File No: STD/1549

June 2015

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1,2,3-Propanetricarboxylic acid, 2-hydroxy-, nickel(2+) salt (1:1)

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.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This 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

TABLE OF CONTENTS

SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1549	Grace Australia Pty Ltd	1,2,3-Propanetricarboxylic acid, 2-hydroxy-, nickel(2+) salt (1:1)	Yes	≤ 5 tonnes per annum	Component of a catalyst products used in the petroleum refining industry

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Acute Toxicity (Category 4)	H302 – Harmful if swallowed H332 – Harmful if inhaled
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction
Respiratory sensitisation (Category 1)	H334 – May cause allergy or asthma symptoms or breathing difficulties if inhaled
Specific target organ toxicity (repeated exposure) (Category 1)	H372 – Causes damage to organs through prolonged or repeated exposure by inhalation
Mutagenicity (Category 2)	H341 – Suspected of causing genetic defects
Carcinogenicity (Category 1A)	H350 – May cause cancer by inhalation
Toxic to Reproduction (Category 1B)	H360 – May damage fertility or the unborn child

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase(s):

- R20/22: Harmful by inhalation and if swallowed
- R42/43: May cause sensitisation by inhalation and skin contact
- R48/23: Danger of serious damage to health by prolonged exposure through inhalation
- R68: Possible risk of irreversible effects
- R49: May cause cancer by inhalation
- R61: May cause harm to the unborn child

The environmental hazard classification according to the *Globally Harmonised System for the 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 Toxicity (Category 2)	H401 - Toxic to aquatic life
Chronic Toxicity (Category 1)	H410 – Very toxic to aquatic life with long lasting effects

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

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

Environmental risk assessment
On the basis of the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Acute Toxicity (Category 4): H302/332 – Harmful if swallowed or inhaled
  - Skin Sensitisation (Category 1): H317 – May cause an allergic skin reaction
  - Respiratory Sensitisation (Category 1): H334 – May cause allergy or asthma symptoms or breathing difficulties if inhaled
  - Specific target organ toxicity (repeated exposure) (Category 1): H372 – Causes damage to organs through prolonged or repeated exposure by inhalation
  - Mutagenicity (Category 2): H341 – Suspected of causing genetic defects
  - Carcinogenicity (Category 1A): H350 – May cause cancer by inhalation
  - Toxic to Reproduction (Category 1B): H360 – May damage fertility or the unborn child

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

- Due to the ecotoxicity of the notified chemical, the notifier should consider their obligations under the Australian Dangerous Goods Code.

Health Surveillance

- As the notified chemical is considered to be a sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Enclosed, automated processes, where possible
  - Adequate ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid contact with skin
  - Avoid inhalation
  - Avoid leaks and spills during use

- 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:
  - coveralls
  - impervious gloves
  - respiratory protection

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

- A copy of the (M)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 for the 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.

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.

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical 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(2) of the Act; if
- the function or use of the chemical has changed from a component of catalyst products used in the petroleum refining industry, 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.

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Grace Australia Pty Ltd (ABN: 41 080 660 117)
40 Scanlon Drive
Epping VIC 3076

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: analytical data.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: hydrolysis as a function of pH, partition coefficient, dissociation constant, particle size, explosive and oxidising properties, acute inhalation toxicity, repeated dose toxicity, bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
Europe (2013)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, nickel(2+) salt (1:1)
Nickel(2+) hydrogen citrate
ICR/HOP/DX/GR or AT Grade catalyst products (≤ 10% notified chemical)

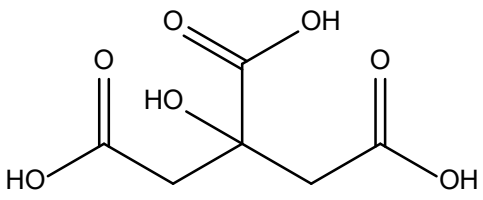
CAS NUMBER
18721-51-2

CHEMICAL NAME
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, nickel(2+) salt (1:1)

OTHER NAME(S)
Nickel(2+) hydrogen citrate
Nickel citrate
Nickel(II) citrate
Citric acid, nickel(2+) salt (1:1)
Nickel Hydrogencitrate
Nickel Hydrogencitrat

MOLECULAR FORMULA
$C_6H_8O_7.Ni$

STRUCTURAL FORMULA



. Ni(II)

MOLECULAR WEIGHT
250 Da

ANALYTICAL DATA
Reference C^{13}-NMR, IR, MS, and UV-VIS spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
99-100%

IDENTIFIED IMPURITIES/RESIDUAL MONOMERS

Chemical Name	1,2,3-Propanetricarboxylic acid, 2-hydroxy- (Citric acid)		
CAS No.	77-92-9	*Weight %*	0–1%

ADDITIVES/ADJUVANTS
None.

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Greenish powder.

