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March 2020

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

D-Glucopyranose, oligomeric, 2-ethylhexyl glycosides

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (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 conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Agriculture, Water and the Environment.

This Public Report is 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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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1680	IXOM Operations Pty Ltd	D-Glucopyranose, oligomeric, 2-ethylhexyl glycosides	Yes	≤ 800 tonnes per annum	A component of cleaning products

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the available information, the notified chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the notified chemical/polymer is presented in the following table.

Hazard Classification	*Hazard Statement*
Serious Eye Damage/Eye Irritation (Category 1)	H318 – Causes serious eye damage

Human Health Risk Assessment
Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

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

Environmental Risk Assessment
On the basis of the PEC/PNEC ratios, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  – Serious Eye Damage/Eye Irritation (Category 1): H318 – Causes serious eye damage

  In the absence of data for end-use products, concentrations at ≥ 3% are classified as Category 1 causing serious eye damage according to the GHS criteria.

  The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation:
  – Enclosed/automated processes
  – Adequate general ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid contact with skin and eyes
  - Use in a well ventilated area

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Safety glasses or goggles
  - Impervious gloves
  - Protective clothing
  - Respiratory protection if inhalation exposure may occur

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Public Health

- The Delegate should consider the notified chemical for listing on the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

- Formulators should take into account the potential for the notified chemical to cause serious eye damage when manufacturing consumer products containing the notified chemical.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

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 final use concentration of the notified chemical exceeds 6% in cleaning products;

or

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

- the function or use of the chemical has changed from a component of cleaning products, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

Safety Data Sheet
The SDS of the products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
IXOM Operations Pty Ltd (ABN: 51 600 546 512)
70 Marple Avenue
VILLAWOOD NSW 2163

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include: analytical data, degree of purity, impurities, use details, and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for hydrolysis as a function of pH, dissociation constant, particle size, explosive properties, oxidising properties, and reactivity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2010)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
SIMULSOL AS 48 (containing the notified chemical at up to 60% concentration)

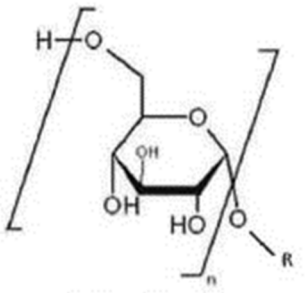
CAS NUMBER
161074-93-7

CHEMICAL NAME
D-Glucopyranose, oligomeric, 2-ethylhexyl glycosides

OTHER NAME(S)
2-Ethylhexyl glucoside
A mixture of 2-ethylhexyl mono-D-glucopyranoside and 2-ethylhexyl di-D-glucopyranoside

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



R= 2-ethylhexyl
N=1-2

MOLECULAR WEIGHT
The molecular weight depends on the degree of polymerisation (DP).

MW = 292 - 617 g/mol where the DP = 1 to 3, MW = 392.4 g/mol where the DP=l.62.

3. COMPOSITION

DEGREE OF PURITY
> 60% (the chemical is a UVCB)

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Solid. Clear viscous liquid (as imported)*

Property	*Value*	*Data Source/Justification*
Melting Point/Freezing Point	-5 °C	Solidification occurred at about -5 °C
Boiling Point	> 275 °C at 101.3 kPa	Decomposition reaction began at about 275 °C
Density	1,183 kg/m^3 at 20 °C	Measured
Vapour Pressure	5 × 10^{-8} kPa at 25 °C	Measured
Water Solubility	> 790 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Notified chemical is not expected to hydrolyse under normal environmental conditions (pH 4-9).
Partition Coefficient (n-octanol/water)	log Pow = 1.1 at 20 °C	Measured
Surface Tension	30.2 mN/m	Measured
Adsorption/Desorption	log Koc = 0.6	Measured
Dissociation Constant	Not determined	Notified chemical is not expected to dissociate under normal environmental conditions (pH 4-9).
Particle Size	Not determined	The notified chemical will be introduced as a liquid into Australia.
Flash Point	> 110 °C at 101.7 kPa	Measured
Flammability	Non flammable	Measured
Autoignition Temperature	> 400 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties

* The notified chemical at up to 60% concentration (as SIMULSOL AS 48)

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical Hazard Classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported at up to 60% concentration for reformulation into finished end-use industrial, and household cleaning products at up to 6% concentrations. The notified chemical may also be imported as finished cleaning products.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	≤ 800	≤ 800	≤ 800	≤ 800	≤ 800

PORT OF ENTRY
Melbourne and Sydney

IDENTITY OF MANUFACTURER
SEPPIC SA.
Paris La Défense
50 boulevard National – CS 90020
92257 La Garenne Colombes Cedex
France

TRANSPORTATION AND PACKAGING
The notified chemical at up to 60% concentration will be introduced in HPDE plastic containers of 1,000 kg and in PEHD plastic drums of 200 kg. The formulated end-use products containing the notified chemical at up to 6% concentration will be transported by road and Rail.

USE
The notified chemical will be used as a component (at concentrations up to 6%) of industrial, institutional and household cleaning products.

OPERATION DESCRIPTION

Reformulation into cleaning products
The notified chemical will not be manufactured in Australia. The imported products containing the notified chemical (at up to 60% concentration) will be reformulated with additional components to form the finished end-use products at up to 6% concentration. Reformulation procedures are expected to vary depending on the nature of the cleaning products being made, and may involve both automated and manual transfer steps. In general, it is expected that the reformulation processes will involve blending operations that will normally be automated and occur in an enclosed system, followed by automated filling of the finished products into retail containers of various sizes. Samples may be collected during the blending process for quality control testing.

End-use
Household cleaning products containing the notified chemical at up to 6% concentration may be used by consumers and professional cleaners. The cleaning products will be generally applied with a cloth or sponge, mop or brush, or by spray followed by wiping. In some cases the cleaning product will be diluted with water prior to application.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and Storage	1	12
Laboratory activities	1	330
Reformulation	1	12
Packers (Dispensing & Capping)	1	12
Store Persons	1	12
End Users	8	330

EXPOSURE DETAILS

Transport and storage
Transport, storage and warehouse workers may come into contact with the notified chemical at up to 60% concentration only in the event of accidental rupture of containers.

