File No.: LTD/2093

January 2020

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Loctite HB S109 Purbond

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 the Environment and Energy.

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
LTD/2093	Henkel Australia Pty Limited	Chemical in Loctite HB S109 Purbond	ND	< 1 tonne per annum	Component of industrial adhesives

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the limited toxicity data provided, the notified chemical cannot be classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

The environmental hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard Classification	*Hazard Statement*
Acute Aquatic Toxicity (Category 3)	H402 – Harmful to aquatic life

Human Health Risk Assessment
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 reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- 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 in the product:
  - Avoid contact with skin and eyes

- 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 in the product:
  - Coveralls
  - Gloves
  - Goggles

  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.

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 importation volume exceeds one tonne per annum notified chemical;
  - the notified chemical is imported other than as a component of an industrial adhesive at ≤ 5% concentration;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of industrial adhesives, 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 product containing the notified chemical provided by the notifier was 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)
Henkel Australia Pty Limited (ABN: 82 001 302 996)
135-141 Canterbury Road
KILSYTH VIC 3137

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, additives/adjuvants, use details, import volume and identity of manufacturer

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for melting point, adsorption/desorption, flammability and oxidising properties

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
REACH

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Loctite HB S109 Purbond (containing the notified chemical at 1-5% concentration)

MOLECULAR WEIGHT
< 500 g/mol

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

3. COMPOSITION

DEGREE OF PURITY
> 99% (UVCB/Multi-constituent substance)

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: colourless homogeneous liquid

Property	*Value*	*Data Source/Justification*
Melting Point	< -20 °C	Estimated by notifier
Boiling Point	305 °C at 101.3 kPa	Measured
Density	921.9 kg/m^3 at 20 °C	Measured
Viscosity	Kinematic viscosity: 4.43 mm^2/s at 20 °C, 2.84 mm^2/s at 40 °C Dynamic viscosity: 4.08 mPa.s at 20 °C, 2.57 mPa.s at 40 °C	Measured
Vapour Pressure	3.7×10^{-5} kPa at 20 °C 6.5×10^{-5} kPa at 25 °C 8.3×10^{-4} kPa at 50 °C 0.19 kPa at 125 °C	Measured
Water Solubility	23 g/L at 20 °C	Measured

Property	*Value*	*Data Source/Justification*
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities but hydrolysis is not expected in the environmental pH range of 4-9
Partition Coefficient (n-octanol/water)	log Pow = 2.21 at 23 °C	Measured. The chemical is surface active, which may affect the accuracy of the result
Surface Tension	44.9 mN/m at 20 °C	Measured. Surface active
Adsorption/Desorption	Not determined	Expected to be mobile in soil based on high water solubility
Dissociation Constant	Not determined	Does not contain dissociable functionalities
Flash Point	123 °C at 101.3 kPa	Measured
Lower flammability limit	0.45% by volume	SDS
Autoignition Temperature	295 °C	Measured
Explosive Properties	Not explosive	Measured
Oxidising Properties	Predicted negative	Contains no functional groups that would imply oxidising properties.

DISCUSSION OF PROPERTIES
Studies were carried out on the notified chemical, which contains several constituents. 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.

The notified chemical has a flash point of 123 ºC which is greater than 93 °C. Based on *Australian Standard AS1940* definitions for combustible liquid, the notified chemical may be considered as a Class C2 combustible liquid if the chemical has a flash point below the boiling point.

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 industrial adhesives at ≤ 5% concentration.

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

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

PORT OF ENTRY
Sydney

IDENTITY OF RECIPIENTS
Henkel Australia Pty Limited

TRANSPORTATION AND PACKAGING
The finished adhesives containing the notified chemical at ≤ 5% concentration will be imported into Australia by sea in 200 kg drums or 1,000 L Flexi bag with a polypropylene outer and foil inner, and will be transported within Australia by road.

USE
The notified chemical will be used as a component of moisture cured polyurethane adhesives at ≤ 5% concentration in the production of engineered wood products for structural and non-structural end use applications.

OPERATION DESCRIPTION
At the timber processing site, the imported adhesives containing the notified chemical at ≤ 5% concentration will be decanted into a holding tank and pumped through metered equipment to an application system which generally consists of a multiple nozzle application head. The adhesive is under a degree of pressure to achieve an even layer of adhesive on the wood products. Some applications of adhesive are automated, with operators some distance from the adhesives while other application involved manual handing of the wood planks by the operators. Open time (time during which the adhesive remains active without curing after being applied to the substrate) cure is 5 minutes with full cure in 24 hours.

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)*
Warehouse (2-5 workers)	< 1	10-20
Transport (2-5 workers)	< 1	4-12
Application (6-10 workers)	2-4	150-220

EXPOSURE DETAILS
Transport and storage
Transport and storage workers, and retail workers may come into contact with the notified chemical at ≤ 5% concentration only in the unlikely event of an accidental breach of the imported packaging.

End use
At end use sites, dermal and perhaps accidental ocular exposure to the notified chemical at ≤ 5% concentration may occur during application of adhesives containing the notified chemical. Inhalation exposure is not expected as the notified chemical has a low vapour pressure, and it is not expected that aerosols will be generated during this process. The product containing the notified chemical contains other ingredients which are hazardous, and potential for exposure to the notified chemical would be minimised through controls related to these chemicals. The product SDS specifies the use of ventilation controls and personal protective equipment (PPE), including coveralls, gloves, and goggles, and respiratory protection if inhalation exposure may occur.

Once the product containing the notified chemical has cured, the notified chemical will be reacted and incorporated into the adhesive matrix in the wood products, and is not expected to be available for exposure.