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Decomposed from ~ 150 °C	Measured.
Density	1,845 kg/m^3 ± 0.5 °C	Measured.
Vapour Pressure	1.55 x 10^{-7} kPa at 25 °C 1.29 x 10^{-7} kPa at 20 °C	Measured.
Water Solubility	34.73 ± 1.07 g/L at 20 °C	Measured.
Hydrolysis as a Function of pH	Not determined	No significant hydrolysis is expected under environmental conditions (pH 4- 9).
Partition Coefficient (n-octanol/water)	Citric acid: log Pow = - 1.64 at 20 °C	Analogue (citric acid), KOWWIN v1.67, EPI Suite 4.11
Surface Tension	61.93 mN/m at 20 °C	Measured.
Adsorption/Desorption	log Koc < 1.5 at 25 °C	Measured.
Dissociation Constant	Citric acid: pKa = 2.79	Analogue (citric acid), IUPAC, Chemical; Data Series No. 23 (1979). At very acidic conditions (pH = 1-2), the tri-citrate is available as uncharged citric acid. At the physiological pH of about 7.4, nickel hydrogen citrate is predominately present in ionic forms. Under normal environmental conditions, nickel hydrogen citrate is predominantly present in highly mobile dissociated forms.
Particle Size	Inhalable fraction (< 100 μm): 0% Respirable fraction (< 10 μm): 0%	Measured (study report not provided). The notified chemical will be imported adsorbed onto a matrix (reported diameter 2-5 mm; reported length 2-15 mm).
Flammability	Not highly flammable	Measured.
Autoignition Temperature	1) 263 °C 2) Not a self-heating substance	1) Measured. 2) Measured. Sample maintained at an oven temperature of ~140 °C for 24 hours.
Explosive Properties	Not determined	Contains no functional groups that

Oxidising Properties	Not determined	imply explosive properties. Contains no functional groups that imply oxidative properties.

DISCUSSION OF PROPERTIES
For full 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. The notifier has indicated that the notified chemical may be corrosive to metals and should be classified as such.

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

Hazard classification	***Hazard statement***
Corrosive to metals (Category 1)	H290 – May be corrosive to metals

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. The notified chemical will be imported into Australia as part of catalyst products at ≤ 10% concentration.

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

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

PORT OF ENTRY
Brisbane (QLD)
Sydney (NSW)
Adelaide (SA)
Bunbury and Fremantle (WA)
Geelong and Melbourne (VIC)

IDENTITY OF MANUFACTURER/RECIPIENTS
Grace Australia Pty Ltd (various recipients throughout Australia)

TRANSPORTATION AND PACKAGING
The products containing the notified chemical (at ≤ 10%) will be transported from the port to customers by road in ~ 900 kg UN approved intermediate bulk containers (IBCs), carried in closed trailers.

USE
The notified chemical will be imported into Australia as a component (≤ 10%) of a solid hydrotreating/hydroprocessing catalyst for use in the petroleum refining industry.

OPERATION DESCRIPTION
The notified chemical will not be manufactured or reformulated in Australia. The catalyst products containing the notified chemical (at ≤ 10% concentration) will be transferred from the IBCs into a reactor by trained personnel using refilling equipment. The notified chemical is expected to be completely consumed during the activation of the catalyst products. The used catalyst will be removed and recycled to recover the metals contained in the catalyst.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and warehousing	Not specified	Not specified
Reactor worker (loading & refilling)	4	4
Bale packer	0.5	4
Cleaners/reactor maintenance	0.5	4

EXPOSURE DETAILS
It is anticipated that transport drivers and warehouse workers would only be exposed to the material in the event of an accident.

At the end-use sites dermal, ocular and inhalation exposure to the notified chemical at ≤ 10% concentration may occur during unloading of the IBCs containing the notified chemical, adding to reactors using refilling equipment, bale packing of used bags and cleaning/maintenance processes. The catalysts may be loaded into the reactor vessels over a period of hours-days. Exposure is expected to be limited by the use of exhaust ventilation, dust filters and appropriate personal protective equipment (PPE), which may vary depending on the tasks being carried out (e.g. PPE may include gloves, filter mask and full body suit). Workers are not expected to be exposed to the notified chemical during the normal hydroprocessing/hydrotreating processes.

6.1.2. Public Exposure

The catalyst products containing the notified chemical are intended for industrial use only, and will not be available to the public. It will be consumed during use and is not expected to be present in the fuels. Direct exposure of the public would therefore not be expected.

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 300 – 2,000 mg/kg bw; harmful
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	inadequate evidence of sensitisation
Mutagenicity – bacterial reverse mutation	mutagenic
Genotoxicity –in vitro chromosome aberration	genotoxic
Genotoxicity – in vivo erythrocyte micronucleus	genotoxic

The notified chemical is considered to have similar properties to other soluble nickel compounds (see for example, TERA, 1999; ATSDR, 2005; NICNAS, 2013). For systemic effects, provided that it can be assumed that the counter-anion does not contribute to the observed toxicity, it is assumed that it is the absorbed dose of nickel ion that will be related to the toxicity of the source nickel compounds (Henderson *et al.*, 2012a and 2012b). This is assumed to be the case for the notified chemical, noting that citric acid is considered to be of low toxicity (OECD SIDS, 2001). Therefore, in addition to studies conducted on the notified chemical, information on other soluble nickel compounds is briefly discussed below and is considered to support the health hazard classifications of the notified chemical.