Reformulation
During reformulation dermal and ocular exposure of workers to the notified chemical at up to 60% concentration may occur during handling of drums, during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. It is expected that exposure will be minimised through the use of enclosed systems, and workers wearing personal protective equipment (PPE) such as protective clothing, eye protection and impervious gloves, as stated by the notifier. Inhalation exposure is not expected given the low vapour pressure of the notified chemical.

End-use
Exposure to the notified chemical in end-use products (at up to 6% concentration) may occur in professions where the services provided involve in the use of cleaning products. The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible. Such professionals may use some PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the products containing the notified chemical (see section 6.1.2).

6.1.2. Public Exposure

There will be repeated exposure of the public to the notified chemical at up to 6% concentration through the use of household cleaning products. The main route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray/applicators.

Data on typical use patterns of household cleaning product categories (SCCS, 2012; Cadby et al., 2002; ACI, 2010) in which the notified chemical may be used are shown in the following tables. For the purposes of the exposure assessment via the dermal route, Australian use patterns for the various product categories are assumed to be similar to those in Europe. In the absence of dermal absorption data, a dermal absorption (DA) of 100% was assumed for the notified chemical (ECHA, 2017). A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

Household products (Indirect dermal exposure - from wearing clothes):

Product type	Amount (g/use)	C (%)	Product Retained (PR) (%)	Percent Transfer (PT) (%)	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	230	6	0.95	10	0.2048
Fabric softener	90	6	0.95	10	0.0802
Total					**0.2850**

C = maximum intended concentration of notified chemical
Daily systemic exposure = (Amount × C × PR × PT × DA)/BW

Household products (Direct dermal exposure):

Product type	Frequency (use/day)	C (%)	Contact Area (cm^2)	Product Use C (g/cm^3)	Film Thickness (cm)	Time Scale Factor	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	1.43	6	1980	0.01	0.01	0.007	0.0019
Dishwashing liquid	3	6	1980	0.009	0.01	0.03	0.0150
All-purpose cleaner	1	6	1980	1	0.01	0.007	0.1299
Total							**0.1468**

C = maximum intended concentration of notified chemical
Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor × DA)/BW where C = concentration, DA = Dermal absorption rate, BW = Average bodyweight

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical at the maximum intended concentrations

specified by the notifier in various product types. This would result in a combined internal dose of 0.4318 mg/kg bw/day for the notified chemical.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Acute oral toxicity – rat	LD50 > 5,000 mg/kg bw; low toxicity
Acute dermal toxicity – rat	LD50 > 2,380 mg/kg bw; low toxicity
Skin irritation – rabbit	non-irritating
Eye irritation – rabbit	severely irritating
Skin sensitisation – guinea pig, Maximisation test	inconclusive
Repeat dose oral toxicity – rat, 90 days	NOAEL = 150 mg/kg bw/day
Repeat dose oral toxicity – rat, 28 days	NOAEL = 750 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration - human lymphocytes	non genotoxic
Genotoxicity – *in vitro* mouse lymphoma	non genotoxic

Toxicokinetics, Metabolism and Distribution
No toxicokinetic data was provided for the notified chemical.
For dermal absorption, molecular weights below 100 g/mol are favourable for absorption and molecular weights above 500 g/mol do not favour absorption (ECHA, 2017). Additionally Log P values between 1 and 4 favour dermal absorption particularly if water solubility is high (ECHA, 2017). The notified chemical has a molecular weight of 292 - 617 g/mol, very high water solubility (> 790 g/L) and a log Pow of 1.1 at 20 °C, indicating potential for absorption.

Following dermal exposure alky glucosides, such as the notified chemical, are metabolised by glucoside hydrolases in the skin into the separate glucoside and fatty alcohol components (Fiume *et al*., 2013).

Acute Toxicity
The notified chemical was shown in studies to be of low acute toxicity to rats via the oral and dermal routes. There is no information available on the acute inhalation toxicity of the notified chemical.

Irritation and Sensitisation
The notified chemical was non-irritating to skin of rabbits. In an eye irritation test on one rabbit, the notified chemical was considered to be severely irritating to eyes.

In a guinea pig maximisation test on the notified chemical at up to 50% topical induction concentration (in distilled water), dermal reactions were observed in some test animals following challenge. The dermal responses were seen in 5/30 test animals which were more marked than those for the controls and 4/30 test animals showed inconclusive responses. The notified chemical is comprised of D-glucopyranoside (mono or di) and 1-hexanol, 2-ethyl-. 1-Hexanol, 2-ethyl-, is not expected to be a skin sensitiser (NICNAS), and the D-glucopyranosides that are used for the synthesis of the notified chemical are predominantly glucose and maltose which are not reported as being dermal sensitisers. Studies on similar alkyl glucosides have shown them to generally be non-sensitising or weak sensitisers (Fiume *et al*., 2013). Nonetheless, some alkyl glucosides have been reported to cause allergic skin reactions in people exposed to products containing them; the specific glucosides reported in the majority of cases were decyl glucoside, lauryl glucoside, cetearyl glucoside and coco glucoside (Loranger *et al*., 2017). Therefore, the potential for the notified chemical to cause skin sensitisation is expected to be low, but cannot be ruled out entirely.

Repeated Dose Toxicity
A 90 day repeated dose oral toxicity study in rats was conducted on the notified chemical with dose levels of 0, 50, 150 and 450 mg/kg bw/day. Under the conditions of this study, the NOAEL was established at 150 mg/kg bw/day.

A 28 day repeated dose oral toxicity study in rats was conducted on the notified chemical with dose levels of 0, 15, 150, and 750 mg/kg bw/day. The No Observed Adverse Effect Level NOAEL was established as 750 mg/kg bw/day in this study, based on an absence of toxicologically relevant adverse effects at this dose.

Mutagenicity/Genotoxicity
The notified chemical tested negative in a bacterial reverse mutation assay, in an *in vitro* mammalian chromosome aberration test using cultured human lymphocytes cells and in an *in vitro* mammalian cell gene mutation test using mouse lymphoma/L5178Y cells.

Toxicity for Reproduction
There was no data provided on the reproductive and developmental toxicity of the notified chemical. The notified chemical is expected to be reduced by hydrolysis to produce 1-hexanol, 2-ethyl- (CAS number 104-76-7). 1-Hexanol, 2-ethyl- is suspected of being toxic to development with a NOAEL of 130 mg/kg bw/day (NICNAS).

