File No: STD/1307

December 2008

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Silan 449029 VP

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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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Wacker Chemie AG (ABN 11 607 113 062)
1/35 Dunlop Road
MULGRAVE VIC 3170

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Spectral data, Methods of detection and determination, Purity, Impurities, Import volume, Use details, Identity of manufacturer/recipients.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU submission (December 2007)

2. IDENTITY OF CHEMICAL

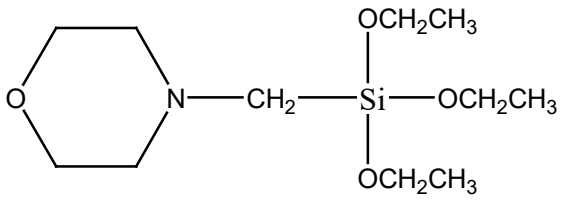
MARKETING NAME(S)
Silan 449029 VP
Silan Morph TEO
SLM 449029
EL 8000N TRAN S1 (containing < 2% notified chemical)
EL 9500 N versch. Farben (containing < 2% notified chemical)

CAS NUMBER
21743-27-1

CHEMICAL NAME
Morpholine, 4-[(triethoxysilyl)methyl]-

MOLECULAR FORMULA
$C_{11}H_{25}NO_4Si$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
263.4 Da

ANALYTICAL DATA
Reference NMR, IR, GC, and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 90%

ADDITIVES/ADJUVANTS None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Colourless to yellowish liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -100°C	Measured
Boiling Point	239.4°C at 101.3 kPa	Measured
Density	1001.5 kg/m^3 at 20°C	Measured
Vapour Pressure	≤ 4 x 10^{-3} kPa at 20°C	Measured
Water Solubility	Not determined	Reacts readily with water.
Hydrolysis as a Function of pH	Half-life < 1 minute at 25°C and pH 4, 7 and 9	Measured
Partition Coefficient (n-octanol/water)	Not determined	Reacts readily with water.
Adsorption/Desorption	Not determined	Reacts readily with water.
Dissociation Constant	Not determined	Reacts readily with water.
Particle Size	Not determined	Liquid at room temperature.
Flash Point	81°C at 97.4 kPa	Measured
Flammability	Not expected to be highly flammable	Estimated from measured flash point.
Autoignition Temperature	190°C	Measured
Explosive Properties	Not expected to be explosive	The structural formula contains no explosophores

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

The notified chemical has a low vapour pressure.

Reactivity
The notified chemical reacts exothermically with water (air humidity) and acids to release a flammable gas (ethanol) and form siloxane polymer.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported as a component of high viscosity silicone sealant mixtures at a concentration of < 2%.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.1-2	0.1-3	0.1-4	0.1-5	0.1-8

PORT OF ENTRY
Sydney

TRANSPORTATION AND PACKAGING
The notified chemical will be imported by sea in polyethylene or steel drums (220 L) within aluminium coated polyethylene liners, or polyethylene cartridges (280, 300 or 310 ml), and transported by road from the wharf to the warehouse, where they will be stored in a cool, dry and well-ventilated area.

USE
Additive for silicone sealant formulations.

OPERATION DESCRIPTION
No reformulation or repackaging of the notified chemical imported in cartridges will occur in Australia. The cartridges containing the notified chemical (< 2%) will be delivered to the end-user in the same form in which they are imported.

The drummed proportion of the product (< 2% notified chemical) will be refilled into cartridges using an automated process. The surface of the imported silicone sealant formulation in the polyethylene liner will be further covered with a polyethylene sheet. The refiller will open the lid of the drum and the liner bag, and will then remove the polyethylene cover sheet. A steel pressing plate with a hole equipped with a hose will be placed on top of this package, and the formulation will be mechanically pressed out through the hose into a cartridge filling line. The cartridge filling line will be fully automated.

At the end of the refilling process, cleaning of the refilling line may be required dependant on the colour and/or crosslinking system of the next batch to be refilled. To avoid laborious cleaning, refillers are expected to use dedicated filling lines for one product.

End-use
The sealant silicone formulations will be applied by both professional applicators and DIY users to joints using a spittle or a scraper.