Toxicokinetics.
No toxicokinetic data was provided for the notified chemical. Similarly to other soluble nickel compounds (ATSDR, 2005), it is possible that the notified chemical will be absorbed via inhalation, ingestion and to a limited extent following dermal exposure. The extent of absorption (oral and dermal routes) of the notified chemical is supported by studies conducted on the notified chemical (see below), in which mortalities were observed following oral exposure to the notified chemical, whereas dermal exposure resulted in the absence of clinical signs of toxicity.

Acute toxicity.
The notified chemical is harmful via the oral route (LD50 300 - 2,000 mg/kg bw in rats). All of the animals treated at 2,000 mg/kg bw died during the study (~24-72 hours post treatment). Various clinical signs were observed preceding death, including a decrease in spontaneous activity, associated with partial or complete ptosis, decrease in body weight, piloerection and bradypnea. A decrease in muscle tone and righting reflex and an increase in lacrymation were also noted. Macroscopical examination reportedly revealed several effects in these animals, including a thinning of the forestomach and the corpus of the stomach, accompanied with spotting and discolouration. The intestine also presented with red spots and viscous green content in certain animals. No mortalities, treatment-related clinical signs or macroscopic findings were observed in the animals treated at 300 mg/kg bw.

The notified chemical is of low acute dermal toxicity (LD50 > 2,000 mg/kg bw in rats). A decrease in body weight (day 2-day 0 following treatment with gains evident at subsequent observations) and local signs of toxicity were noted in all treated female animals. No effects were reported in male animals.

No data is available on the acute inhalation toxicity of the notified chemical. Information on soluble nickel compounds, e.g. nickel sulfate (CAS no. 7786-81-4), indicates the potential for acute inhalation toxicity effects to be associated with these compounds, and nickel sulfate is considered to be harmful by inhalation (ATSDR, 2005; HSIS, 2015). The notifier has indicated that, as a worst case scenario, the notified chemical is considered to be harmful if inhaled.

Irritation.
In a skin irritation study in male rabbits, no cutaneous reactions (erythema or oedema) were noted in animals at any observation interval (1, 24, 48 or 72 hours), following treatment with the notified chemical for 4 hours. However, it is noted that local signs of toxicity were noted in all female animals treated with the notified chemical in an acute dermal toxicity study in rats (see above).

In an eye irritation study in rabbits, moderate conjunctival redness and slight chemosis were noted in all test animals 1 hour after instillation. Both signs were fully reversible between days 2 and 7. Conjunctival discharge was seen in all animals at the 1 hour observation and remained in 1 animal at the 24 hour observation. Iridial congestion (lesion) was noted in 1 animal 1 hour after instillation, but had reversed by day 2.

Based on the results of these studies, classification of the notified chemical as a skin or eye irritant was not warranted.

Sensitisation.
The notified chemical was found to be a non-sensitiser in a Local Lymph Node Assay (LLNA) study in mice. Concentrations of 10, 25, and 50% of the notified chemical were tested, producing stimulation indices of 0.72, 0.99 and 0.60, respectively. However, nickel (Ni^{2+}) is reported to be the most common cause of allergic contact dermatitis and it is noted that false-negative findings can occur in the LLNA during the testing of certain metals, such as nickel (OECD, 2010; EPA, 2011; Kimber *et. al*, 2011), for example, as has been seen with nickel chloride (ECVAM, 2008).

Inhalation exposure to nickel can also lead to sensitisation (TERA, 1999). An exposure standard is associated with nickel, soluble compounds (as Ni), 0.1 mg/m^3 time weighted average, with a notice to indicate that the substances are known to act as sensitisers and that caution should be exercised in the industrial use of the substances (HSIS, 2015).

Some nickel compounds, such as nickel sulfate, are classified for their potential to cause sensitisation by inhalation and skin contact (HSIS, 2015), and the notifier has indicated that the notified chemical should be classified as such.

Repeated dose toxicity.
No data was provided on the repeated dose toxicity of the notified chemical.

Many studies have been conducted on soluble nickel compounds, with the chemicals thought to present a concern for serious damage to health by prolonged exposure via the inhalation route (TERA, 1999; EU RAR, 2008; ATSDR, 2005; NICNAS, 2013). Some nickel compounds, such as nickel sulfate, are classified for their

potential to cause repeated dose toxicity effects via the inhalation route (HSIS, 2015) and the notifier has indicated that the notified chemical should be classified as such.

Mutagenicity/Genotoxicity.
In a bacterial reverse mutation assay, a significant increase in revertant colony counts was noted with the tester strain TA98 in the presence of metabolic activation. The study authors reported a dose-dependent relationship, and the result was reproduced in the confirmatory assay. No cytotoxicity was detected.