Health Hazard Classification
Based on the available information, the notified chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the notified chemical is presented in the following table.

Hazard Classification	*Hazard Statement*
Serious Eye Damage/Eye Irritation (Category 1)	H318 – Causes serious eye damage

6.3. Human Health Risk Characterisation
Based on the studies provided, the notified chemical is severely irritating to eyes. The skin sensitisation potential of the notified chemical is inconclusive, but it is not expected to be a strong sensitiser.

6.3.1. Occupational Health and Safety
Dermal and ocular exposure to the notified chemical at up to 60% concentration may occur during reformulation. As stated by the notifier use of PPE such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate) and engineering controls including automated/enclosed processes and local exhaust ventilation will limit worker exposure.

Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described (use of enclosed systems, and workers wearing PPE), the notified chemical is not considered to pose an unreasonable risk to the health of workers during reformulation.

End-use
Workers involved in professions where the services provided involve the use of cleaning products, may come into contact to the notified chemical at ≤ 6% concentration. Products containing the chemical at ≥ 3% are classified as severe eye irritants according to the GHS criteria. The risk to workers who regularly use these products is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health
Household cleaning products containing the notified chemical at ≤ 6% concentration will be available to the public. The main route of exposure is expected to be dermal with some potential for accidental ocular or oral exposure.

The notified chemical is a severe eye irritant at concentrations ≥ 3% according to the GHS criteria and therefore consumer products in retail containers should be labelled with appropriate safety directions for use. However, accidental ocular exposure to the notified chemical in cleaning products is expected to be an infrequent event and therefore the risk to the public is not expected to be unreasonable at the proposed use concentration.

The repeat dose toxicity potential was estimated by calculation of the margin of exposure (MOE) of the notified chemical using the worst case exposure scenario from use of multiple products containing the notified chemical as 0.4318 mg/kg bw/day (see Section 6.1.2). Using the NOAEL of 150 mg/kg bw/day, as determined in a 90-day repeated dose toxicity study a MOE of 347 was estimated. A MOE value ≥ 100 is considered acceptable to account for intra- and inter-species differences, and to account for long-term exposure; therefore, the MOE is considered to be acceptable.

An expected metabolite (1-hexanol, 2-ethyl-) of the notified chemical is a potential developmental toxicant with a NOAEL of 130 mg/kg bw/day. 1-Hexanol, 2-ethyl- comprises < 42% of the notified chemical by weight and therefore the maximum expected exposure to 1-hexanol, 2-ethyl- would be < 0.1735 mg/kg bw/day which would give an MOE of > 749.

When used at a maximum concentration of 6% in household cleaning products with warnings on the label for any potential risks and safety directions for use, the notified chemical is not considered to pose an unreasonable risk to public health.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical is not manufactured in Australia, therefore there is no environmental release associated with this activity. Environmental release is only likely during transportation, storage, reformulation and repackaging of the notified chemical. Reformulation and repacking processes are typically highly automated and occur inside of closed environments. The release volume from these processes is expected to be low and but may occur from the disposal of waste washings, empty containers and spilt materials. Accidental spills are to be collected using an inert, absorbent material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be primarily washed into the sewers during use of the end-use household, industrial and institutional cleaning products, but some industrial uses will result in direct release to the environment, including the marine environment.

RELEASE OF CHEMICAL FROM DISPOSAL

Waste from spills during transportation and reformulation are to be disposed of to landfill. Approximately 3% of the import volume of the notified chemical is expected to remain as residues which will be disposed of into landfill.

7.1.2. Environmental Fate

The notified chemical will enter sewers and be subsequently treated at sewage treatment plants (STPs) following its use in cleaning products available to the general public. A ready biodegradability test determined that the notified chemical is readily biodegradable (90% after 28 days). See Appendix C for further details.

Based on its low partition coefficient, the notified chemical is not expected to bioaccumulate. Based on the low Koc the notified chemical is not expected to sorb to soils or sediments and will eventually degrade via biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

Release to Sewer

A Predicted Environmental Concentration for waterways ($PEC_{waterways}$) for a worst case scenario has been calculated. Based on the reported use of the notified chemical in household and industrial cleaning products, a release of 100% of the annual import volume to sewers on a nationwide basis over 365 days per year has been used for the notified chemical. The extent to which the notified chemical is removed from the effluent in STP processes based on the properties of the notified chemical has not been considered in this worst-case scenario.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	800,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	800,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2191.78	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	

Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10	
PEC - River:	449.40	µg/L
PEC - Ocean:	44.94	µg/L

Direct Release to the Marine Environment

Direct discharge of the notified chemical into the marine environment is likely from offshore use. The predicted environmental concentration in seawater (PEC_{water}) has been calculated based on the CHARM model (Thatcher et al., 2005) and discharges of notified chemical from cleaning has been identified as the main route for release. The notified chemical is discharged in batches and the greatest effect will occur within a radius (r) of 500 m from the discharge line. Assuming that none of the chemical is depleted or transformed between addition and discharge, the discharge concentration equals to the initial concentration (mg/L). For the worst case scenario, the PEC_{water} in the water column due to cleaning discharge is calculated using following equation:

$$PEC_{water} = C_{i,cleaning} * D_{batch,cleaning}$$

In this relationship,
PEC_{water} = Predicted Environmental Concentration in the water column (mg/L);
C_i = Initial concentration of the notified chemical in the product (mg/L);
$D_{batch, mixwater}$ = Batchwise dilution factor for cleaning fluids.

The initial dosage of the notified chemical in cleaning fluids is up to 6% w/v. Therefore, the original dose for the notified chemical in cleaning fluids is calculated to be 60,000 mg/L. The default dilution factor for cleaning fluids is set at 7.7×10^{-5} in the CHARM model under the batch-wise discharge scenario (Thatcher et al., 2005, p. 52).

Therefore, the resulting PEC_{water} is calculated to be:

$$PEC_{water} = C_{i,cleaning} * D_{batch,cleaning} = 60\,000 \text{ mg/L} \times 7.7\text{x}10^{-5} = 4.62 \text{ mg/L} = 4620 \text{ µg/L}.$$

The $PEC_{sediment}$ for a batch-wise discharge scenario is not calculated in the CHARM model because it is assumed that there would be insufficient time to allow the establishment of equilibrium between the high short-term levels of notified chemical in the water column arising from batch-wise release and the levels of the notified chemical in sediments near the discharge point. Furthermore, as the notified chemical is highly water soluble and is expected to readily disperse and biodegrade in the aqueous compartment, it is not expected to reach ecotoxicologically significant concentrations in the sediment compartment.