6.1.2. Public Exposure
Products containing the notified chemical at ≤ 5% concentration are for industrial use only, and will not be available to the public. The public may come into contact with the glued wooden articles containing the notified chemical. However, once the adhesives are cured, the notified chemical will be reacted into the adhesive matrix in the wood products, and is not expected to be available for exposure.

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 > 2,000 mg/kg bw; low toxicity
Skin irritation – rabbit	slightly irritating
Eye irritation – rabbit	slightly irritating
Skin sensitisation – mouse local lymph node assay	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic
Dose range-finding test – combined repeated dose toxicity study with reproduction/developmental toxicity screening test – rat	NOAEL not established

Endpoint	*Result and Assessment Conclusion*
Dose range-finding test – prenatal developmental study - rat	NOAEL not established
Combined repeated dose toxicity study with reproduction/developmental toxicity screening test – rats	NOAEL = 750 mg/kg bw/day*

*Established by the study authors for systemic toxicity and reproductive/developmental effects.

Toxicokinetics
Based on the molecular weight of the notified chemical (< 500 g/mol) and its log Pow (2.21), there is potential for the chemical to cross biological membranes (ECHA, 2017). The chemical class of which the notified chemical is a member (short chain ethylene glycol ethers) are absorbed by all routes of exposure (US EPA, 2010).

Acute Toxicity
The notified chemical was found to have low acute oral toxicity in rats.

Irritation
The notified chemical was slightly irritating to the skin and eyes in studies of rabbits.

Sensitisation
In a mouse local lymph node assay, the notified chemical did not show evidence of skin sensitisation when tested up to 100% concentration.

Mutagenicity/Genotoxicity
The notified chemical was non-mutagenic in a bacterial reverse mutation assay.

Repeated Dose Toxicity
A No Observed Adverse Effect Level (NOAEL) of 750 mg/kg bw/day (the highest dose tested) was established by the study authors in a combined repeated dose toxicity study with a reproduction/developmental toxicity screening test in rats (OECD TG 422). Changes in haematological parameters in high dose males, and mild effects seen in liver, kidney and spleen may be indicative of effects that can be caused by the chemical class of glycol ethers, of which the notified chemical is a member.

Toxicity for Reproduction
In a combined repeated dose toxicity study with reproduction/developmental screening (OECD TG 422), the study authors established a NOAEL of 750 mg/kg bw/day. Increases in pre-implantation loss in all treatment groups from 100 mg/kg bw/day and post-implantation loss at 750 mg/kg bw/day were seen, as well as an increase in the M/F sex ratio, but all of these were not statistically significant. A non-statistically significant reduction in litter weight at this dose level was attributed to lower numbers of pups from 3/11 litters. In the earlier dose range-finding study using a very small number of animals, litter weight, male litter weight and M/F sex ratio were reduced at 750 mg/kg bw/day, compared to historical controls. Effects seen in a dose range finding study for prenatal development toxicity included a substantial increase in post implantation loss in all treatment groups from 250 mg/kg bw/day and slightly reduced number of males and male litter weight at 500 and 750 mg/kg bw/day.

Overall, based on the test results and known characteristics of some glycol ethers, potential effects observed cannot be ruled out as unrelated to treatment.

Health Hazard Classification
Based on the limited toxicity data provided, the notified chemical cannot be classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation
The notified chemical is slightly irritating to skin and eyes. There is uncertainty on the toxicity for systemic effects and reproduction/developmental effects for the notified chemical.

6.3.1. Occupational Health and Safety
The expected use of personal protective equipment (PPE) including coveralls, gloves, and goggles should minimise the risk from the notified chemical for workers applying the adhesive products containing the notified chemical at

≤ 5% concentration. Once cured, the notified chemical will be reacted into the adhesive matrix and worker exposure is not expected.

Therefore, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

6.3.2. Public Health

The adhesive products containing the notified chemicals at ≤ 5% concentration are intended for industrial use only and will not be available to the public. The public may come into contact with the cured adhesives containing the notified chemical after application. However, once the adhesives are cured, the notified chemical will be reacted into the adhesive matrix in the wood products and is not expected to be available for exposure.

Therefore, when used in the proposed manner, 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 will be imported as a component of finished adhesives. No reformulation or repackaging of the notified chemical will occur in Australia. Spills or accidental release of the products containing the notified chemical during import, storage, and transport are expected to be collected on suitable absorbents and disposed of by approved waste management facilities, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The notified chemical is used as a component of moisture cured polyurethane adhesives in the production of engineered wood products for structural and non-structural end use applications. The adhesives will be cured after being applied on the wood products and will not be available for release to the environment. Wastes and residues in empty packaging are expected to be disposed of by approved waste management facilities, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM DISPOSAL

The notified chemical is expected to share the fate of the wood products in which it has been incorporated, and be disposed of to landfill at the end of their useful lives.

7.1.2. Environmental Fate

A biodegradability study conducted on the notified chemical indicates that it is not readily biodegradable but shows inherent biodegradability (52-100% degraded over 28 days in OECD 301B test; 10-day-window was not passed). The notified chemical is a multi-constituent substance and the difference in biodegradability of various constituents may contribute to the large variation in the test results. For details of the biodegradability study, refer to Appendix C.