The study authors also considered that positive results were obtained in an *in vitro* chromosome aberration assay. Statistically and toxicologically significant increases in the number of cells with structural aberrations were noted in both the presence (2 highest concentrations tested; concentration-effect relationship at these concentrations not evident) and absence (highest concentration) of metabolic activation. It is noted that the positive effects were only seen at cytotoxic concentrations. The study authors considered that the highest concentration tested should be evaluated for the induction of chromosomal damage, as the cytotoxic damage (mitotic indices ~20% of solvent control) was not so large as to inhibit structural evaluation. A confirmatory test was not conducted.

An *in vivo* micronucleus assay also showed positive results. An increase in the induction of micronuclei was seen in female animals of the highest dose groups after 44 and 68 hours treatment, compared to the negative control data and/or the historical data range. These increases were deemed biologically relevant by the study authors. However, it is noted that the increase 68 hours after treatment was not statistically significant.

Carcinogenicity.
No data was provided on the carcinogenicity potential of the notified chemical. It is considered that there is sufficient evidence in experimental animals for the carcinogenicity of nickel compounds and nickel metal and that nickel compounds are carcinogenic to humans (Group 1; IARC, 2012). The chemicals cause cancers of the lung and of the nasal cavity and paranasal sinuses (IARC, 2012).

Toxicity for reproduction.
No data was provided on the reproductive and developmental toxicity of the notified chemical.

It is reported that absorbed nickel can cross the placenta and accumulate in fetal tissues (TERA, 1999). Many reproductive and developmental toxicity studies have been conducted on nickel compounds, with the outcomes of the studies indicating conflicting results (TERA, 1999; ATSDR, 2005). Some nickel compounds, such as nickel sulfate, are classified for their potential to cause harm to the unborn child (HSIS) and the notifier has indicated that the notified chemical should be classified as such.

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

Hazard classification	***Hazard statement***
Acute Toxicity (Category 4)	H302 – Harmful if swallowed H332 – Harmful if inhaled
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Mutagenicity (Category 2)	H341 – Suspected of causing genetic defects
Carcinogenicity (Category 1A)	H350 – May cause cancer by inhalation
Toxic to Reproduction (Category 1B)	H360 – May damage fertility or the unborn child

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase(s):

- R20/22: Harmful by inhalation and if swallowed

- R42/43: May cause sensitisation by inhalation and skin contact
- R48/23: Danger of serious damage to health by prolonged exposure through inhalation
- R68: Possible risk of irreversible effects
- R49: May cause cancer by inhalation
- R61: May cause harm to the unborn child

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Exposure of workers to the notified chemical during end-use as a component of catalyst products used in the petroleum refining industry (at ≤ 10% concentration notified chemical) may occur via the dermal, ocular and inhalation routes.

Based on the available information, the notified chemical presents a concern for a number of acute and chronic health effects. Therefore, exposure to the notified chemical should be avoided.

Nickel compounds have an exposure standard associated with them (HSIS). The notifier has indicated that the notified chemical will be imported adsorbed onto a matrix, with 0% particles < 100 µm. Where possible, processes involving the notified chemical should be automated and occur in enclosed and/or ventilated environments. In addition, if the potential for exposure to the notified chemical exists, PPE, such as impervious gloves, coveralls and respiratory protection should be worn.

It is also noted that while the notified chemical may be corrosive to metals, appropriate storage of the notified chemical is expected. The notified chemical is expected to be consumed during use and is not expected to be present in fuels.

Overall, provided measures are in place to minimise exposure of workers to the notified chemical, including the use of automated processes (where possible), enclosed and/or ventilated environments and PPE, the risk to workers from use of the notified chemical is not considered to be unreasonable.

6.3.2. Public Health

The notified chemical is only intended for use in industrial settings. Therefore, when used in the proposed manner, the risk to public health from the notified chemical is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured or reformulated in Australia. Therefore, release of the notified chemical from these activities is not expected. Release of the notified chemical to the environment during import, storage, and transport is also unlikely. Release from residues in storage and shipping containers is expected to be minimal.

During end-use, the notified chemical is used in a closed system within an industrial setting. Vacuum equipment will be used to remove any loose particulates or dust during the catalyst loading process. The notified chemical is expected to be consumed during this process. Therefore, emission to air will be minimal.

The notified chemical is not expected to be released to municipal waste water treatment facilities or directly to surface waters. Emission to water or soil is unlikely because the notified chemical is a solid and it will be reformulated in a closed system, and it is expected to be consumed during refining processes.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be used as a component of a solid hydrotreating catalyst for use in the petroleum refining process. Discharge of the notified chemical is expected to be minimal since the notified chemical is contained in a solid catalyst (asymmetric quadrilobe extrudates reported to be 2-5 mm in diameter) that will be

delivered in closed containers. Hydrotreating catalysts will be loaded into a reactor vessel over a period of hours to days, depending on the quantity of material required to fill the vessel volume. Vacuum equipment will be used to remove any loose particulates or dust during the catalyst loading process. The notified chemical will be consumed during use, therefore is not present in any treated hydrocarbon product that may be available to the consumer. Used catalyst that is removed from the hydro treating units will not contain the notified chemical.