A PEC from use in firefighting foams was not calculated. However, it is not expected to be greater than the single batch release, which assumes that the notified chemical becomes evenly distributed in a 500 m radius, from the discharge point, shortly after release. The actual PEC will be strongly influenced by the circumstances under which firefighting foam is used, but is not expected to exceed that calculated from a rapid point release.

When used in in firefighting foams in non-marine environments the PEC will be site-specific and strongly influenced by the circumstances of the firefighting foam use. However, as the notified chemical is of low aquatic hazard, the risk from this use pattern is not considered unreasonable unless there is significant direct contamination of waterways.

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	LC50 > 310 mg/L	Not harmful to fish
Daphnia Toxicity	EC50 > 100 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity	EC50 > 98 mg/L (100 mg/L nominal)	Not harmful to algal growth

Based on the above ecotoxicological endpoints for the notified chemical, it is not expected to be acutely or chronically toxic to aquatic organisms. Therefore the notified chemical is not formally classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC $_{waterways}$) was calculated using the most sensitive end-point (algae, EC50 > 98 mg/L) with an assessment factor of 100 as the endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Algae)	> 98	mg/L
Assessment Factor	100	
Mitigation Factor	1	
PNEC:	> 980	µg/L

The PNEC $_{Pelagic\ acute}$ for offshore use was calculated using the most sensitive end-point (algae, EC50 > 98 mg/L) with an assessment factor of 100 as the acute endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Acute Pelagic Compartment		
EC50 (Algae)	> 98	mg/L
Assessment Factor	10	
Mitigation Factor	1	
PNEC:	> 9,800	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	449.4	> 980	< 0.46
Q - Ocean:	44.9	> 980	< 0.046
Q – Offshore:	4620	> 9,800	<4.71

The risk quotient (Q=PEC/PNEC) has been calculated based on the worst-case assumption of complete release into the waterways with no removal in STPs. The Q values are less than 1 for both river and ocean compartments and are based on studies were no ecotoxicity results could be established. Therefore they are regarded as the upper bound of the Q values and it is highly unlikely that the notified chemical will reach ecotoxicologically significant concentrations based on the proposed annual importation and use these patterns. For offshore use the Q value exceeds 1, indicating a potential risk. However, as described previously this is regarded as an upper bound. Furthermore, Thatcher et al., (2005), recommend against using an extrapolation factor of 10 for acute-to-chronic extrapolation for batch-wise releases due to the very short exposure times expected at the peak PEC of 4620 µg/L. Therefore the assessment factor for batch-wise release from offshore uses is 10, rather than 100. This is mathematically equivalent to dividing the Q value above by 10 which results in a modified Q value of 0.47 for offshore use. Therefore, based on the PEC/PNEC ratios, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point -5 °C

Method British Standard 4633:1970 using a standard crystallising point method
Remarks No freezing point in the classical sense but solidification occurred at about -5 °C
Test Facility Confidential (1993)

Boiling Point > 275 °C at 101.3 kPa

Method OECD TG 103 Boiling Point
EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks Decomposition began at about 275 °C and a rapid reaction was observed at about 338 °C. The boiling point test was performed after a drying procedure in an oven at 105 ± 5 °C for about 15 hours.
Test Facility Confidential (2013)

Relative Density 1.1829

Method A.3 Relative Density Pycnometer method.
Remarks The test item density was determined to be 1182.9 kg/m^3 in two tests.
Test Facility Confidential (1993)

Vapour Pressure 5×10^{-8} kPa at 25 °C

Method A.4 Vapour Pressure
Remarks Vapour Pressure Balance method
Test Facility Confidential (1993)

Water Solubility > 790 g/L at 20 °C

Method In-house method equivalent to OECD TG 105 Water Solubility
Remarks Flask Method
Test Facility Confidential (1993a)

Partition Coefficient (n-octanol/water) log Pow = 1.1 at 20 °C

Method In-house method equivalent to OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks Shake Flask Method
Test Facility Confidential (1993a)

Surface Tension 30.2 mN/m at 23 °C

Method In-house method equivalent to OECD TG 115 Surface Tension of Aqueous Solutions
Remarks Concentration: 1% w/v solution
Test Facility Confidential (1993a)

Adsorption/Desorption – screening test log Koc = 0.6 at 20 °C

Method OECD TG 106 Adsorption – Desorption Using a Batch Equilibrium Method

Soil Type	*Adsorption (%)*	*Koc (mL/g)*
Sandy loam	3.7	2
Loam	7.5	7
Clay loam	21.5	7
Silt loam	6	2
Clay	16.6	5

Remarks	Rapid degradation of the test substance was observed in the preliminary test, therefore in the screening test the soils were sterilised with ɣ-radiation and heat (160 °C). The soils were analysed after treatment and showed no signs of structural change. The mean Koc of 5 was used to calculate the log Koc for the test substance. Due to low adsorption, desorption and advanced tests were not performed.
Test Facility	Confidential (2006)

Flash Point > 110 °C at 101.7 kPa

Method	A.9 Flash Point (ASTM D93-80)
Remarks	Pensky-Martens closed cup method. The test flame extinguished from approximately 70 °C onwards. The test item started boiling at 105 °C, with the emission of white fumes. The test was terminated at 110 °C
Test Facility	Confidential (1993)

Flammability Non flammable

Method	A.10 Flammability (Solids)
Remarks	Determined by using a test mould and an ignition source. Flammability is defined as the time taken for a pile of test substance to burn a distance of 100 mm after having burned a distance of 80 mm. The test substance melted to a black liquid with evolution of copious amounts of white/grey smoke, but failed to ignite after 1 minute in all six of the tests.
Test Facility	Confidential (1993)