The majority of the notified chemical will be present as cured solids and share the fate of the wood products in which it has been incorporated, and be disposed of to landfill at the end of their useful lives. As it is cured in a solid matrix, the notified chemical will be neither bioavailable nor mobile. A minor amount of the notified chemical may also be disposed of to landfill as collected spills and empty container residues. The minor amount of the notified chemical in landfill is expected to be mobile and inherently biodegradable. The notified chemical is not expected to bioaccumulate based on its low log Pow. The notified chemical is expected to eventually degrade via biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated as release of the notified chemical to the aquatic environment will be limited, based on its reported use pattern.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 210 mg/L (measured)	Not harmful to fish
Daphnia Toxicity	48 h EC50 = 65.4 mg/L (nominal)	Harmful to aquatic invertebrates
Algal Toxicity	72 h EC50 = 74.6 mg/L (nominal) 72 h NOEC = 10.2 mg/L (nominal)	Harmful to algae
Inhibition of Bacterial Respiration*	3 h IC50 = 3,500 mg/L (nominal)	Not inhibitory to bacteria at sewage treatment plants

*English language abstract only

Based on the above ecotoxicological endpoints for the notified chemical, it is expected to be harmful to aquatic invertebrates and algae. Therefore, the notified chemical is formally classified as "Acute Category 3: Harmful to aquatic life" under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009). Although the notified chemical is not strictly considered readily biodegradable (see Appendix C), it is a complex multicomponent substance. Therefore, the 10-day window criterion may be waived and the pass level applied at 28 days. Therefore the notified chemical can be considered to be rapidly degradable for the purposes of GHS. Also, since the log Kow of the notified chemical is less than 4, no classification is applied for long-term hazard.

7.2.1. Predicted No-Effect Concentration (PNEC)

The predicted no-effects concentration (PNEC) has been calculated based on the most sensitive endpoint for Daphnia as shown in the table below. An assessment factor of 100 was used given the acute endpoint for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
48 h EC50 for Daphnia	65.4	mg/L
Assessment Factor	100	
Mitigation Factor	1	
PNEC	0.65	mg/L

7.3. Environmental Risk Assessment

The Risk Quotient (PEC/PNEC) for the aquatic compartment has not been calculated as release of the notified chemical to the aquatic environment will be limited based on its reported use pattern. Therefore, on the basis of the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

8. OVERSEAS ACTIONS

Two of the components of the notified chemical are the subject of regulatory action in the USA, being subject to a Significant New Use Rule (SNUR) if introduced or processed for particular uses. The rationale for this rule "Ethylene Glyol Ethers; Significant New Use Rule" is that there is potential for the chemicals to cause reproductive and/or developmental toxicity, genotoxicity and toxicity to blood and blood forming organs (US EPA, 2014).

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Boiling Point 305 ± 8 °C at 101.3 kPa

Method OECD TG 103 Boiling Point
Remarks Differential scanning calorimetry was used.
Test Facility Clariant (2012a)

Density 921.9 ± 0.1 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids
Remarks The vibrating U-tube method was used.
Test Facility Clariant (2012b)

Viscosity Kinematic viscosity: 4.43 ± 0.03 mm^2/s at 20 °C
2.84 ± 0.02 mm^2/s at 40 °C
Dynamic viscosity: 4.08 mPa.s at 20 °C
2.57 mPa.s at 40 °C

Method OECD TG 114 Viscosity of Liquids
Remarks A capillary viscometer (Ubbelohde) was used.
Test Facility Clariant (2012c)

Vapour Pressure 3.7×10^{-5} kPa at 20 °C
6.5×10^{-5} kPa at 25 °C
8.3×10^{-4} kPa at 50 °C
0.19 kPa at 125 °C

Method OECD TG 104 Vapour Pressure
Remarks Dynamic method was used.
Test Facility Siemens AG (2011a)

Water Solubility 23 g/L at 20 °C

Method OECD TG 105 Water Solubility
Remarks Flask Method; the notified chemical was determined by gas chromatography.
Test Facility Clariant (2011a)

Partition Coefficient (n-octanol/water) log Pow = 2.21 at 23 °C

Method OECD TG 107 Partition Coefficient (n-octanol/water): Shake Flask Method
Remarks The notified chemical is surface active, which is not in the applicability domain of the OECD TG 107 method; the analysis of the notified chemical was determined by gas chromatography.
Test Facility Clariant (2011b)

Surface Tension 44.9 mN/m at 20 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions
Remarks Concentration: 1g/L; the notified chemical is surface active.
Test Facility Clariant (2012d)

Flash Point 123 ± 2 °C at 101.3 kPa

Method EC Council Regulation No 440/2008 A.9 Flash Point
Remarks The Pensky-Martens method (DIN EN ISO 2719) was used.
Test Facility Clariant (2012e)

Autoignition Temperature 295 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Remarks	DIN 51794 was used.
Test Facility	Siemens AG (2011b)

Explosive Properties The test substance has no explosive properties.

Method	EC Council Regulation No 440/2008 A.14 Explosive Properties. Using OECD TG 113 Screening Test for Thermal Stability and Stability in Air as a screening method, the thermal stability was measured for explosive properties, involving the differential scanning calorimetry (DSC) method.
Remarks	*Thermal stability* Two DSC-measurements conducted were not successful. The first measurement showed an exothermal effect in the temperature range 345 - 405 ºC with an energy of 137 J/g. It was stopped at 410 ºC to avoid bursting of the glass crucible due to high pressure. The second measurement showed no exothermal effects in the temperature range 25 - 500 ºC. Due to the high pressure, a leakage of the stainless steel crucible at approximately 440 ºC occurred. *Explosive properties* No explosion was noted in the test of thermal sensitivity or mechanical sensitivity with respect to shock. A test of mechanical sensitivity with respect to friction was not required for a liquid chemical.
Test Facility	Siemens AG (2011c)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 401 Acute Oral Toxicity (before 2002) – Limit Test
Species/Strain	Rat/Wistar
Vehicle	Sesame oil
Remarks – Method	Only IUCLID 6 summary was provided in English.

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity	On the day of application the treated animals responded with a range of non-specific intoxication signs, including changes to respiration and to reflex responses. All these effects disappeared within 24 hours.
Effects in Organs	Not provided.
Remarks – Results	The treated animals showed normal body weight development in the observation period of 14 days.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	The original report (1993) was presented in German.