The catalyst is made of high-value materials, so any unusable catalyst will be reactivated, or sent for metals recovery. Catalyst reactivation is standard in the refining industry. The notified chemical is not expected to be released to municipal waste water treatment facilities or directly to surface waters.

RELEASE OF CHEMICAL FROM DISPOSAL

Any waste generated is anticipated to be as a result of an accidental release of products containing the notified chemical. In this case, any spillage would be collected and reused, collected and sent for metals recovery or collected for disposal by an approved waste management company. The amount of waste of the notified chemical is expected to be negligible. The notified chemical is not expected to be released to municipal waste water treatment facilities or directly to surface waters.

7.1.2. Environmental Fate

The notified chemical is not expected to be released to the environment because it will be used within a closed system. In the unlikely event that the notified chemical is released in the environment, it is assumed that under environmental conditions only minor amounts will be present in a bioavailable form due to its reported level of biodegradability of 29.5% biodegradation after 28 days. Therefore, while the notified chemical is not considered readily biodegradable, it is expected to be biodegradable in the environment. The notified chemical is not expected to be persistent due to its high water solubility, low adsorption coefficient (log Koc < 1.5) and biodegradability. The notified chemical is not expected to bioaccumulate due to a bioconcentration factor (BCF) of 1613. Therefore, the notified chemical is not expected to either bioaccumulate or be bioavailable and has very limited potential for exposure to the aquatic compartment.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) was not calculated since no significant release to the aquatic environment is expected based on the 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 these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	EC_{50} (96 h) > 100 mg/L	Not harmful to fish
Daphnia Toxicity	EC_{50} (48 h) = 25 mg/L	Harmful to aquatic invertebrates
Algal Toxicity	ErC_{50} (72 h) = 1.4 mg/L	Toxic to algae
	$NOEC_r$ = 0.07 mg/L	Very toxic to algae with long lasting effects
Inhibition of Bacterial Respiration	NOEC (3 h) = 10 mg/L	Not expected to inhibit bacterial respiration

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is acutely not harmful to fish, acutely harmful to aquatic invertebrates and acutely toxic to algae. The notified chemical is therefore formally classified 'Acute Category 2; Toxic to aquatic life'. As the notified chemical is not readily biodegradable and has chronic $NOEC_r$ = 0.07 mg/L, it is formally classified under the GHS as 'Chronic Category 1; Very toxic to aquatic invertebrates with long lasting effects'.

7.2.1. Predicted No-Effect Concentration

The PNEC has not been calculated as no significant aquatic exposure is expected based on the reported use pattern.

7.3. Environmental Risk Assessment

A Risk Quotient is unable to be quantified as a PEC and PNEC were not calculated. There is no significant aquatic release of the notified chemical anticipated based on its reported use pattern. The notified chemical is consumed during use. The notified chemical is not expected to persist in the environment due to its biodegradability. The notified chemical is not expected to be bioaccumulative due to its limited bioavailability. Therefore, based on the assessed use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point Decomposed from ~150 °C.

Method	OECD TG 102 Melting Point/Melting Range.
Remarks	Capillary method (aluminium block). 3 experimental determinations were conducted. The test item showed signs of decomposition (evidenced by colour change), beginning at ~150 °C.
Test Facility	LAUS GmbH (2009a)

Density 1,845 ± 0.5 kg/m^3

Method	OECD TG 109 Density of Liquids and Solids.
Remarks	Determined using the pycnometer method. 2 experimental determinations were conducted at reported temperatures of 22.4°C and 21.8°C, respectively.
Test Facility	LAUS GmbH (2009b)

Vapour Pressure 1.55 x 10^{-7} kPa at 25 °C
1.29 x 10^{-7} kPa at 20 °C

Method	OECD TG 104 Vapour Pressure.
Remarks	Determined using the effusion (Knudsen cell; weight loss) method. 9 determinations were conducted at different temperatures. Experiments 1 to 4 (nominal temperatures 30-75 °C) showed no significant weight loss and were not used in the evaluation. The final 5 experiments (nominal temperatures 90-150 °C) were to calculate the vapour pressure. The study authors note that it is possible that loss of water and decomposition processes took place at elevated temperatures, leading to a weight loss, which may misleadingly appear as "vapour pressure".
Test Facility	LAUS GmbH (2009c)

Water Solubility 34.73 ± 1.07 g/L at 20 °C

Method	OECD TG 105 Water Solubility.
Remarks	Flask Method. The individual results from each sample did not differ by more than 15%.
Test Facility	LAUS GmbH (2009d)

