were prepared in triplicate. The test was repeated in an independent experiment after an interval of at least 3 days

RESULTS

Metabolic	*Test Substance Concentration (µg/plate) Resulting in:*

Activation	*Cytotoxicity in the Test*	*Precipitation*	*Mutagenic Effect*
Absent			
Test 1	> 5000	≥ 1500	negative
Test 2	> 5000	≥ 1500	negative
Present			
Test 1	> 5000	≥ 1500	negative
Test 2	> 5000	≥ 1500	negative

Remarks – Results

In both the initial and repeat study, the number of spontaneous revertants observed using each of the five strains was close to those previously established in the laboratory.
The results with the positive control substances also confirmed the sensitivity of the test system.
Using the same test conditions, there was no significant increase in the number of revertants in the treated plates compared to the control plates.

CONCLUSION

The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY

King Harnasch (2001a)

B.12. Genotoxicity – in vitro

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 473 In vitro Mammalian Chromosome Aberration Test.

Cell Type/Cell Line: Human peripheral blood lymphocytes

Metabolic Activation System: A liver homogenate fraction (S9) from Aroclor 1254 treated male rats

Vehicle: Ethanol

Remarks – Method: No significant variations from the protocol.
The test was repeated in an independent experiment after an interval of at least 14 days.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 50*, 150*, 500*	24 hours	24 h
Test 2	0*, 150*, 500*, 1000*	4 hours	24 h
Present			
Test 1	0*, 50*, 150*, 500*	3.5 hours	24 h
Test 2	0*, 150*, 500*, 1000*	3.5 hours	24 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	N/A			
Test 1		≥ 150	> 500	positive
Test 2		> 500	> 1000	positive
Present	N/A			
Test 1		≥ 150	> 500	positive
Test 2		≥ 500	> 1000	positive

Remarks – Results

The results showed the spontaneous value of aberrations observed were within the historical range, and that the positive control substances confirmed the efficacy of the test system.

The highest concentration tested (500 µg/mL in test 1 and 1000 µg/mL in test 2) induced 50% (test 1) and 48% cytotoxicity (test 2) in the absence and 33% (test 1) and 62% (test 2) cytotoxicity in the presence of S9-mix. At concentrations above 1000 µg/mL cytoxicity increased sharply to a nearly complete loss of surviving cells at 1500 µg/mL.
At the concentrations tested, the notified chemical induced a dose related increase in the number of chromosome aberrations in cultural human blood lymphocytes in the presence and absence of a metabolising system. The effect reached 1% significance after treatment with a dose of 1000 µg/mL for 4 hours in the absence and for 3.5 hours in the presence of S9-mix.

CONCLUSION — The notified chemical induced chromosome aberrations in human peripheral blood lymphocytes in vitro in the presence and absence of a metabolising system under the experimental conditions.

TEST FACILITY — King Harnasch (2001b)

B.13. Genotoxicity – in vivo

TEST SUBSTANCE — Notified chemical

METHOD — OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
- Species/Strain: NMRI outbred mice
- Route of Administration: Intraperitoneal injection
- Vehicle: Corn oil
- Remarks – Method: No significant variations from the protocol.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5 per sex	0	24 hours
II (low dose)	5 per sex	500	24 hours
III (mid dose)	5 per sex	1000	24 hours
IV (high dose)	5 per sex	2000	24 hours
V (high dose)	5 per sex	2000	48 hours
VI (positive control, CP)	5 per sex	50	24 hours

CP=cyclophosphamide.

RESULTS
- Doses Producing Toxicity: After dosing, the animals of all groups treated with the test substance showed no signs of toxicity. In comparison to the negative controls in the groups treated with the test substance, the proportion of immature erythrocytes among total erythrocytes was changed only slightly. Therefore it cannot be confirmed that the test substance reached the bone marrow.
- Genotoxic Effects: The test substance induced in male animals of some of the test groups a slight but not statistically significant increase in the frequency of micronucleated immature erythrocytes above the control level. The percentage of micronucleated immature erythrocytes in all test groups and the control was within historical vehicle controls, and positive controls were consistent with historical data.

CONCLUSION — The notified chemical was not mutagenic in the micronucleus test with bone marrow cells of mice under the experimental conditions.