B.2. Skin Irritation – Rabbit

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation) EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation)
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 (sex not reported)
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive
Remarks – Method	Only IUCLID 6 summary was provided in English.

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	1.3	1.3	1.3	2	< 14 days	0
Oedema	0.3	0	0.3	1	< 14 days	0

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

Remarks – Results	The animals showed transient erythema and oedema that were fully reversible within 14 days of observation period.
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	The original report (1993) was presented in German.

B.3. Eye Irritation – Rabbit

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	2 M, 1 F
Observation Period	72 hours
Remarks – Method	Only IUCLID 6 summary was provided in English.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva – Redness	0	0.3	0.3	1	< 48 hours	0
Conjunctiva – Chemosis	0	0	0	1	< 24 hours	0
Conjunctiva – Discharge	0	0	0.3	2	< 48 hours	0
Corneal Opacity	0	0	0	0	-	0
Iridial Inflammation	0	0	0	0	-	0

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

Remarks – Results	The animals exhibited transient conjunctiva redness (maximum score of one) that were fully reversible within 72 hours of observation period.
CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	The original report (1993) was presented in German.

B.4. Skin Sensitisation – LLNA

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay (2010)
Species/Strain	Mouse/CBA/CaOlaHsd
Vehicle	Acetone/olive oil (4:1 v/v)
Preliminary study	Yes
Positive control	Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using p-phenylenediamine.
Remarks – Method	No protocol deviations

RESULTS

Concentration (% w/w)	*Number and Sex of Animals*	*Proliferative Response (DPM/lymph node)*	*Stimulation Index (test/control ratio)*
Test Substance			
0 (vehicle control)	5 F	650.3 ± 120.6	1.0
25*	5 F	1023.2 ± 190.9	1.6 ± 0.3
50*	5 F	1147.2 ± 126.9	1.8 ± 0.2
100	5 F	1672.2 ± 340.1	2.6 ± 0.5
Positive Control			
0	5 (sex unknown)	951.7 ± 356.5	1.0
1	5 (sex unknown)	8591.6 ± 608.7	9.0 ± 0.6

*An outlier result from one animal in this group with high results was not included in calculating DPM/lymph node.

Remarks – Results	All animals survived and showed no clinical signs during the study. All animals showed the expected body weight development.

CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Bioservice (2012a)

B.5. Genotoxicity – Bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test (1997) Plate incorporation procedure (test 1)/Pre incubation procedure (test 2)
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone induced rat liver
Concentration Range in Main Test	Test 1: with and without metabolic activation: 0, 31.6, 100, 316, 1,000, 2,500 and 5,000 µg/plate Test 2: with and without metabolic activation: 0, 31.6, 100, 316, 1,000, 2,500 and 5,000 µg/plate (for TA 98, TA 1537 and TA 102) and 0, 10, 31.6, 100, 316, 1,000, 2,500 and 5,000 µg/plate (TA 100 and TA1535)
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks – Method	*Escherichia coli* was not one of strains tested.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	≥ 2,500			
Test 1		≥ 1,000	> 5,000	negative
Test 2		≥ 1,000	> 5,000	negative
Present	≥ 5,000			
Test 1		≥ 5,000	> 5,000	negative
Test 2		≥ 2,500	> 5,000	negative

Remarks – Results	No precipitation of the test substance was observed in any tester strain used in tests 1 and 2, with and without metabolic activation. Cytotoxicity of the test substance was observed in all tester strains in tests 1 and 2 at high concentrations. No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, either with or without metabolic activation. The positive controls produced satisfactory responses, confirming the activity of the S9-mix and the sensitivity of the bacterial strains.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Bioservice (2011)

B.6. Dose Range Finding Study for Prenatal Developmental Toxicity – Rat

TEST SUBSTANCE	Notified chemical
METHOD	Dose range-finder for OECD TG 414 Prenatal Developmental Toxicity Study (2001)
Species/Strain	Rat/Wistar Crl:WI(Han)
Route of Administration	Oral – gavage
Exposure Information	Exposure days: from gestation day 5 to 19
Vehicle	Corn oil

Remarks – Method	Non-GLP. Fewer animals per group were used than is required in the OECD TG 414 Guideline. Statistical analysis was not carried out.

RESULTS

Group	*Number of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
1	8 F	0	0/8
2	8 F	250	0/8
3	8 F	500	0/8
4	11 F	750	0/11

Mortality and Time to Death

No unscheduled deaths occurred. All females were sacrificed on the gestation day 20. Males were sacrificed after completion of mating of all females.

Effects on Dams

Clinical signs were seen only in the 500 and 750 mg/kg bw/day group females, and included: reduced spontaneous activity (1/8), piloerection (2/8), prone position (1/8), ataxia (1/8) and moving the bedding (2/8) in the 500 mg/kg bw/day group; reduced spontaneous activity (3/11), piloerection (6/11), prone position (1/11), ataxia (1/11), moving the bedding (9/11) and salivation (3/11) in the 750 mg/kg bw/day group.

Substantial decrease in mean body weight change in the 500 and 750 mg/kg bw/day groups when compared to corresponding control over most of the treatment period was considered to be of toxicological relevance.

Slight decrease in mean food consumption in the 250 mg/kg bw/day groups noted during the entire gestation period and substantial decrease in the 500 and 750 mg/kg bw/day groups during most of the treatment period was considered to be of toxicological relevance.

No macroscopic findings in dams were observed in control or treatment groups.

Reproductive performance

Slight increase in number of early and total resorptions in all treatment groups, substantial decrease in mean M/F sex ratio in the 500 mg/kg bw/day group and substantial increase in mean post implantation loss in all treatment groups when compared to control were noted. The early and total resorption and post implantation loss were considered by the study authors as possibly related to the treatment.