Autoignition Temperature > 400 °C

Method	EEC Directive 67/548 A.16 Relative Self-Ignition Temperature for Solids
Remarks	Determination of self-ignition at elevated temperatures. A steady rise in temperature of the oven and the sample was observed with no indication of auto ignition of the test substance. No trace of the sample was left in the cube or oven at the end of the test.
Test Facility	Confidential (1993)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	EC Methods for the determination of toxicity, Directive 84/449/EEC (OJ No. L251, 19.9.84). Part B, Method B.1. Acute Toxicity (oral)
Species/Strain	Rat/Crl CD (SD) BR VAF plus
Vehicle	Distilled water
Remarks – Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5 per sex	5,000	4/10
2	5 per sex	2,000	0/10

LD50	> 5,000 mg/kg bw
Signs of Toxicity	A total of four rats (two male and two female) died when dosed at 5,000 mg/kg bw. Pilo-erection, hunched posture, waddling, lethargy, decreased respiratory rate and pallor of the extremities were observed in all animals dosed at either 2,000 or 5,000 mg/kg bw. Ptosis, ataxia and prostration were also observed but only in rats dosed at 5,000 mg/kg bw. Recovery of surviving rats was observed by Day 3 for groups treated at 2,000 mg/kg bw, Day 4 for male rats treated at 5,000 mg/kg bw and Day 5 for female rats treated at 5,000 mg/kg bw.
Effects in Organs	Congestion of the blood vessels of the small and large intestines was noted in animals that died during the study. No abnormalities were noted at the macroscopic examination on Day 15 for animals that survived until the end of the study.
Remarks – Results	Body weight loss (11.3%) was observed in one female treated at 2,000 mg/kg bw and slightly low bodyweight gains were observed on Day 8 on two males treated at 2,000 mg/kg bw and one at 5,000 mg/kg bw. These rats reached the expected gains on Day15 and the rest of rats throughout the study.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	Confidential (1992a)

B.2. Acute Dermal Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	EEC Methods for the determination of toxicity, Directive 84/449/EEC (OJ No. 19.09.84), Part B, Method B.3. Acute Toxicity (dermal)
Species/Strain	Rat/Hsd/Ola SD(CD)
Vehicle	Water
Type of dressing	Occlusive.
Remarks – Method	Similar to EC Council Regulation No 440/2008 B.3 Acute Toxicity (Dermal).

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M	2,380 mg/kg bw	0/5
2	5F	2,380 mg/kg bw	0/5

LD50	> 2,380 mg/kg bw
Signs of Toxicity – Local	No irritation, erythema, oedema or other dermal changes were observed on any animals.
Signs of Toxicity – Systemic	Slightly low bodyweight gains were noted.
Effects in Organs	No abnormalities were noted at the macroscopic examination.
Remarks – Results	No mortality occurred in both groups treated at 2,380 mg/kg bw.

CONCLUSION The notified chemical is of low acute toxicity via the dermal route.

TEST FACILITY Confidential (1993b)

B.3. Skin Irritation – Rabbit

TEST SUBSTANCE Notified chemical

METHOD EEC Methods for the determination of toxicity, Directive 84/449/EEC (OJ No. L251, 19.9.84), Part B, Method B.4 Acute Toxicity (Skin Irritation)

Species/Strain	Rabbit/New Zealand White
Number of Animals	Three
Vehicle	None
Observation Period	4 days
Type of Dressing	Semi-occlusive
Remarks – Method	Similar to EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation)

RESULTS

Remarks – Results	No signs of toxicity in any rabbit during the observation period were noted. No dermal reaction to treatment was observed in any rabbit during the observation period.

CONCLUSION The notified chemical is non-irritating to the skin.

TEST FACILITY Confidential (1992b)

B.4. Eye Irritation – Rabbit

TEST SUBSTANCE Notified chemical

METHOD EEC Methods for the determination of toxicity, Directive 84/449/EEC (OJ No. L251, 19.9.84), Part B, Method B.5. Acute toxicity (eye irritation)

Species/Strain	Rabbit/New Zealand White
Number of Animals	One male
Observation Period	21 days
Remarks – Method	No significant protocol deviations.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva – Redness	2	2	21 days	1
Conjunctiva – Chemosis	2	2	7 days	1
Conjunctiva – Discharge	N/A	N/A		N/A
Corneal Opacity	2	3	21 days	3
Iridial Inflammation	1	1	3 days	1

* Calculated on the basis of the scores at 24, 48, and 72 hours

Remarks – Results	No signs of systemic toxicity were noted. Cornea dulling was observed one hour after instillation followed by development of corneal opacity. This persisted after 21 days with neo-

vascularisation also present. Iridial inflammation persisted until Day 3. Conjunctival irritation persisted for 21 days.

CONCLUSION The notified chemical is severely irritating to the eye.

TEST FACILITY Confidential (1992c)

B.5. Skin Sensitisation – Guinea Pig - Maximisation Test (GMPT)

TEST SUBSTANCE Notified chemical

METHOD EC Directive 84/449/EEC B.6 Skin Sensitisation – Maximisation test

Species/Strain Guinea pig/Dunkin Hartley

PRELIMINARY STUDY Maximum non-irritating concentration:
Intradermal: 0.5% v/v in water
Topical: Induction: 50% v/v in distilled water
Challenge: 10 and 5% v/v in distilled water

MAIN STUDY

Number of Animals Test Group: 30 Control Group: 10

Vehicle Distilled water

Positive Control Formalin (not conducted in parallel with the test substance).

INDUCTION PHASE Induction concentration:
Intradermal: 0.5% v/v in water
Topical: 50% v/v in distilled water

Signs of Irritation Necrosis was observed at intradermal injection sites that received the test substance along with Freund's Complete Adjuvant (50%) in water. Slight irritation was seen at intradermal injection sites where the test substance was diluted with only water.
Slight to moderate erythema was seen at the topical induction sites.

CHALLENGE PHASE

Challenge Intradermal: None
Topical: 10% v/v in distilled water (Anterior site of the animal)
Topical: 5% v/v in distilled water (Posterior site of the animal)

Remarks – Method No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: Challenge*		
		24 h	*48 h*	*72 h*
Test Group	10%	9/30	5/30	2/30
	5%	0/30	0/30	0/30
Control Group	10%	0/9	0/9	0/9
	5%	0/9	0/9	0/9

Remarks – Results No signs of toxicity were observed in the treated animals.

One control animal died following topical application, with the cause of death not determined. A post mortem showed no macroscopic abnormalities.

Slight to well defined erythema was seen in 9/30 test animals at the 24 hour observation, with the irritant effects reducing over time.