Surface Tension 61.93 mN/m at 20 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions.
Remarks	Determined using a tensiometer (plate of roughened Pt/Ir). The test item was considered to be 'not surface active'.
Test Facility	LAUS GmbH (2009e)

Adsorption/Desorption log K_{oc} < 1.5 at 25 °C

Method	OECD TG 121 Estimation of the Adsorption Coefficient on Soil and on Sewage Sludge using HPLC.
Remarks	The study was performed using a HPLC with a cyanopropyl chemical bound resin on a silica base column. Six reference items with different retention times were used to produce a calibration curve, since retention time on cyanopropyl columns and Koc are correlated. The reference items were chosen based on the retention time of the test item on the column.
Test Facility	LAUS GmbH (2009f)

Flammability Not highly flammable

Method	EC Council Regulation No 440/2008 A.10 Flammability (Solids).
Remarks	The combustion with flame of the test item did not propagate.

Test Facility LAUS GmbH (2009g)

Autoignition Temperature (1) 263 °C

Method EC Council Regulation No 440/2008 A.16 Relative Self-Ignition Temperature for Solids.
Remarks A drastic increase in the temperature of the sample, in comparison to the laboratory oven, was detected, with ignition observed at an oven temperature of 263 °C (oven heated at 0.5 K/min).
Test Facility LAUS GmbH (2009h)

Autoignition Temperature (2) Not a self heating substance

Method UN-Method N.4: 'Test method for self-heating substances', 4.rev. (2003).
Remarks No signs of ignition were observed and no increase in the temperature of the sample in comparison to the oven was detected (sample maintained at an oven temperature of ~140 °C for 24 hours; temperature of the test substance after 24 hours was ~117 °C).
Test Facility LAUS GmbH (2009i)

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/Sprague Dawley
Vehicle	Distilled water
Remarks - Method	No significant protocol deviations. GLP Certificate.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	6F	2,000	6/6
2	6F	300	0/6

LD50	300 – 2,000 mg/kg bw All of the animals treated at 2,000 mg/kg bw died during the study period, at approximately 24 hours (1/6), 48 hours (2/6) and 72 hours (3/6) post administration. There were no mortalities in the lower dose group
Signs of Toxicity	In the animals treated at 2,000 mg/kg bw, various clinical signs were observed preceding death. These included a decrease in spontaneous activity (6/6), associated with partial or complete ptosis (3/6), piloerection (6/6) and bradypnea (4/6). A decrease in muscle tone (1/6) and righting reflex (1/6) and an increase in lacrymation (1/6), were also noted. On day-2 post-administration, a decrease in body weight was noted for the remaining 3 animals (day 2 – day 0). In the animals treated at 300 mg/kg bw, no clinical signs were attributed to the test item and no body weight losses were noted during the study period.
Effects in Organs	In the animals treated at 2,000 mg/kg bw, macroscopical examination reportedly revealed several effects. A thinning of the forestomach (5/6) associated with a red (5/6) or green (1/6) colouration with spots red (2/6) or white (3/6) in colour was noted. Also thinning of the corpus (5/6) of the stomach, associated with red (4/6) or green (2/6) colouration with spots red (4/6) or black (1/6) in colour. The intestine presented with red spots (2/6) and viscous green content (1/6). In the animals treated at 300 mg/kg bw, no treatment-related macroscopic findings were observed at necropsy.
CONCLUSION	The notified chemical is harmful via the oral route.
TEST FACILITY	Phycher Bio Developpement (2009a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 402 Acute Dermal Toxicity.
Species/Strain	Rat/Sprague Dawley
Vehicle	Distilled water
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations. GLP Certificate.

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	Cutaneous reactions were noted during the study in female animals only and consisted of moderate erythema with red spots on the treated area on days 1-4 (5/5). Between day 2 and day 4, these signs were associated with dryness and on day 5, red spots and scabbing were noted. All dermal symptoms had resolved by day 6 and for the remainder of the observation period.
Signs of Toxicity - Systemic	There were no systemic clinical findings observed during the study.
Effects in Organs	There were no macroscopic findings observed at necropsy.
Remarks - Results	There were no mortalities noted during the study. On day-2 post-administration, a decrease in body weight was noted for all female animals (day 2 – day 0), with weight gains evident at the subsequent observations (day 7 and day 14, post-administration).

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

TEST FACILITY Phycher Bio Developpement (2009b)

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	3M
Vehicle	Moistened with distilled water.
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations. GLP Certificate. The first animal was initially exposed to the test substance for 3 minutes, then 1 hour and then for 4 hours. The 2 additional animals were subsequently treated for 4 hours.

RESULTS

Remarks - Results	No cutaneous reactions (erythema or oedema) were noted at any observation interval (1, 24, 48 or 72 hours post-patch removal).

CONCLUSION The notified chemical was non-irritating to the skin, under the conditions of the test.

TEST FACILITY Phycher Bio Developpement (2012a)

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	3F
Observation Period	7 days
Remarks - Method	No significant protocol deviations.

GLP Certificate.

The eyes of all animals were rinsed with physiological saline 1 hour after instillation.