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)*
Chemical plant	< 10	4 h	≤ 10
Construction	100	8 h	≤ 50

EXPOSURE DETAILS
Exposure to the notified chemical during the importation, transport and storage is not expected, except in the unlikely event of an accident where the packaging may be breached.

Dermal and ocular exposure may occur to the notified chemical (at < 2%) by chemical plant workers when opening the drums, when handling and applying the steel pressing plate, during maintenance and cleaning of cartridge filling machines, and by construction workers when applying the silicone sealants to joints.

Construction workers will likely make dermal contact with the silicone sealant after application. However, once dried and cured, the notified chemical will be reacted into the polymer matrix and will not be bioavailable.

Inhalation exposure is not expected due to the low vapour pressure of the notified chemical.

All workers likely to come into dermal contact with the notified chemical are expected to wear gloves as a minimum, which will further reduce the extent of exposure.

6.1.2. Public exposure

Given the public may or may not wear gloves, the exposure to the notified chemical (at < 2%) in silicone sealants is expected to be identical, or of a slightly greater extent, than that experienced by construction workers using the same sealant.

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	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOAEL > 1000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test (Chinese hamster V79 cells)	genotoxic

Toxicokinetics, metabolism and distribution

The notified chemical has a relatively low molecular weight (263.4 Da) and rapidly hydrolyses to form ethanol and siloxane polymer (half-life < 1 minute at 25°C and pH 4, 7 and 9). Due to this reaction, the notified chemical is expected to undergo hydrolysis if in contact with mucous membranes lining the respiratory system, eyes and to a lesser extent the skin. The effects seen in the toxicological studies are therefore likely to be due to the breakdown products and adducts at the site of contact.

Acute toxicity

The notified chemical has been shown to be of low acute oral and dermal toxicity.

No toxicological data was received to establish the potential of the notified chemical for inducing acute inhalation toxicity. Low molecular weight alkoxysilanes are a known concern for lung toxicity, due to inhalation of vapours or aerosols causing irreversible lung damage at low doses (US EPA, 1994). An analogous chemical 3-aminopropyltriethoxysilane (APTES, CAS No. 919-30-2), which has a similar acute oral and dermal toxicity profile to the notified chemical (OECD SIDS, 2004) and hydrolytic instability, has been shown to have a very low acute inhalation toxicity when tested on the hydrosylate, with a lethal concentration of > 7.35 mg/L/4 hours (SIDS, 2004). Based on the results on the analogous chemical, the notified chemical is expected to have low acute inhalation toxicity. However, the vapour pressure of the notified chemical is very low ($\leq 4 \times 10^{-3}$ kPa) and therefore inhalation of the vapour of the notified chemical is not expected to occur under normal environmental conditions unless aerosols are formed.

Irritation and Sensitisation

The notified chemical was found to be a slight eye irritant based on redness, swelling and discharge of the conjunctiva, which was particularly evident at the 1-hour observation period. These symptoms persisted for several days but had completely resolved in all animals tested by 7 days. However, the severity of this effect was insufficient to warrant classification of the notified chemical as a potential eye irritant according to the *Approved Criteria* (NOHSC, 2004).

No evidence of skin irritation or sensitisation using the LLNA test was observed with the notified chemical.

Repeated Dose Toxicity

In a 28-day repeat oral dose study, no treatment-related effects were observed in rats at the highest dose level tested (1000 mg/kg bw/day). Variations in body weight, food consumption and organ weights compared to the control group for some of the animals were not considered to be dose related.

Mutagenicity
The notified chemical was found to be negative in a bacterial reverse mutation study, but positive in an *in vitro* chromosome aberration study in the absence of metabolic activation. APTES has been tested in several bacterial reverse mutation/Ames assays, *in vitro* V79 hamster lung cell and Chinese hamster fibroblast chromosome aberration assays, two Chinese hamster ovary cell HGPRT gene mutation assays, and an *in vitro* mouse micronucleus assay. In all studies on APTES, no evidence of genotoxicity was observed.

Given the positive chromosome aberration test result, any potential of the notified chemical for mutagenicity cannot be definitively excluded.