TEST FACILITY — King Harnasch (2002)

B.14. Phototoxicity

TEST SUBSTANCE	Notified chemical 20% in paraffin oil
METHOD	Clinical evaluation on human volunteers –in-house method
Study Group	15 F, 5 M; age range 21-65
Vehicle	Paraffin oil
Irradiations	Two irradiated sites (Control and Test substance) at 0.75 minimal erythemal dose (total spectrum = UVA + UVB) on days 2 and 4.
Application area	Scapular zones
Quantity and concentration applied	25 µL 20%
Frequency	Non-irradiated zone: twice – days 1 and 3. Irradiated zone: twice – days 1 and 3
Contact time	Non-irradiated zone: 48 hours Irradiated zone: 24 hours
Application conditions	The test substance was placed into a cupule of the occlusive patch (Finn Chambers on Scanpor) and applied to the volunteer's back. The patch containing no test substance was applied under the same conditions to serve as a non-treated control. Both of them were applied to the back, to the zone not to be irradiated. Another set of patches, identical to the first one, was applied to a different section of the back, to the zone to be irradiated. During the whole study, the treated zones were kept dry.
Remarks - Method	Irradiation was with UVA+UVB. Determination of the minimal erythemal dose was not described in detail in the study report. The numerical scoring system for assessing the phototoxic effects rated pigmentation, erythema, edema, dryness and vesicle formation.
RESULTS	
Remarks - Results	The clinical examinations did not show any skin reactions of the phototoxic type and had a zero score.
CONCLUSION	Under these study conditions, the test substance can be considered non-phototoxic.
TEST FACILITY	Eurofins ATS (2007a)

B.15. Photosensitisation

TEST SUBSTANCE	Notified chemical
METHOD	Clinical evaluation on human volunteers –in-house method
Study Group	20 F, 5 M; age range 21-62
Vehicle	Paraffin oil
Irradiations	Induction phase: Two irradiated sites (Control and Product) at 0.75 minimal erythemal dose (total spectrum = UVA + UVB) on days 2, 4, 9, 11, 16 and 18. Challenge phase: Four irradiated sites (Control irradiated with UVA + UVB, test substance irradiated with UVA + UVB, Control irradiated with UVA and test substance irradiated with UVA) on day 36. Irradiation doses: UVA + UVB at 0.75 minimal erythemal dose and UVA at 10J/cm^2.
Test substance application	The product was applied to the volunteer's back.
Application area	Scapular zones
Quantity and concentration applied	25 µL 20% in paraffin oil

Frequency	Non-irradiated zone: 6 times – Days 1, 3, 8, 10, 15 and 17 Irradiated zone: 6 times – Days 1, 3, 8, 10, 15 and 17
Contact time	Non-irradiated zone: 48 hours Irradiated zone: 24 hours
Application conditions	Induction phase: The test substance was placed in a cupule of the occlusive patch (Finn Chambers on Scanpor). The patch containing no test substance was applied under the same conditions to serve as a non-treated control. Both of them were applied to the back, to the zone to be irradiated. Another set of patches, identical to the first one, was applied to a different section of the back, to the zone not to be irradiated. Challenge phase: Three sets of patches were applied to the parallel scapular zone: the first for UVA+UVB irradiations, the second for UVA irradiations and the last one for non-irradiated areas. During the whole study, the treated zones were kept dry.
Remarks - Method	The minimal erythemal dose was determined by irradiation on day 1 and rating of effects on day 2. The numerical scoring system for assessing the phototoxic effects rated pigmentation, erythema, edema, desquamation and vesicle formation.

RESULTS

Remarks - Results	During the induction phase, the clinical examinations did not show any skin reactions of the photo-irritation type (score zero). During the challenge phase, the clinical examinations did not show any skin reactions of the photo-sensitisation type (score zero).

CONCLUSION	Under these study conditions, the test material can be considered as non-sensitising.
TEST FACILITY	Eurofins ATS (2007b)

B.16. Percutaneous Absorption In Vitro

TEST SUBSTANCE	Notified chemical
METHOD	Not specified. The notified chemical has been applied in the form of emulsion at 8% on the well recognised model of *ex vivo* pig skin. As original study report was in German, a summary in English was provided by the notifier.

RESULTS

In the test, the recovery rate from the quantity of the notified chemical which was applied is 92% (8% loss). From this recovery quantity, 55% came from the skin surface and 45% from within the skin. The portion recovered from the skin was distributed as follows:

- 94.7% in the *stratum corneum*,
- 3.4% in the epidermis,
- 1.9% in the dermis,
- and 0% in the reception phase (dosage by HPLC method, with a detection limit of roughly 0.2 µm/mL), usual and validated approach of the systemic bioavailability.