There was slight decrease in mean number of males and male litter weight in the 500 and 750 mg/kg bw/day groups when compared to controls. The lower pregnancy rate in treatment groups (75%, 75 % and 72.7% respectively with increasing dose) compared to controls (87.5%) was considered by the study authors to be incidental.

Effects on Pups

No gross external abnormalities were observed in the control and 250 mg/kg bw/day groups. Hooked tail, misshapen and elongated snout, micrognathia and malrotated forelimb (right) in one foetus in the 500 mg/kg bw/day group and hematoma (left forelimb and hindlimb, dorsal lumbar region and tail) in one foetus in the 750 mg/kg bw/day were considered isolated incidences.

A range of visceral abnormalities were seen in the different test groups, with only short innominate artery and enlarged spleen in the 750 mg/kg bw/day group considered by the study authors as toxicologically relevant. The other findings were considered incidental due to lack of dose response or due to their presence in an individual foetus of litter.

A range of abnormalities were shown in the cranio-facial examination, but were considered incidental by study authors due to lack of dose response or due to their presence in individual foetus of litter.

Skeletal examination showed a range of abnormalities in different groups. Incidences such as cervical rib, dumbbell shaped thoracic vertebral centres, enlarged anterior fontanella, full rib, incomplete ossification of sacral vertebral body, 4th metacarpal, 4th stemebrum and temporal in the 750 mg/kg bw/day group were

considered by the study authors as toxicologically relevant. Other observations were considered incidental due to lack of dose response or due to their presence in individual foetus of litter.

Remarks – Results

The study authors noted that effects in dams included decrease in food consumption in all dose groups and decrease in body weight gain at 500 mg/kg bw/day and above. In all dose groups there was a slight increase in early and total resorptions and a substantial increase in post-implantation loss. A slight decrease in the number of male pups and male litter weight was seen at 500 and 750 mg/kg bw/day. An increased incidence of some visceral and skeletal abnormalities was seen at 750 mg/kg bw/day.

CONCLUSION

Based on the results from this dose range finding study, 100, 250 and 750 mg/kg bw/day were proposed for the subsequent Dose Range Finding Study for Reproduction/Developmental Toxicity Screening Test and Combined Toxicity Screening.

TEST FACILITY Bioservice (2012b)

B.7. Dose Range Finding Study for Reproduction/Developmental Toxicity Screening Test and Combined Toxicity Screening – Rat

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 421 Reproduction/Developmental Toxicity Screening Test (1995)
Species/Strain	Rat/Wistar Crl:WI(Han)
Route of Administration	Oral – gavage
Exposure Information	Exposure days: daily during 14 days pre mating and 14 days mating period in both males and in females, during gestation period and up to postnatal day 3 in females. Males were dosed for a total of 29 days.
Vehicle	Corn oil
Remarks – Method	Results were compared with historical controls rather than with the concurrent control for some parameters, due to low fertility in that group. Statistical analysis was not performed.

RESULTS

Group	*Number of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
1	3 per sex	0	0/6
2	3 per sex	250	0/6
3	3 per sex	500	0/6
4	3 per sex	750	0/6

Mortality and Time to Death

There were no unscheduled deaths.

Effects on Dams

There were a range of clinical signs, most occurring in the 500 and 750 mg/kg bw/day groups and considered toxicologically relevant. These included salivation, nasal discharge and moving the bedding. Breathing difficulty in one 750 mg/kg bw/day male was attributed to the gavaging cannula.

Slight reductions in mean body weight gain were seen in both males and females over some of the time intervals. Reduced body weight was considered toxicologically relevant for 750 mg/kg bw/day females, compared to historical controls. A reduction in mean food consumption was also noted in males and females, and consistent decrease in food consumption of 750 mg/kg bw/day females was considered toxicologically relevant.

There was no significant difference in group mean litter weight and female litter weight on post natal day 0 and 4 in treatment groups compared with the historical controls. However, substantial decrease for total litter weight and male litter weight was noted on post natal day 0 and 4 in the 750 mg/kg bw/day group compared with the historical control, and considered to be caused by the test substance treatment.

No treatment related effect was noted on precoital interval, duration of gestation and fertility index in treatment groups compared with the historical control. All pregnancies resulted in normal births.

Compared with the historical control, slight decrease for number of corpora lutea, implantation sites and live pups born on post natal day 0 in the 750 mg/kg bw/day group was considered toxicologically relevant. However, compared with the historical control, substantial increase in percent pre implantation loss in the 250 mg/kg bw/day group and post implantation loss in the 250 and 750 mg/kg bw/day groups was considered incidental by the study authors due to lack of dose response pattern.

Compared with the historical control, no treatment related effect were noted for number of female pups, still births and runts on post natal day 0 and number of female pups on post natal day 4. However, slight decrease for total number of pups born and number of live pups (post natal day 0 and 4) in the 750 mg/kg bw/day group was shown. Substantial decrease in number of male pups and sex ratio on post natal day 0 and 4 in the 750 mg/kg bw/day group was observed. These findings were considered toxicologically relevant to the treatment by the study authors.

No treatment related effect on copulation index, fertility index, delivery index and viability index in treatment groups was noted compared with the historical control.

At necropsy, no findings were considered to be of toxicological relevance except for a few random observations in males, such as small epididymides in one animal in the control group, crystalline mass within the urinary bladder in one animal in the 250 mg/kg bw/day group and yellowish epididymides-right in one animal in the 750 mg/kg bw/day group. In females, there were no macroscopic findings observed in control and treatment groups.

No treatment related effect were noted for the absolute and relative (to terminal body weight) organ weights in all animals compared with the controls.

The mean and individual haematological values in all animals were within the historical control range and comparable with the control except for a few incidental findings in the males, such as slight decrease observed for mean haemoglobin value and substantial increase in white blood cell value in the 250 mg/kg bw/day group and slight decrease in mean platelet value in the 500 mg/kg bw/day group.