Health hazard 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
Given the low potential of the notified chemical to induce systemic toxicity in animal studies following oral or dermal exposure (with acute or repeated dosing), the potential for systemic toxicity in exposed workers is not expected to be significant. The risk of systemic or lung toxicity resulting from inhalation exposure is not known, but data from an analogous chemical would suggest that this risk would be low for acute exposures. In addition, inhalation exposure is not expected given the low vapour pressure of the notified chemical and high viscosity of the sealant in which it is contained.

Acute dermal exposure is not expected to cause irritation or sensitisation. Ocular exposure is expected to cause slight irritation in exposed workers. Given workers will only be exposed to low concentrations of the notified chemical in a highly viscous product, the risk of eye irritation will be reduced. Any risk of mutagenicity of the notified chemical is uncertain based on the positive chromosome aberration test. However given the weight of evidence from the available animal test data, the risk of mutagenicity is expected to be low.

Given the notified chemical releases a flammable gas readily on contact with water, there is the potential of a fire risk, particularly in circumstances where the product is stored in an enclosed environment such as during transportation and storage. However, given the low concentration of the notified chemical (< 2%), the risk of fire is expected to be low.

Given the low hazard of the notified chemical and proposed use in low concentrations in a viscous formulation, the risk to the health and safety of workers is not considered to be unacceptable. However, additional information on the genotoxic potential of the chemical would further characterise the risk.

6.3.2. Public health
The exposure and hazard of the notified chemical to the members of the public during the use of silicone sealants containing the notified polymer are expected to be identical or similar to that experienced by construction workers. Therefore, the risk of the notified chemical to the health of the public is not considered to be unacceptable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical is imported into Australia as a minor ingredient in finished products (silicone sealant formulations).

RELEASE OF CHEMICAL FROM USE
No environmental release is expected from the use of products containing the notified chemical because of its instability. The notified chemical has moderate volatility, but is rapidly cured into the matrix of the silicone sealant. Curing starts upon diffusion of air humidity into the product and the notified chemical reacts with silicone polymer within the product to form a three-dimensional polymeric network. This reaction consumes 100% of the notified chemical and is irreversible. After curing of the silicone sealant the notified chemical is bound within a polymeric matrix and cannot be released into the environment. Surplus product that is left over during application of the sealant product also cures and these remains can be disposed of with standard waste streams.

RELEASE OF CHEMICAL FROM DISPOSAL
The notified chemical will not be released to the environment when products containing it are disposed of because of its instability.
Material which cannot be used or chemically reprocessed should be disposed of at an approved facility in accordance with any applicable governmental regulations. Containers should be completely emptied before recycling as specified in government regulations. Empty containers should be sent to an approved recycling facility.
Product residues (silicone sealants formulations containing less than 2% of the notified substance) should be left to cure and can then be disposed of with the usual solid waste streams, typically to landfill.

7.1.2 Environmental fate

Aquatic exposure to the notified chemical is not expected when it is used as proposed in sealant products. If the sealant products are washed to water, for example following spills or cleaning of residues from application equipment, the notified chemical will degrade rapidly because of its hydrolytic instability.
The notified chemical is considered not to be biodegradable based on its behaviour in a manometric respirometry test, but an inherent biodegradation potential was found. This biodegradation test method measures the oxygen uptake of microorganisms and would not detect the rapid hydrolysis of the notified chemical.
Bioaccumulation was not tested, but would not be expected to occur because of the rapid hydrolysis of the notified chemical.
For the details of the environmental fate studies please refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

It is not possible to determine a predicted environmental concentration as no aquatic exposure to the notified chemical is expected when it is used as proposed in sealant products. The notified chemical would not be expected to occur in water because of its hydrolytic instability.

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 > 95.7 mg/L	Not harmful
Daphnia Toxicity	EC50 > 144 mg/L	Not harmful
Algal Toxicity	EC50 = 25 mg/L	Harmful
Inhibition of Bacterial Respiration	IC50 > 1000 mg/L	Not harmful

Aquatic toxicity testing with the notified chemical is precluded by its hydrolytic instability. These tests were performed in order to demonstrate that the hydrolysis products of the notified chemical had no toxic effects on the test organisms (fish, daphnids and algae). The exposure concentrations were confirmed by analysis, but using nonspecific methods (measurement of organic carbon) that are unable to identify the test substance or its hydrolysis products. Results from the fish and algal tests are expressed as measured concentrations, and for the daphnid test as nominal concentrations. There was no analytical confirmation for the respiration inhibition test.