No percutaneous penetration is identified for the notified chemical on this pig skin model with characteristics of skin absorption and percutaneous penetration close to human skin.

CONCLUSION

Under the conditions of the study, the application of an emulsion with 8% concentration of the notified chemical does not result in percutaneous penetration through *ex vivo* pig skin.

TEST FACILITY	Beiersdorf AG, Forschung & Entwicklung Cosmed (2002)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1 Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	
Analytical Monitoring	TOC
Remarks – Method	25 mg notified chemical was weighed out on aluminium foil. The notified chemical along with the aluminium foil was added to test vessels to give a test concentration of 100 mg/L.

RESULTS

Notified chemical		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	0	4	57
10	1	10	80
14	1	14	84
20	2		
24	4		
28	4	28	88

Remarks – Results	Sodium benzoate showed 84% degradation after 14 days thus confirming the validity of the test. The toxicity control exceeded the required degradation within the study, indicating the test material was not inhibiting to the bacteria at the test concentration of 100 mg/L.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Bayer Ag (2007d)

C.2 Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test static/semi-static with renewal of test solutions after 24 h exposure EC Directive 92/69/EEC C.1 Acute Toxicity for Fish static test
Species	*Danio rerio*
Exposure Period	96 hours
Auxiliary Solvent	Reconstituted water
Water Hardness	228.5 mg $CaCO_3$/L
Analytical Monitoring	
Remarks – Method	Reconstituted water was prepared according to the recommendations of ISO 7346. This freshly prepared standard dilution water is used for both, the maintenance of the test animals under flow-through conditions and the preparation of stock and test solutions. To produce the test concentration 5.0 mg of the notified chemical was added to 5 litre of dilution water, treated with ultra turrax for 60 seconds and afterwards stirred for 24 h on a magnetic stirrer. Finally undissolved

particles of the notified chemical was removed by filtration to give the Water Accommodated Fraction (WAF).

RESULTS

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

LC50	≥ 1 mg/L WAF at 96 hours.
NOEC	1 mg/L WAF at 96 hours.
Remarks – Results	The results are expressed in terms of nominal concentrations. Considering the low solubility of the notified chemical (< 0.1 mg/L) no specific analysis was established.
CONCLUSION	The notified chemical is not toxic to *Danio rerio* up to the limit of its water solubility.
TEST FACILITY	Bayer AG (2007a)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – static. EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – static test. /semi-static with renewal of test solutions after 24 h exposure
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Reconstituted water.
Water Hardness	287.5 mg $CaCO_3$/L
Analytical Monitoring	
Remarks – Method	Reconstituted water (so-called 'M4 medium') was prepared according to the recommendations of Bundesgesundeitsamt Berlin. This standard solution was used for both, the maintenance of the test animals and the preparation of stock and test solutions. To produce the test concentration 1.1 mg of the notified chemical was added to 1 litre of dilution water, treated with ultra turrax for 60 seconds and afterwards stirred for 24 h on a magnetic stirrer. Finally undissolved particles of the notified chemical were removed by filtration to give the Water Accommodated Fraction (WAF). The criterion of adverse effects used in this study was substance induced alteration of the normal mobility behaviour and the loss of locomotory actions of the neonates, observed at 24 and 48 hours.

RESULTS

Concentration mg/L Nominal	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
1.1	20	0	0

EC0	≥ 1.1 mg/L WAF at 24 hours ≥ 1.1 mg/L WAF at 48 hours
NOEC	1 1 mg/L at 48 hours

Remarks – Results	The results are expressed in terms of nominal concentrations. Considering the low solubility of the notified chemical (< 0.1 mg/L) no specific analysis was established.
CONCLUSION	The notified chemical is not harmful to *Daphnia magna* up to the limit of its water solubility.
TEST FACILITY	Bayer AG (2007b)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Directive 92/69/EEC C.3 Algal Inhibition Test.
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 1 mg/L
Auxiliary Solvent	
Water Hardness	Not given
Analytical Monitoring	
Remarks - Method	1.2 mg of the notified chemical was directly added to 1 litre of dilution water and treated for 60 seconds with an ultra turrax and afterwards stirred for 24 h on a magnetic stirrer. Finally undissolved particles of the notified chemical was removed by filtration to give the Water Accommodated Fraction (WAF)..