The mean values of all clinical biochemistry parameters in all animals were within the historical control range, except for the lower mean total protein value in the 250 mg/kg bw/day group females. However some individual values were outside these limits, for both males and females. An increase in mean alanine amino transferase compared to the concurrent control in high dose males and a decrease in mean creatinine in mid and high dose males were considered to be toxicologically relevant.

For urinalysis, all parameters were comparable to controls in all treated animals except for higher blood value in one isolated female in the 750 mg/kg bw/day group.

Effects on Foetus

Compared with the historical control, the test substance treatment did not affect the survival of the pups from post natal day 0 to 4.

In pups, no macroscopic findings were observed at necropsy.

Remarks – Results

There were clinical signs in females at 500 and 750 mg/kg bw/day, including consistent decrease in body weight and food consumption of females at 750 mg/kg bw/day.

There was substantial decrease for total litter weight and male litter weight at 750 mg/kg bw/day. There was slight to substantial decrease or number of corpora lutea, implantation sites, live pups born, live pups, number of male pups and sex ratio at 750 mg/kg bw/day.

CONCLUSION
Based on the results from this dose range finding study, 100, 250 and 750 mg/kg bw/day were used for the subsequent Combined Repeated Dose Toxicity with the Reproduction/Developmental Toxicity Screening Test.

TEST FACILITY Bioservice (2012c)

B.8. Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test – Rat

TEST SUBSTANCE Notified chemical

METHOD OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test

Species/Strain	Rat/Wistar Crl:WI
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 14 days pre mating and 14 days mating period in both male and female animals, during gestation period and up to post natal day 3 in females. Males were dosed for 28 days. Dose regimen:7 days per week Post-exposure observation period: 14 days
Vehicle	Corn oil
Remarks – Method	A detailed qualitative examination of the testes was carried out. Collection of urine samples of recovery males was inadvertently not carried out at necropsy, but was not considered to affect the validity of the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	12 per sex	0	0/24
Low Dose	12 per sex	100	0/24
Mid Dose	12 per sex	250	0/24
High Dose	12 per sex	750	0/24
Control Recovery	6 M	0	0/6
High Dose Recovery	6 M	750	0/6

Mortality and time to death
There were no unscheduled deaths.

Effects on parental animals
Clinical signs in the high dose groups such as salivation and piloerection were attributed to the unpleasant taste of the test substance. No treatment related effects were seen in functional and behavioural examinations.

Dose related reduced body weight gains (mostly not statistically significant) were seen in both sexes in treatment groups, but not in the male recovery group. Food consumption was slightly reduced in high dose males and females. No effect was seen in recovery males.

Statistically significant changes in haematological parameters were seen in high dose males but not females. These included decrease in red blood corpuscles, haemoglobin and haematocrit. An increase in mean corpuscular volume was dose related but statistically significant only at the mid dose. Eosinophils were reduced in treatment groups, with statistical significance in the low and mid doses. In high dose recovery males, basophils and neutrophils were increased and lymphocytes reduced, all with statistical significance. Dose related increase of activated partial prothrombin time was seen in treatment males, statistically significant at the high dose. A non-statistically significant increase in this parameter was seen in high dose females and the recovery high dose males. Most values were within the historical controls.

In males there were several changes in clinical chemistry parameters, including an increase in alanine aminotransferase, statistically significant in the low and high dose groups, and elevated in the recovery group. Raised cholesterol, total protein and sodium were statistically significant in all treated groups. Non-statistically

significant change in females included a decrease in alkaline phosphatase in all treatment groups. Urine changes in males did not show a dose response pattern.

Macroscopic changes were observed at necropsy only in the low and mid doses, and included epididymides with a yellow spot, and one mid dose animal with small left testes and epididymis. The main changes in organ weights related to increased liver weights, which were statistically significant in males and females in the mid and high dose treatment groups, and in recovery males (relative weight only). Slight reductions in epididymides absolute weights (~5%) were seen in high dose treatment and recovery animals and relative weights in high dose treatment animals only. In high dose males, relative heart weight, relative prostate weight (including seminal vesicle and coagulating gland) were significantly reduced. In females, increased absolute kidney weight was statistically significant at the low and high doses and increased absolute adrenal weight at the low and mid doses. The weight changes for adrenal (males and females), heart (males), prostate (males) and kidney (females) was not considered to be toxicologically relevant to the test substance treatment as there were no microscopic changes and no dose response pattern.

Histopathological changes included a higher incidence of minimal glycogen storage in livers of all treatment groups without dose relationship, and a minimal centrilobular hepatocellular hypertrophy in one high dose male. Yellow spots on the epididymidis were seen in 2 males in the low dose group, one corresponding to spermatic granuloma, and 3 males in the mid dose group, without dose relationship, and were considered spontaneous.

In the kidney of female rats, minimal cortical tubular degeneration in 1 animal in the mid dose group and 3 rats in the high dose group was noted against a background change of minor or mild cortical tubular regeneration in a portion of treated and control animals. No renal change to correspond the higher kidney weight was observed in the treated groups. However, the observed effects may be possibly caused by the test substance treatment.

In the spleen of female animals in the high dose group, a minimal tendency towards higher grades of extramedullary hematopoiesis was noted. Minimal golden-brown pigment storage was noted only in 4/6 of high dose females. Without corresponding haematological changes, the study authors considered the effects were related to the test substance treatment, however, they were not likely to be adverse.

Reproductive effects

No statistically significant difference was noted on precoital interval, duration of gestation, successful mating results and fertility index compared with the controls. All pregnancies resulted in normal births. No statistically significant difference for corpora lutea, implantation sites, live pups on post natal day 0, percentage pre and post implantation loss were noted.