Harmful effects were only seen in algae, possibly reflecting surface interaction with fine particles rather than absorption of toxic hydrolysis products.

7.2.1 Predicted No-Effect Concentration

As data are available for three trophic levels, the PNEC can be estimated by application of an assessment factor of 100 to the median effect concentration for algal growth inhibition. Note that this PNEC applies to the hydrolysis products of the notified chemical, and not to the chemical itself.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (algae)	25	mg/L
Assessment Factor	100	
Mitigation Factor	1.00	
PNEC:	250	µg/L

7.3. Environmental risk assessment

It is neither necessary nor meaningful to estimate the PEC/PNEC ratio as the notified chemical is not expected to enter aquatic environments and would hydrolyse rapidly in water if it did.

On the basis of the hydrolytic instability of the notified chemical and available data on ecotoxicity of the hydrolysis products and the reported use pattern, the notified chemical is not considered to pose a risk to the environment.

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 inapplicable as the notified chemical is hydrolytically unstable.

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 public health.

Environmental risk assessment

On the basis of the hydrolytic instability of the notified chemical and available data on ecotoxicity of the hydrolysis products 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

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the notified chemical itself, however, these should be selected on the basis of all ingredients in the formulation.

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *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.

Disposal

- The notified chemical should be disposed of by landfill.

Emergency procedures

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

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
  - further information on the genotoxic potential of the chemical becomes available,
  - the concentration of the notified chemical is > 10% in the imported silicone sealant formulations.

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from an additive for silicone sealant formulations, or is likely to change significantly;
  - the amount of chemical being introduced has increased from 8 tonnes per annum, or is likely to increase, significantly;
  - if 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.

Material Safety Data Sheet
The MSDS of the products containing the notified chemical provided by the notifier were 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/Freezing Point < -100°C

Method EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Differential scanning calorimetry
Test Facility Wacker Chemie AG (2007)

Boiling Point 239.4°C at 101.3 kPa

Method EC Directive 92/69/EEC A.2 Boiling Temperature.
Differential scanning calorimetry
Test Facility Wacker Chemie AG (2007)

Density 1001.52 kg/m^3 at 20°C

Method EC Directive 92/69/EEC A.3 Relative Density.
Test Facility Wacker Chemie AG (2007)

Vapour Pressure 4 x 10^{-3} kPa at 20°C (standard batch)

Method EC Directive 92/69/EEC A.4 Vapour Pressure.
Dynamic method
Test Facility Wacker Chemie AG (2007)

Vapour Pressure < 1 x 10^{-3} kPa at 20°C (cleaned batch)

Method EC Directive 92/69/EEC A.4 Vapour Pressure.
Dynamic method
Test Facility Wacker Chemie AG (2007)

Vapour Pressure 1.9 x 10^{-4} kPa at 20°C (cleaned batch)

Method EC Directive 92/69/EEC A.4 Vapour Pressure.
Effusion method by loss of weight
Test Facility Wacker Chemie AG (2007)

Hydrolysis as a Function of pH

Method EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH.

pH	*T (°C)*	$t_{½}$
4	25	< 1 minute
7	25	< 1 minute
9	25	< 1 minute

Remarks This was a preliminary test only. The reaction was conducted in deuterated water and monitored by ^{1}H NMR, with the first spectrum being taken within 90 seconds of mixing. Hydrolysis was already complete by this time, as indicated by the presence of ethanol signals and the absence of ethoxysilane signals.
Test Facility Wacker Chemie AG (2008)

Flash Point 81°C at 97.4 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Test Facility Wacker Chemie AG (2007)

Autoignition Temperature 190ºC

Method	EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Test Facility	Wacker Chemie AG (2007)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE Notified chemical

METHOD OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain Rat/WIST (Full-Barrier)
Vehicle Cottonseed oil
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 F	2000	0
2	3 F	2000	0

LD50 > 2000 mg/kg bw
Signs of Toxicity No treatment related clinical effects observed.
Effects in Organs No treatment related effects observed.
Remarks - Results No deaths occurred during the 14-day study.