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	1.67	1.33	0.67	3	< 7 days	0
Conjunctiva: chemosis	1.33	0.33	0.33	2	< 7 days	0
Conjunctiva: discharge	1	0	0	3	< 48 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0.33	0	0	1	< 48 hours	0

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

Remarks - Results: Moderate conjunctival redness and slight chemosis was noted in all test animals 1 hour after instillation. Both signs were fully reversible between days 2 and 7. Conjunctival discharge with moistening of the eyelids and around the eye was seen in all animals at the 1 hour observation and remained in 1 animal at the 24 hour observation. Iridial congestion (lesion) was noted in 1 animal 1 hour after instillation, but had reversed by day 2.

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

TEST FACILITY: Phycher Bio Developpement (2012b)

B.5. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 429 Skin Sensitisation: Local Lymph Node Assay

Species/Strain: Mouse/CBA/CaOlaHsd (4F per dose group)

Vehicle: Ethanol:water (3:7 v/v)

Remarks - Method: No significant protocol deviations.
GLP Certificate.

Based on the results of a solubility study, it was determined that the highest technically feasible concentration was a 50% suspension in ethanol:water (3:7).

A pre-screen test was conducted to determine the highest non-irritant test concentration (1 animal/dose; tested at 50% and 25% concentration). The increase in ear weight/thickness and ear irritation seen did not exceed the threshold values, and no signs of systemic toxicity were observed in any of the test animals.

No concurrent positive control test was run, however, it had been previously conducted in the test laboratory with α-Hexylcinnamaldehyde in acetone:olive oil (4:1 v/v) using the same strain of test mice.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	354.1	1.00
10	255.3	0.72

25	350.1	0.99
50	211.6	0.60

Remarks - Results

On day 2 only, the animals treated with the high dose showed erythema (score 1) of the ear skin. No other irritation of the ears was observed.

No test substance related mortalities occurred, and no clinical signs of toxicity were observed.

While the above results do not provide evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical, false negative results can be obtained from the testing of nickel compounds in LLNA studies (ECVAM, 2008; Kimber, 2011), therefore, the results of this study should be treated with caution.

CONCLUSION

The notified chemical may have skin sensitising ability but the test conditions employed may be inadequate. Therefore, on the basis of inadequate evidence, no conclusion is made.

TEST FACILITY

Harlan (2012)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE

Notified chemical.

METHOD

OECD TG 471 Bacterial Reverse Mutation Test.
Plate incorporation procedure/Pre incubation procedure

Species/Strain	*S. typhimurium*: TA1535, TA98, TA100, TA102, TA97a
Metabolic Activation System	S9 fraction from Aroclor 1254-induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 0.15 – 5,002 µg/plate b) Without metabolic activation: 0.15 – 5,002 µg/plate
Vehicle	Water demin.
Remarks - Method	No significant protocol deviations. GLP Certificate.

Test 1 (plate incorporation method) was conducted with a concentration range of 50-5,002 µg/plate.

Tests 1 and 2 (pre-incubation method) were conducted on separate days. The concentration range was amended in Test 2 (0.15-15 µg/plate).

Vehicle [water and dimethyl sulfoxide (DMSO)] and positive controls were used in parallel with the test material.

Positive controls: i) without S9: 4-Nitro-1,2-phenylene diamine (TA97a, TA98 and TA102) and sodium azide (TA100, TA1535); ii) with S9: 2-aminoanthracene (TA97a, TA100, TA102 and TA1535) and benzo-a-pyrene (TA98). All positive controls were prepared in DMSO, except sodium azide which was diluted in water.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,002	≥ 5,002	negative
Test 2	> 15	> 15	negative
Present			
Test 1	> 5,002	≥ 5,002	positive
Test 2	> 15	> 15	positive

Remarks - Results	In both experiments, no signs of toxicity towards the tested strains could be observed. The background lawn was visible and the number of revertant colonies was not reduced. As no complete dissolution was possible at the highest concentration (the test substance was suspended in water), undissolved particles were seen on the plates. A significant increase in the number of revertant colonies could be seen in the strain TA98 (with metabolic activation) in the mutagenicity assays of both experiments. A weak concentration-related increase over the tested range was reported. The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	The notified chemical was mutagenic to bacteria under the conditions of the test.
TEST FACILITY	LAUS GmbH (2012a)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain	Human
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	S9 fraction from Aroclor 1254-induced rat liver
Vehicle	Culture medium without fetal calf serum
Remarks - Method	No significant protocol deviations. GLP Certificate. Experiment 1 was initially treated as a pre-experiment, however based on its results, a second experiment was deemed unnecessary. Vehicle and positive controls (ethyl methanesulphonate without metabolic activation and cyclophosphamide with metabolic activation) were used in parallel with the test material.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	19.6, 39.2*, 78.3, 156.5*, 313*, 625.9. 1251.7 and 2,503.4*	4 hours	22 hours
Test 2	-	-	-
Present			
Test 1	19.6, 39.2*, 78.3, 156.5*, 313, 625.9. 1251.7* and 2,503.4*	4 hours	22 hours
Test 2	-	-	-