The study authors noted that in 5 of the animals that had dermal reactions the responses were more marked than those of the controls, whilst in the other 4 animals with a lower level of dermal reactions and therefore the responses were inconclusive. The study authors conclude that the test substance produced evidence of skin sensitisation in only 5/30 animals.

CONCLUSION	There was limited evidence of reactions indicative of skin sensitisation to the notified chemical in less than 30% of the treated animals under the conditions of the test. The GHS criteria for a chemical to be considered as a skin sensitiser in GPMT- Freunds Complete Adjuvant – test, a response rate of at least 30% of the animals should be positive. Therefore the chemical cannot be classified as a skin sensitiser.
TEST FACILITY	Confidential (1993c)

B.6. Repeat Dose Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents (1998) EC Directive 67/548/EEC, B Repeated Dose (90 days) Toxicity (oral) (2001)
Species/Strain	Rat/ Wistar Crl:(WI) BR
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week Post-exposure observation period: 28 days
Vehicle	Water (Milli-U)
Remarks – Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	10M, 10F	0	0/20
Low Dose	10M, 10F	50	0/20
Mid Dose	10M, 10F	150	0/20
High Dose	10M, 10F	450	1/20
Control Recovery	10M, 10F	0	0
High Dose Recovery	10M, 10F	450	1/20

Mortality and Time to Death

One male in the 450 mg/kg bw/day recovery group and one female in the 450 mg/kg bw/day main group died on days 29 and 21, respectively. Clinical signs in the deceased animals consisted of laboured respiration, hunched posture and piloerection. Observations from the necropsy consisted of severe necrosis in addition to an exudation of the tracheal mucosa, autolysis and red foci on the lungs, and red discolouration of the mesenteric lymph nodes. The pathology report noted the cause of the deaths as gavage errors.

Clinical Observations

Clinical signs in the animals dosed at 450 mg/kg bw/day included rales (4M, 8F), laboured respiration (1M, 3F), hunched posture (2M, 3F), gasping (1F), and piloerection (1M, 1F) and lethargy (2M). All animals treated at high dose showed salivation during both main and recovery tests. Incidental findings were also observed such as a purple colouration of the toes or ear (noted in two control males and one male treated at 50 mg/kg bw/day), alopecia, scabs, swelling of the ears, a wound on the mouth, focal erythema of the ear, and brown staining of the fur. These observations were considered by the study authors signs of no toxicological significance as these findings were often noted in rats of this age and strain. One female animal dosed at 150 mg/kg bw/day was reported to have rales.

There were no treatment related changes in motor activity or functional observation parameters when compared to the controls.

There were no differences in food or water consumption, or changes in bodyweight that were related to treatment.

No ophthalmoscopic findings in treated animals were observed when compared to controls during the study period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Haematology

There were statistically significant increases (80%) in the level of neutrophils in male animals dosed at 150 and 450 mg/kg bw/day. This was not seen in the recovery group or in female animals. Mean corpuscular haemoglobin showed a statistically significant decreases of 3.1% and 2.8% in female animals dosed at 150 and 450 mg/kg bw/day respectively. This was not seen in male animals or in the recovery group. All other statistically significant changes in haematology parameters showed no dose response relationship or were only present in the recovery group.

Clinical chemistry and Urinalysis

Total protein values were statistically significantly higher (4.2%) in male animals treated at 450 mg/kg bw/day compared to controls. The increase in total protein was not observed in females or males in the recovery group. Female animals dosed at 50, 150 and 450 mg/kg bw/day showed decreased alanine aminotransferase and aspartate aminotransferase with increased phosphorus levels. Female animals dosed at 150 and 450 mg/kg bw/day had decreased glucose levels and increased potassium levels. None of the statistically significant changes seen at the highest doses in the female test groups were present in the female recovery group. All other statistically significant changes in clinical chemistry and urinalysis parameters showed no dose response relationship or were only present in the recovery group.

Effects in Organs

Except for the two dead animals, the incidence and severity of gross and microscopic lesions observed were similar in both treated animals and control animals.

The absolute liver weights of females at 150 and 450 mg/kg bw/day showed a statistically significant decrease. No statistically significant decrease in absolute or relative liver weights was observed in the recovery group females or in male animals. There were no histopathological changes. All other statistically significant changes in organ weights showed no dose response relationship or were only present in the recovery group.

Remarks – Results

No adverse treatment related changes were noted in animals dosed at 50 or 150 mg/kg bw/day.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 150 mg/kg bw/day.

TEST FACILITY Confidential (2003)

B.7. Repeat Dose Oral -Gavage Toxicity – in Rat

TEST SUBSTANCE Notified chemical

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents
EEC Methods for the determination of toxicity, Directive 84/449/EEC (OJ No. L251, 19.9.84), Part B, Method B7. Subacute toxicity (oral)

Species/Strain	Rat/Sprague Dawley (Crl:CD BR VAF Plus)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Distilled water
Remarks – Method	No significant protocol deviations Doses were selected based on a preliminary seven day study at doses of 250, 500 and 750 mg/kg bw/day.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	5M, 5F	0	0/10
Low Dose	5M, 5F	15	0/10
Mid Dose	5M, 5F	150	0/10
High Dose	5M, 5F	750	0/10

Mortality and Time to Death
All animals survived the scheduled treatment and were killed and examined macroscopically on Day 29.

Clinical Observations
Increased salivation was noted in all rats treated at 750 mg/kg bw/day of the test substance. Three female rats treated at 750 mg/kg bw/day had a thin looking appearance in week 3 of treatment. There were no clinical signs noted for all rats treated at 150 or 15 mg/kg bw/day.

There were no statistically significant changes in food consumption or body weight between treated and control rats. However, overall bodyweight gain for females treated at 750 mg/kg bw/day was statistically significantly lower (20%) than the control group. Bodyweight gains for all treated male rats were comparable to those of the control groups throughout the study period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Mean corpuscular volume showed a slight but statistically significant decrease in all three treated groups of male animals. There were no other statistically significant changes noted in haematological parameters measured.