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

TEST FACILITY BSL (2005a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE Notified chemical

METHOD OECD TG 402 Acute Dermal Toxicity – Limit Test.
Species/Strain Rat/WIST (Full-Barrier)
Vehicle None
Type of dressing Occlusive
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 M	2000	0
2	5 F	2000	0

LD50 > 2000 mg/kg bw
Signs of Toxicity - Local No treatment related effects observed.
Signs of Toxicity - Systemic No treatment related effects observed.
Effects in Organs No treatment related effects observed.
Remarks - Results No deaths occurred.

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

TEST FACILITY BSL (2007a)

B.3. Irritation – skin

TEST SUBSTANCE Notified chemical

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 (Females)
Vehicle None
Observation Period 3 days
Type of Dressing Semi-occlusive.
Remarks - Method The notified chemical was not removed by washing after the 4-hour exposure period.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0	0	0	0	0	0
Oedema	0	0	0	0	0	0

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

Remarks - Results No treatment related effects observed.

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

TEST FACILITY BSL (2005b)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 (Female)
Observation Period 7 days
Remarks - Method As signs of irritation were observed in two of the three animals at the 72-hour observation period, the observation time was extended for these animals until all the symptoms had disappeared i.e. 7 days. Fluoroscein examination was carried out at 72 hours and at the end of the observation period.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value after 72 hours*
	1	2	3			
Conjunctiva: redness	1.0	1.3	0.7	2.0	6 days	1.0
Conjunctiva: chemosis	1.0	1.0	0.3	2.0	6 days	1.0
Conjunctiva: discharge	0.3	1.3	0	2.0	5 days	1.0
Corneal opacity	0	0	0	0	N/A	0
Iridial inflammation	0	0	0	0	N/A	0

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

Remarks - Results No clinical effects were observed. No signs of corneal or iridial irritation was observed in any of the animals treated. All animals showed some degree of redness, swelling and discharge of the conjunctiva, which was particularly evident at the 1-hour observation period. These symptoms had completely resolved at the 72-hour observation period for one animal

and at the 7-day observation period for the other two.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY BSL (2005c)

B.5. Repeat dose toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.

Species/Strain	Rats/Wistar
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: 0 days
Vehicle	Corn oil
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M, 5F	0	0
low dose	5M, 5F	20	0
mid dose	5M, 5F	150	0
high dose	5M, 5F	1000	0

Mortality and Time to Death

No mortalities occurred at any dose level.

Clinical Observations

No clinical signs of toxicity were observed in test or control animals throughout the study period.

There were no treatment-related changes in sensory reactivity and in the behavioural and functional parameters measured.

The animals of the female dose group, in particular the high dose group, showed higher weight gain compared to the corresponding control group. Individually diminished weight gains were observed in all male groups. Food consumption was slightly lower for the female dosage groups compared to the control group.

The findings regarding weight gain and food consumption were not considered to be an adverse effect, as both parameters were within the expected dose range for the dosage groups.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No toxicologically significant changes were detected in blood chemistry analysis or haematological investigations.

Effects in Organs

No macroscopic or histopathological organ changes were observed related to administration of the notified chemical. However, slight increases in organ weights were found for the absolute liver weights in the female high dose group, for the absolute spleen weights in the female low dose group, for the absolute heart weights of the female high dose group and for the absolute brain weights in the male low dose and high dose groups. Significantly decreased relative brain weights were found in female high dose group. The findings on organ weights were considered to be of no toxicological relevance.

Remarks – Results

No adverse effects attributable to the notified chemical were observed even at the highest dose level (1000 mg/kg bw/day).

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as > 1000 mg/kg bw/day in this study, as no adverse effects were observed at the highest dose level used in this study.