A substantial increase in percentage pre implantation loss in all treatment groups and post implementation loss in the high dose group was seen compared with the controls, without statistical significance and with high variations among the individual values, especially for 3 females in the high dose group. These changes were not considered to be caused by the test substance treatment by study authors.

No statistically significant differences for litter weight between the treatment and control groups were noted. Substantial decrease for total litter weight and female litter weight in the high dose group on post natal day 0 and 4 was caused by lower number of live pups in 3 females, in which increased pre and post implantation loss was observed. Lower numbers of female pups in other two females also contributed to lower female litter weight. Therefore these changes were not considered to be adverse.

Effects on Pups

Difference for total number of pups born, number of male and female pups, sex ratio, live pups, still birth and runt on post natal day 0 and total number of live pups and sex ratio on post natal day 4 was not statistically significant. Slight decrease in total live pups in the high dose group was likely to be caused by lower number of pups in three isolated females. This change was not considered to be related to the test substance treatment as it was limited to three female animals only. No treatment related effects were found through gross examination of dead pups.

Remarks – Results

The study authors considered that effects observed in the liver, kidney and spleen cannot be ruled out as substance-related. All the effects were considered by the study authors not to be adverse.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 750 mg/kg bw/day by the study authors for systemic effects and reproductive/developmental toxicity.

TEST FACILITY Bioservice (2013)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test
Inoculum	Activated sludge from a municipal STP
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Titration method
Remarks – Method	No major deviations from the test guidelines were reported. The test substance was added to the test vessels and ultra-sonicated for 10 minutes. A toxicity control was run.

RESULTS

Test Substance		*Sodium benzoate*	
Day	*% Degradation**	*Day*	*% Degradation*
7	2 - 9	7	49
14	9 - 59	14	61
21	36 - 93	21	63
28	52 - 100	28	67

*(8 replicates)

Remarks – Results	The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The test temperature was stated to vary from 19.5 to 23 °C but no further details were provided. The overall mean biodegradation after 28 days was 81%. However, the result of each of eight replicates varied greatly (52-100%) and three out of eight replicates did not meet the 10 day window criterion. The notified chemical is a multi-constituent substance and the difference in biodegradability of various constituents may contribute to the large variation in the test results.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Dr. U. Noack Laboratorien (2012)

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	*Danio rerio* (zebrafish)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	39 mg $CaCO_3$/L
Analytical Monitoring	Gas Chromatography Mass Spectrometry (GCMS)
Remarks – Method	The definitive test concentrations were selected based on a preliminary test result. No major deviations from the test guidelines were reported. The test substance was directly added to the test vessels. The test water was sampled at the start and at the end of the experiment for analysis of the test substance.

RESULTS

Concentration (mg/L)		*Number of Fish*	*Mortality (%)*			
Nominal	*Measured*		*24 h*	*48 h*	*72 h*	*96 h*
Control	Control	7	0	0	0	0
20.0	19.9	7	0	0	0	0
40.0	42.0	7	0	0	0	0
80.0	85.8	7	0	0	0	0
160	139	7	0	0	0	0
320	317	7	100	100	100	100

LC50 210 mg/L at 96 hours

Remarks – Results All validity criteria for the test were satisfied. During the test, DO was ≥ 97%. The measured concentrations of the test substance varied from 79 to 115% of the nominal concentrations. As this was outside the 80-120% range, the results were presented based on measured concentration. The LC50 was the geometric mean value of the concentrations with 0% and 100% mortality.

CONCLUSION The test substance is not harmful to fish.

TEST FACILITY Dr. U. Noack Laboratorien (2013a)

C.2.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Static

Species *Daphnia magna*

Exposure Period 48 hours

Auxiliary Solvent None

Water Hardness 253 mg $CaCO_3$/L

Analytical Monitoring GCMS

Remarks – Method The definitive test concentrations were selected based on a preliminary test result. No major deviations from the test guidelines were reported. A stock solution of 200 mg/L of the test substance was prepared and used as the highest test concentration. Lower test concentrations were achieved by further diluting the stock solution. The test water was sampled at the start and at the end of the experiment for analysis of the test substance. A reference test with potassium dichromate was run (approximately one month prior to the current study).

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Immobilised (%)*	
Nominal	*Initial measured*		*24 h*	*48 h*
Control	Control	20	0	0
12.5	12.9	20	0	0
25	26.2	20	0	0
50	45.5	20	0	30
100	103	20	40	80
200	188	20	65	100

EC50 65.4 mg/L (CI: 58.6-73.8 mg/L) at 48 hours

Remarks – Results All validity criteria for the test were satisfied. During the test, DO was ≥ 8.1 mg/L. The measured concentrations of the test substance were in the range of 91-119% of the nominal concentrations. Therefore, the results were presented based on nominal concentration. The EC50 was

	calculated by sigmoidal dose-response regression. The EC50 of *D.magna* exposed to potassium dichromate was within historical range.
CONCLUSION	The test substance is harmful to aquatic invertebrates.
TEST FACILITY	Dr. U. Noack Laboratorien (2013b)

C.2.3. Algal Growth Inhibition Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 10.2, 25.6, 64.0, 160, 400 mg/L Initial measured: 11.6, 26.6, 67.6, 163, 395 mg/L
Auxiliary Solvent	None
Water Hardness	0.24 mmol Ca+Mg/L
Analytical Monitoring	GCMS
Remarks – Method	The definitive test concentrations were selected based on a preliminary test result. No major deviations from the test guidelines were reported. A stock solution of 400 mg/L of the test substance was prepared and used as the highest test concentration. Lower test concentrations were achieved by further diluting the stock solution. The test water was sampled at the start and at the end of the experiment for analysis of the test substance. A reference test with potassium dichromate was run (less than 3 months prior to the current study.).