Total protein was decreased in male and female animals at 150 and 750 mg/kg bw/day and also in male animals at 15 mg/kg bw/day. Globulin levels were also decreased in both male and female animals in the 150 and 750 mg/kg bw/day dose groups and also in females dosed at 15 mg/kg bw/day. The albumin/globulin ratio showed a statistically significant increase for females in all three treatment groups in comparison to the controls. Chloride and sodium levels showed a slight but statistically significant increase in male animals dosed at 150 and 750 mg/kg bw/day, and chloride in male animals dosed at 15 mg/kg bw/day.

Effects in Organs
Male rats treated at 750 mg/kg bw/day showed higher relative liver weights than control groups, however, this finding was not associated with histopathological or biochemical changes.

All treated male rats showed a statistically significantly lower adrenal weight than control groups. However, individual values for treated rats were within the expected range for rats of this age and strain and most of the individual values for control groups were high. Therefore, this finding was not treatment related. No other statistically significant differences in organ weight between treated and control animal groups were noted.

Macroscopic and microscopic effects in the organs noted in the treated animals were at a similar level and frequency to those seen in the control groups

Remarks – Results
Test substance-related adverse effects observed included lower food consumption and lower mean body weight gain for female rats treated at the high dose. However, the final bodyweights of the animals were comparable to control animals. In addition, the high liver weights in the high dose males may possibly be adaptive in nature and not considered to be of toxicological importance in the absence of histopathological or biochemical changes.

CONCLUSION
The No Observed Adverse Effect Level NOAEL was established at the highest dose of 750 mg/kg bw/day in this study, based on no toxicologically relevant adverse effects at this dose level.

TEST FACILITY	Confidential (1994)

B.8. Genotoxicity – Bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test EEC Directive 79/831/EEC, Annex V (Directive 84/449/EEC), Method B.14: *Salmonella typhimurium* – Reverse Mutation Assay Pre incubation procedure
Species/Strain	*Salmonella typhimurium*: TA1538, TA1535, TA1537, TA98, TA100

Metabolic Activation System	Liver preparation from Aroclor 1254-induced rats
Concentration Range in Main Test	a) With metabolic activation: 0-5,000 µg/plate b) Without metabolic activation: 0-5,000 µg/plate
Vehicle	DMSO
Remarks – Method	No significant protocol deviations. Positive controls used: *In the absence of S9-Mix:* *N*-ethyl-*N*'-nitro-*N*-nitrosoguanidine for strains TA 1535 and TA 100 9-aminoacridine for strain TA 1537 2-nitrofluorene for strains TA 1538 and TA 98 *In the presence of S9-Mix:* 2-aminoanthracene for all tested strains

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000	> 5,000	-	Negative
Test 2		> 5,000	-	Negative
Present				
Test 1	> 5,000	> 5,000	-	Negative
Test 2		> 5,000	-	Negative

Remarks – Results	There was no evidence of mutagenic activity that was seen at any concentration level of the test substance in either mutation test. The positive and vehicle controls gave satisfactory responses, confirming the validity and sensitivity of the test system.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Confidential (1992d)

B.9. Genotoxicity – *In Vitro* Mammalian Chromosome Aberration Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test EEC Methods for Determination of Toxicity, Directive 84/449/EEC (OJ No. L251, 19.9.84), Part B, Method B.10. In vitro Mammalian Cytogenetic Test
Species/Strain	Human
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	S9 fraction from Aroclor 1254-induced rat liver
Vehicle	Water
Remarks – Method	No significant protocol deviations. Positive controls used were: ethylmethanesulphonate in the absence of metabolic activation, and cyclophosphamide in the presence of metabolic activation.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 9.8, 19.5, 39.1, 78.1, 156.3*, 312.5, 625*, 1,250*, 2,500, 5,000	3 h	18 h
Test 2	0*, 8.2, 16.4, 32.8, 65.6, 131.3*, 262.5, 525*, 1,050*, 2,100, 4,200	3 h	32 h
Present			

Test 1	0*, 9.8, 19.5, 39.1, 78.1, 156.3, 312.5, 625*, 1,250, 2,500* and 5,000*	3 h	18 h
Test 2	0*, 9.8, 19.5, 39.1, 78.1, 156.3, 312.5*, 625, 1,250*, 2,500*, 5,000	3 h	32 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				
Test 1	-	≥ 2,500	≥ 1,250	Negative
Test 2	-	≥ 2,100	≥ 2,100	Negative
Present				
Test 1	-	> 5,000	> 5000	Negative
Test 2	-	> 5,000	> 5000	Negative

Remarks – Results

In the presence of metabolic activation and after 18 h harvest, cells dosed at 5,000 µg/mL showed a statistically significant increase (6%) in the mean percentage of chromosomal aberrations including gaps. This is within the historical control range (0 – 6.5%) and subsequently was not considered to be indicative of clastogenic activity.

In the absence of metabolic activation and after a 32 h harvest, cells dosed at 525 and 1,050 µg/mL showed a statistically significant increase in the mean percentage of chromosomal aberrations (4.0% (both including and excluding gaps) at 525 µg/mL or 2.5% (including gaps only) at 1,050 µg/mL). These values are within the historical control ranges of 0 – 5.25% and 0 – 6.5% for excluding and including gaps, respectively, and subsequently was not considered to be indicative of clastogenic activity.

The positive and vehicle controls gave satisfactory responses, confirming the validity of the test system.

CONCLUSION

The notified chemical was not clastogenic to cultured human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY

Confidential (1993d)

B.10. Genotoxicity – *In Vitro* Mammalian Cell Gene Mutation Test

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test
EC Directive 2000/32/EC B.17 Mutagenicity – *In vitro* Mammalian Cell Gene Mutation Test

Species/Strain: Mouse
Cell Type/Cell Line: Lymphoma/L5178Y
Metabolic Activation System: S9 fraction from Aroclor 1254-induced rat liver
Vehicle: DMSO (dimethyl sulfoxide)
Remarks – Method: No significant protocol deviations.
Positive controls used were: Ethylmethanesulphonate (EMS) in the absence of metabolic activation, and Dimethylnitrosamine (DMN) in the presence of metabolic activation.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				