RESULTS

Biomass		*Growth*	
EbC50 *mg/L at 72 h*	*NOEC* *... mg/L*	*ErC50* *mg/L a t72 h*	*NOEC>* *... mg/L*
> 1.2	1.2	> 1.2	1.2

Remarks - Results	The results are expressed in terms of nominal concentrations. Considering the low solubility of the notified chemical (< 0.1 mg/L) no specific analysis was established.
CONCLUSION	The notified chemical is not toxic to *Desmodesmus subspicatus* up to the limit of its water solubility.
TEST FACILITY	Bayer AG (2007c)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated sludge
Exposure Period	3 hours
Concentration Range	Nominal: 1000 mg/L
Remarks – Method	3,5–Dichlorophenol was used as a reference. Physico-chemical oxygen consumption is carried out since some substances can also consume oxygen by chemical activity.
RESULTS	The notified chemical showed 39.8% respiration inhibition of activated sludge at a test concentration of 10000 mg/L.
EC50	> 10000 mg/L

NOEC	10000 mg/L
Remarks – Results	Because of strong respiration of the activated sludge only 0.32 g/L suspended solids were used. The physico-chemical oxygen consumption was determined at 10000 mg/L concentration. No physico-chemical oxygen consumption has been determined. Therefore lower concentrations of the notified chemical caused no phisico-chemical oxygen consumption. Test concentrations are given as nominal concentrations and have not been confirmed by analytical methods. The reference substance (3,5-Dichlorophenol) concentration result from the quantities used in the preparations had not been confirmed by analytical methods.
CONCLUSION	The notified chemical is not toxic to bacteria
TEST FACILITY	Bayer AG (2007e)

BIBLIOGRAPHY

Bayer AG (2007a) Acute Fish Toxicity of Corapan TM TQ TM, Study No 1133 N/01 F. WD-UWS Institute of Environmental Analysis and Evaluation, Building W 15, Leverkusen 51368

Bayer AG (2007b) Acute *Daphnia* Toxicity of Corapan TM TQ TM, Study No 1133 N/01 D. WD-UWS Institute of Environmental Analysis and Evaluation, Building W 15, Leverkusen 51368

Bayer AG (2007c) Alga, Growth Inhibition Test of Corapan TM TQ TM, Study No 1133 N/01 A1. WD-UWS Institute of Environmental Analysis and Evaluation, Building W 15, Leverkusen 51368

Bayer AG (2007d) Biodegradability study of Corapan TM TQ TM, Study No 1133 N/01 R. WD-UWS Institute of Environmental Analysis and Evaluation, Building W 15, Leverkusen 51368

Bayer AG (2007e) Toxicity to Bacteria study of Corapan TM TQ TM, Study No 1133 N/01 B. WD-UWS Institute of Environmental Analysis and Evaluation, Building W 15, Leverkusen 51368

Consumer Product Testing Co. (1999a) Primary Dermal Irritation in Rabbits (TSCA), Primary Ocular Irritation in Rabbits (TSCA), Acute Oral Toxicity in Rats-Limit Test (TSCA) and Acute Dermal Toxicity in Rabbits-Limit Test (TSCA). Final Report December 1999, Experiment Reference No. T99-0278 for The C.P. Hall Company, Bedford Park, IL, USA. Consumer Product Testing Co., Fairfield, NJ, USA (Unpublished report provided by notifier).

Consumer Product Testing Co. (1999b) Ames Salmonella/E. Coli Mutagenicity test. Final Report November 1999, Study No. M99-1976 for The C.P. Hall Company, Bedford Park, IL, USA. Consumer Product Testing Co., Fairfield, NJ, USA (Unpublished report provided by notifier).

Consumer Product Testing Co. (1999c) Repeated Insult Patch Test. Final Report August 1999, Experiment Reference No. C99-0571.01 for The C.P. Hall Company, Bedford Park, IL, USA. Consumer Product Testing Co., Fairfield, NJ, USA (Unpublished report provided by notifier).

Eurofins ATS (2007a) Notified chemical: Clinical evaluation of the phototoxic potential of a cosmetic product. Final Report April 2008. Study No: 13423 Eurofins ATS for Symrise France. Eurofins Scientific Test Center, France (Unpublished report provided by the notifier).