RESULTS

Biomass		*Growth*	
EC50 (mg/L at 72 h)	*NOEC (mg/L)*	*EC50 (mg/L at 72 h)*	*NOEC (mg/L)*
74.6 (70.9 – 78.8)	10.2	28.1 (25.9 – 30.3)	10.2

Remarks – Results	All validity criteria for the test were satisfied. The mean cell density in the control increased 185 times after 72 hours. The measured concentrations of the test substance were in the range of 95-114% of the nominal concentrations. Therefore, the results were presented based on nominal concentration. The EC50 was calculated by sigmoidal dose-response regression. The EC50 of alga exposed to potassium dichromate was within historical range.
CONCLUSION	The test substance is harmful to alga.
TEST FACILITY	Dr. U. Noack Laboratorien (2013c)

BIBLIOGRAPHY

Bioservice (2011) [Notified Chemical]: Reverse Mutation Assay with Bacteria (*Salmonella typhimurium*) (BSL Bioservice Study No. 113066, October 2011). Bioservice Scientific Laboratories GmbH, 85152 Planegg, Germany (Unpublished report submitted by the notifier).

Bioservice (2012a) [Notified Chemical]: Test for Sensitisation (BSL Bioservice Study No. 114924, January 2012). Bioservice Scientific Laboratories GmbH, 85152 Planegg, Germany (Unpublished report submitted by the notifier).

Bioservice (2012b) [Notified Chemical]: Dose Range Finding Study for Prenatal Developmental Toxicity in Rat (BSL Bioservice Study No. 113067, January 2012). Bioservice Scientific Laboratories GmbH, 85152 Planegg, Germany (Unpublished report submitted by the notifier).

Bioservice (2012c) [Notified Chemical]: Dose Range Finding Study for Reproduction/Developmental Toxicity Screening Test and Combined Toxicity Screening in Rat (BSL Bioservice Study No. 113068, January 2012). Bioservice Scientific Laboratories GmbH, 85152 Planegg, Germany (Unpublished report submitted by the notifier).

Bioservice (2013) [Notified Chemical]: Combined Repeated Dose Oral Toxicity Study with the Reproduction/Developmental Toxicity Screening Test in Wistar Rats (BSL Bioservice Study No. 114870, January 2012). Bioservice Scientific Laboratories GmbH, 85152 Planegg, Germany (Unpublished report submitted by the notifier).

Clariant (2011a) [Notified Chemical]: Water Solubility (Project No. 11-103202-1, August 2011). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Clariant (2011b) [Notified Chemical]: Partition Coefficient (n-octanol/water): Shake Flask Method (Project No. 11-103202-2, August 2011). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Clariant (2012a) [Notified Chemical]: Boiling Point and State of Substance (Project No. 11-103276, February 2012). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Clariant (2012b) [Notified Chemical]: Density (Project No. 11-103276, February 2012). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Clariant (2012c) [Notified Chemical]: Viscosity (Project No. 11-103276, February 2012). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Clariant (2012d) [Notified Chemical]: Surface Tension (Project No. 11-103276, February 2012). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Clariant (2012e) [Notified Chemical]: Flash Point (Project No. 11-103276, February 2012). Clariant Produkte (Deutschland) GmbH, Clariant Analytical Services Rhein-Main, 65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Dr. U. Noack Laboratorien (2012) [Notified Chemical]: Ready Biodegradability Modified Sturm Test (Study No. AST14923, July 2012). Dr. U. Noack Laboratorien, D-31157 Sarstedt, Germany (Unpublished report submitted by the notifier).

Dr. U. Noack Laboratorien (2013a) [Notified Chemical]: Fish (Zebrafish), Acute Toxicity Test, Static, 96 h (Study No. FAZ14923, April 2013). Dr. U. Noack Laboratorien, D-31157 Sarstedt, Germany (Unpublished report submitted by the notifier).

Dr. U. Noack Laboratorien (2013b) [Notified Chemical]: Acute Immobilisation Test to *Daphnia magna*, Static, 48 h (Study No. DAI14923, August 2013). Dr. U. Noack Laboratorien, D-31157 Sarstedt, Germany (Unpublished report submitted by the notifier).

Dr. U. Noack Laboratorien (2013c) [Notified Chemical]: Alga, Growth Inhibition Test with *Desmodesmus subspicatus*, Static, 72 h (Study No. SSO14923, August 2013). Dr. U. Noack Laboratorien, D-31157 Sarstedt, Germany (Unpublished report submitted by the notifier).

ECHA (2017) Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7c: Endpoint specific guidance, June 2017, version 3.0. European Chemicals Agency, https://echa.europa.eu/documents/10162/13632/information_requirements_r7c_en.pdf.

Siemens AG (2011a) [Notified Chemical]: Vapour Pressure (Project No. 20110218.01, August 2011). Siemens AG, Prozess-Sicherheit, D-65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Siemens AG (2011b) [Notified Chemical]: Auto-ignition Temperature (Liquids and Gases) (Project No. 20110218.03, August 2011). Siemens AG, Prozess-Sicherheit, D-65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

Siemens AG (2011c) [Notified Chemical]: Explosive Properties (Project No. 20110218.02, August 2011). Siemens AG, Prozess-Sicherheit, D-65926 Frankfurt am Main, Germany (Unpublished report submitted by the notifier).

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

US EPA (2010) TSCA New Chemical Program (NCP) Chemical Categories. Accessed at https://www.epa.gov/sites/production/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf November 2019.

US EPA (2014) Ethylene Glycol Ethers; Significant New Use Rule. Federal Register. Vol 79, No. 241 pp 74639-74647. Accessed at https://www.federalregister.gov/documents/2014/12/16/2014-29429/ethylene-glycol-ethers-significant-new-use-rule November 2019.