TEST FACILITY BSL (2007b)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD
- Species/Strain: *S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102.
- Metabolic Activation System: S9 liver microsomal fraction of Phenobarbital and β-naphthoquinone
- Concentration Range in Main Test: a) With metabolic activation: 31.6-5000 µg/plate; b) Without metabolic activation: 31.6-5000 µg/plate
- Vehicle: DMSO
- Remarks - Method: No significant protocol deviations. A preliminary toxicity assay, using eight doses (3.16-5000 µg/plate) tested against the cultures TA98 and TA100, was used to determine the dose-range for the main test.

  Both the plate incorporation (Test 1) and pre-incubation methods (Test 2) were used in the study.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5000	> 5000	> 5000	Negative
Test 2	> 5000	> 5000	> 5000	Negative
Present				
Test 1	> 5000	> 5000	> 5000	Negative
Test 2	> 5000	≥ 2500	> 5000	Negative

Remarks - Results: No toxic effects of the notified chemical were noted in any of the five tester strains used up to the highest dose group evaluated (with and without metabolic activation) in Test 1 (plate incorporation method). In Test 2 (pre-incubation method), toxic effects of the notified chemical were observed in tester strain TA 1535 at a dose of 2500 µg/plate and higher (with metabolic activation) and in tester strains TA 1537 and TA 102 at a dose of 5000 µg/plate (with metabolic activation).

No biologically relevant increases in revertant colony numbers of any of the five tester strains were observed following treatment with the notified chemical at any concentration level, with and without metabolic activation, in the plate incorporation and pre-incubation methods.

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

TEST FACILITY BSL (2005d)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain Chinese hamster
Cell Type/Cell Line V79 (ATCC, CCL-93)
Metabolic Activation System S9 liver microsomal fraction of Phenobarbital and β-naphthoquinone
Vehicle Cell culture medium (MEM)
Remarks - Method No significant protocol deviations

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	125, 250, 500, 1000*, 2500*, 5000*	4 hr	20 hr
Test 2	125, 250, 500, 1000*, 2500*, 5000*		
Present			
Test 1	125, 250, 500, 1000*, 2500*, 5000*	4 hr	20 hr
Test 2	125, 250, 500, 1000*, 2500*, 5000*		

*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	> 5000			
Test 1		> 5000	> 5000	≥ 2500
Test 2		> 5000	> 5000	≥ 2500
Present	> 5000			
Test 1		> 5000	> 5000	Negative
Test 2		> 5000	> 5000	Negative

Remarks - Results

The notified chemical is not cytotoxic at the highest dose level used for the study.

In the main experiment without metabolic activation, the aberration rates of the higher dose groups (2500 and 5000 μg/mL) were above the range of the historical control data of the negative control (up to 4.5%). Aberration rates of 7.0% and 7.5% respectively were found.

All aberration rates with metabolic activation were within the range of the historical control data of the negative control.

No biologically relevant increase in the frequencies of polyploid cells was observed.

CONCLUSION The notified chemical was genotoxic without metabolic activation to V79 Chinese Hamster cells treated in vitro under the conditions of the test.

TEST FACILITY BSL (2007d)

B.8. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified chemical
METHOD	OECD 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain	Mouse/ CBA/Ca01aHsd (female)
Vehicle	Acetone/Olive oil (3:1 v/v)
Remarks - Method	A positive control was not conducted

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	755.0	1.0
10	682.8	0.9
50	706.9	0.9
100	1151.4	1.5

Remarks - Results	All animals showed expected weight development. At the daily clinical observation the animals did not show any visible clinical symptoms. As the stimulation index was below 3.0 for each concentration tested, the notified chemical did not induce sensitisation under the study conditions.
CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	BSL (2005e)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical (25 mg/L)
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge from domestic STP at Darmstadt, Germany
Exposure Period	28 days
Auxiliary Solvent	None. The test substance was dispersed by stirring.
Analytical Monitoring	None
Remarks - Method	The test substance hydrolyses spontaneously in water to form siloxanes.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	12	2	45
12	38	12	87
28	60	28	95