Eurofins ATS (2007b) Notified chemical: Clinical evaluation of the photosensitising potential of a cosmetic product. Final Report May 2008. Study No: 13423 Eurofins ATS for Symrise France. Eurofins Scientific Test Center, France (Unpublished report provided by the notifier).

FORS (Federal Office of Road Safety) (1998) Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 6th Edition, Canberra, Australian Government Publishing Service

Frey-Tox Germany (2001a) Notified Chemical: Primary Skin Irritation Study in the Rabbit. Final Report October 2001, Project HR 01/901992 for Haarmann & Reimer GmbH, Holzminden, Germany. Frey-Tox Osteroda, Germany (Unpublished report provided by notifier).

Frey-Tox Germany (2001b) Notified Chemical: Acute Eye Irritation/Corrosion Study in the Rabbit. Final Report October 2001, Project HR 01/901992 for Haarmann & Reimer GmbH, Holzminden, Germany. Frey-Tox Germany, Osteroda, Germany (Unpublished report provided by notifier).

Frey-Tox Germany (2001c) Notified Chemical: Test for Delayed Contact Hypersensitivity Using the Guinea Pig Maximisation Test. Final Report October 2001, Project HR 01/901992 for Haarmann & Reimer GmbH, Holzminden, Germany. Frey-Tox Germany, Osteroda, Germany (Unpublished report provided by notifier).

Kesla Forschung & Service KG (2001a). Corapan TQ. Determination of the melting point. Final Report December 2001. Study No: KBL/2001/1169 MP for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2001b). Corapan TQ. Determination of the boiling point. Final Report December 2001. Study No: KBL/2001/1169 BP for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2001c). Corapan TQ. Determination of the relative density. Final Report December 2001. Study No: KBL/2001/1169 RDI for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2001d). Corapan TQ. Determination of the water solubility. Final Report December 2001. Study No: KBL/2001/1169 WLO for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2001e). Corapan TQ. Determination of the water solubility. Final Report December 2001. Study No: KBL/2001/1169 WLO for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2001f). Corapan TQ. Determination of the flash point. Final Report August 2001. Study No: KBL/2001/1169 FLP for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2001g). Corapan TQ. Determination of the Partition Coefficient. Study No: KBL/2001/1169 OWV for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

Kesla Forschung & Service KG (2002). Notified Chemical. 28-Day (gavage) Toxicity Study in the Rat with a 14 Day Treatment-Free Recovery Period. Final Report March 2002. Study No: KBL/2001/1214 Rsa for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

King Harnasch (2001a). Notified Chemical. Mutagenicity study in the salmonella typhimurium/mammalian microsome reverse mutation assay (Ames-Test). Final Report October 2001. Project No: AM02201N for Haarmann & Reimer GmbH, MuhlenfeldstraBe 1, D-37603, Holzminden (Unpublished report provided by the notifier).

King Harnasch (2001b). Notified Chemical. Mutagenicity study in the chromosome aberration test with human peripheral blood lymphocytes in vtitro. Final Report December 2001. Project No: HL02301V for Haarmann & Reimer GmbH, MuhlenfeldstraBe 1, D-37603, Holzminden (Unpublished report provided by the notifier).

King Harnasch (2002). Notified Chemical. Mutagenicity study with the micronucleus test in bone marrow cells of mice (NMRI). Final Report March 2002. Project No: MN00202M for Haarmann & Reimer GmbH, MuhlenfeldstraBe 1, D-37603, Holzminden (Unpublished report provided by the notifier).

Noack Laboratorium fur Angewandte Biologie (2001). Corapan TQ. Autoignition temperature. Final Report October 2001. Study No: CPZ80911 for Haarmann & Reimer GmbH, Postfach 1253, D-37601, Holzminden (Unpublished report provided by the notifier).

NTP (2006) NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di(2-Ethylhexyl) Phthalate (DEHP). Center For The Evaluation of Risks To Human Reproduction. National Toxicology Program. U.S. Department of Health and Human Services, November 2006, NIH Publication No. 06-4476.

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

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

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

Sicherheitstechnik (2001). Corapan TQ. Vapour pressure. Final Report December 2001. Report No: 20011280.01 for Kesla Forschung & Service KG, Salegaster Chaussee 3, Germany (Unpublished report provided by the notifier).

United Nations (2003) Globally Harmonised System of Classification and Labelling of Chemicals (GHS). United Nations Economic Commission for Europe (UN/ECE), New York and Geneva.