Test 1	0*, 5, 10, 25*, 50*, 100*, 175*, 225*, 300*, 375*, 500*, 750, 1000	3h	3 days	9-11 days
Test 2	0, 10, 25, 100, 175, 225, 300*, 375*, 500*, 750*, 875*, 1,000*, 1,125*, 1,250*,	24h	2 days	9-11 days
Present				
Test 1	0*, 50*, 100*, 250*, 500*, 750*, 1,000*, 1,250*, 1,500*, 1,750, 2,000, 2,250	3h	3 days	9-11 days
Test 2	0*, 100*, 250*, 500*, 750*, 1,000*, 1,200*, 1,300*, 1,400*, 1,500, 1,600	3h	3 days	9-11 days
Test 3	0*, 1,000*, 1,200*, 1,400*, 1,500*, 1,550*, 1,600*, 1,651*, 1,700	3h	3 days	9-11 days

*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				
Test 1	≥ 994 (3h Treatment)	≥ 500	> 1,000	Negative
Test 2	≥ 994 (24h Treatment)	≥ 1,125	> 1,250	Negative
Present				
Test 1	≥ 3,313 (3h Treatment)	≥ 1,250	> 2,250	Negative
Test 2	-	> 1,400	> 1,600	Negative
Test 3		> 1,500	> 1,700	Negative

Remarks – Results

The maximum concentration level used was limited by the test substance induced cytotoxicity. Cytotoxicity was observed at all dose levels in the absence and presence of S9-mix in all experiments.

The test substance did not induce significant increases in the mutant frequency in the absence or in the presence of S9 metabolic activation in independent repeated experiments.

The positive and vehicle controls gave satisfactory responses, confirming the validity of the test system.

CONCLUSION

The notified chemical was not clastogenic to L5178Y mouse lymphoma cells treated *in vitro* under the conditions of the test.

TEST FACILITY

Confidential (2001)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

Three ready biodegradability studies were provided, one on the notified chemical and two on an analogue of the notified chemical. The two studies on the analogue of the notified chemical did not have sufficient information to determine the validity of the studies, and therefore the study on the notified chemical was considered the most reliable and relevant.

C.1.1. Ready Biodegradability (Study 1)

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	BOD
Remarks – Method	As per OECD test guidelines, no deviations were noted.

RESULTS

Test Substance		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
5	54	5	81
15	83	15	85
28	90	28	106

Remarks – Results	All validity criteria were met. The difference in extremes of replicate values was < 20%, no significant inhibition was observed in the toxicity control, the reference substance reached the pass level by day 5, oxygen depletion was less than 1.5 mg O_2/L in the control samples and the residual O_2 concentration was maintained at > 0.5 mg/L. The pass level of 60% was reached within the 10 day window, therefore the test substance was considered to be readily biodegradable.
CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	Confidential (1992e)

C.1.2. Ready Biodegradability (Study 2)

TEST SUBSTANCE	C_8 branched alkyl polyglycoside an analogue of the notified chemical
METHODS	OECD TG 301 B Ready Biodegradability: CO_2 Evolution test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	DOC
Remarks – Method	No reference test was conducted and the blank sample was not reported on.

RESULTS

Test Substance	
Day	*% Degradation*
6	31
10	49
20	62
28	78

Remarks – Results	The test substance did not meet the 10 day window for ready biodegradability. Control sample data and initial inorganic carbon were not reported. As the validity criteria were not reported on, the results of this study should be treated with caution.
CONCLUSION	The test substance is biodegradable.
TEST FACILITY	Madsen (1996)

C.1.3. Ready Biodegradability (Study 3)

TEST SUBSTANCE	C_8 branched alkyl polyglycoside an analogue of the notified chemical
METHODS	OECD TG 301 D Ready Biodegradability: Closed Bottle Test
Inoculum	Secondary effluent
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	COD
Remarks – Method	No reference test was conducted and the blank sample was not reported on.

RESULTS

Test Substance	
Day	*% Degradation*
28	22

Remarks – Results	The test substance did not meet the 14 d window for biodegradability. The control sample data was not reported and oxygen depletion was not determined. As the validity criteria were not reported on, the results of this study should be treated with caution.
CONCLUSION	The test substance is poorly biodegradable or resistant to microbial mineralisation.
TEST FACILITY	Madsen (1996)

C.2. Ecotoxicological Investigations

C.2.1. Acute Toxicity to Fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-static
Species	*Oncorhynchus mykiss*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	171 ± 12 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks – Method	As per OECD test guidelines, no deviations were noted.

RESULTS

Concentration (mg/L)		*Number of Fish*	*Mortality*				
Nominal	*Measured*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	0	10	0	0	0	0	0
32	31	10	0	0	0	0	0
56	54	10	0	0	0	0	0
100	94	10	0	0	0	0	0
180	170	10	0	0	1	2	2

320	310	10	0	0	0	1	3

LC50	> 310 mg/L at 96 hours
NOEC	54 mg/L at 96 hours
Remarks – Results	All validity criteria were met. Dissolved oxygen was maintained at > 60% air value and test substance concentrations were measured at > 80% of the nominal value throughout the test.

CONCLUSION	The test substance is not harmful to fish
TEST FACILITY	Confidential (1993e)

C.2.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Semi-static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	154 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks – Method	A limit test was conducted, as per OECD test guidelines, with no deviations were noted.

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Number Immobilised*	
Nominal	*Measured**		*24 h*	*48 h*
Control	0	20	0	0
100	100	40	0	0

*Geometric mean of fresh and expired media

EC50	> 100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks – Results	All validity criteria were met. The dissolved oxygen was maintained at > 3 mg/L, pH was maintained between 7.7 - 8.1 and temperature was maintained between 20 - 21°C

CONCLUSION	The test substance is not harmful to aquatic invertebrates
TEST FACILITY	Confidential (1993f)

C.2.3. Algal Growth Inhibition Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test EC Council Regulation No 440/2008 C.3 Algal Inhibition Test
Species	*Selenastrum capricornutum*
Exposure Period	72 hours
Concentration	Nominal: 100 mg/L Measured: 98 mg/L (geometric mean of fresh and expired media)
Auxiliary Solvent	None
Analytical Monitoring	HPLC
Remarks – Method	Only a limit test was conducted as per OECD test guidelines, with no deviations were noted.

RESULTS

Growth rate *ErC50 (mg/L at 72 h)*	*Yield* *EyC50 (mg/L at 72 h)*
> 98	> 98

Remarks – Results	The study meets the validity criterion. The cell concentration in the control groups increased by more than a factor of 16.
CONCLUSION	The test substance is not harmful to algal growth
TEST FACILITY	Confidential (1993g)

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