Remarks - Results	The viability of the test medium was confirmed using the reference substance sodium benzoate. A toxicity control containing test and reference substances found no inhibitory effects on the microbial inoculum. Nitrification of the test substance was considered but not experimentally confirmed. The oxygen demand for the test substance did not reach 60% within the 10-day window but after 28 days of incubation when no nitrification is considered.
CONCLUSION	The hydrolysis products of the notified chemical cannot be considered to be readily biodegradable.
TEST FACILITY	IBACON (2007a)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static.
Species	Rainbow trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	TOC
Remarks – Method	Fish were exposed to hydrolysis products, as the test substance hydrolyses spontaneously in water to form siloxanes, and was introduced into the test medium 24 hours before the fish. The analytic method is non-specific. A limit test only was conducted, at a nominal 110 mg/L (mean measured concentration 95.7 mg/L). Seven fish were tested in exposure and control vessels.
RESULTS	No mortalities occurred. One fish in the test vessel showed symptoms of intoxication (apathy) after 96 hours.

LC50	> 95.7mg/L at 96 hours.
LOEC	95.7 mg/L at 96 hours.
Remarks – Results	The measured concentration declined from 111 mg/L to 81.4 mg/L during the test.
CONCLUSION	The hydrolysis products of the notified chemical are not harmful to fish.
TEST FACILITY	IBACON (2005)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test - static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	DOC
Remarks - Method	Daphnids were exposed to hydrolysis products, as the test substance hydrolyses spontaneously in water to form siloxanes, and was introduced into the test medium 24 hours before the daphnids. The analytic method is nonspecific. Nominal test concentrations were 69, 83, 100, 120 and 144 mg/L (mean measured concentration 93% of nominal). Twenty daphnids were tested in exposure and control vessels.
RESULTS	A single daphnid was immobilised after 48 hours at the highest test concentration.
LC50	> 144 mg/L at 48 hours
NOEC	120 mg/L at 48 hours
Remarks - Results	The measured concentration declined from 97% to 90% of nominal during the test. Slight precipitation was observed at the three highest test concentrations after preparation of the test media, but not after 24 and 48 hours of testing.
CONCLUSION	The hydrolysis products of the notified chemical are not harmful to daphnids.
TEST FACILITY	IBACON (2007b).

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Freshwater Alga and Cyanobacteria, Growth Inhibition Test.
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 0.32, 1.0, 3.2, 10 and 32 mg/L
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	TOC
Remarks - Method	Algae were exposed to hydrolysis products, as the test substance hydrolyses spontaneously in water to form siloxanes, and was introduced into the test medium 24 hours before the algae. The analytic method is nonspecific. The measured concentrations in samples without algae declined from 82% to 75% of nominal over a 72-hour period. The mean recovery from aged algal cultures, after filtration, was 59%, consistent

	with preliminary investigations which found that up to 20% of the hydrolysis products of the test item were removed by filtration. Test media at the highest concentration remained turbid through 72 hours.
RESULTS	The 72-hour EC50s were 25 mg/L based on growth rate and 7.0 mg/L based on biomass production. The NOEC was 0.8 mg/L for either parameter.
Remarks - Results	Control cultures showed a 138-fold increase in cell density through 72 hours, satisfying the validity criterion. Siloxanes would not be expected to show chemical toxicity to algae. It is possible that the effects reflect surface interactions between the algal cells and colloidal material formed by hydrolysis of the notified chemical.
CONCLUSION	The hydrolysis products of the notified chemical are harmful to algae.
TEST FACILITY	IBACON (2007c)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sludge from domestic STP at Darmstadt, Germany
Exposure Period	3 hours
Concentration Range	Nominal: 10, 32, 100, 320 and 1000 mg/L. There was no analysis.
Remarks – Method	Microbes were exposed to hydrolysis products, as the test substance hydrolyses spontaneously in water to form siloxanes, and was introduced into the test medium 24 hours before the sludge.
RESULTS	Less than 20% inhibition was observed at the highest test concentration.
IC50	> 1000 mg/L
NOEC	1000 mg/L
Remarks – Results	The EC50 for the reference substance (3,5-dichlorophenol) met the test validity criteria.
CONCLUSION	The hydrolysis products of the notified chemical are not inhibitory to activated sludge microorganisms.
TEST FACILITY	IBACON (2007d)

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