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:* *Cytotoxicity in Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 313	> 2,503.4	positive
Present			
Test 1	≥ 156.5	> 2,503.4	positive

Remarks - Results	In the absence of metabolic activation, a statistically significant and toxicologically relevant increase of structural chromosomal aberrations was observed at the highest concentration (2,503.4 µg/mL). In the presence of metabolic activation, a statistically significant and toxicoloigically relevant increase of structural chromosomal aberrations was observed at the two highest concentrations (1,251.7 and 2,503.4 µg/mL), without a concentration-effect relationship evident at these concentrations. It is noted that the positive effects were only seen at cytotoxic concentrations. The study authors considered that the highest concentration tested should be evaluated for the induction of chromosomal damage, as the cytotoxic damage (mitotic indices ~20% of solvent control) was not so large as to inhibit structural evaluation. The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	The study authors considered that the notified chemical was clastogenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	LAUS GmbH (2012b)

B.8. Genotoxicity – in vivo

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test
Species/Strain	Mouse/NMRI
Route of Administration	Dermal – single I.P injection
Vehicle	Physiological saline (0.9% NaCl)
Remarks - Method	No significant protocol deviations. GLP Certificate. The test substance was administered by intraperitoneal (I.P.) injection. Peripheral blood samples were collected for micronuclei analysis. A pre-experiment was conducted in which a single mouse was treated I.P. with 2,000 mg/kg bw test substance – the animal died 3 minutes after treatment. Subsequently, 3 animals per sex, were administered with a single I.P. injection (100 mg/kg bw) of the test item. Due to the results obtained, 100 mg/kg bw was chosen as the maximum tolerable dose for the main experiment. Vehicle and positive controls (cyclophosphamide; CP) were used in parallel with the test material. Sampling of the peripheral blood was carried out at 44 hours (all dose groups) and 68 hours (vehicle control and high dose group) after treatment.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5 per sex	0	68 hours
II (low dose)	5 per sex	10	68 hours
III (mid dose)	5 per sex	50	68 hours
IV (high dose)	5 per sex	100	68 hours
V (positive control, CP)	5 per sex	40	68 hours

RESULTS

Doses Producing Toxicity	Following treatment, animals of both sexes in the low dose group showed a reduction of spontaneous activity at the 30 minute observation only. Animals in the mid and high dose groups showed a variety of clinical signs including reduction of spontaneous activity, prone position, constricted abdomen, piloerection, bradykinesia, catalepsis, recumbency, half eyelid to full eye closure. These effects were of varying duration ranging from the 30 minute up to the 24 hour observation and affected animals of both sexes. While the proportion of polychromatic erythrocytes among total erythrocytes was significantly decreased in animals treated with the positive control, relative to negative control animals, in general, it was increased in animals treated with the test substance. The study authors indicated that the increases were not statistically significant and/or were within the range of historical control data.
Genotoxic Effects	A statistically significant increase in the induction of micronuclei was seen in female animals of the high dose group, 44 hours after treatment (0.46%), compared to the negative control data (0.26%) and was above the historical data range limit (0.08-0.31%). An increase was also seen in high dose females 68 hours after treatment (0.37%) relative to control animals (0.24%), however, the increase was not statistically significant. These increases were deemed to be biologically relevant by the study authors.
Remarks - Results	The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.

CONCLUSION	The notified chemical was clastogenic to female mice under the conditions of this in vivo mammalian erythrocyte micronucleus test.
TEST FACILITY	BSL BioService (2012)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 301 C Ready Biodegradability: Modified MITI Test (I).
- Inoculum: Activated Sludge
- Exposure Period: 28 Days
- Auxiliary Solvent: None Reported
- Analytical Monitoring: Biochemical oxygen demand (BOD)
- Remarks - Method: No significant protocol deviations. GLP Certificate.

One of the solutions in the test medium was prepared with EDTA in order to avoid having to prepare the solution immediately before use. As EDTA is a complexing agent, a reaction between Nickel and EDTA might be possible. However, the degradation behaviour suggests toxic effects of Nickel towards the test system; therefore, the complexation is not expected to have influenced the test.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
28	30	2	40
-	-	5	65

Remarks - Results: All validity criteria were met. The positive control reached the pass level of 40% on day 2 (criterion: ≤ 7) and the pass level of 65% on day 5 (criterion ≤ 14). The notified chemical is considered "not readily biodegradable" as a plateau of approx. 29% degradation was reached after 28 days.

CONCLUSION: The notified chemical is not readily biodegradable

TEST FACILITY: LAUS GmbH (2012c)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 203 Fish, Acute Toxicity Test - static system
- Species: *Dania rerio*
- Exposure Period: 96 hours
- Auxiliary Solvent: None
- Water Hardness: 79 mg $CaCO_3$/L
- Analytical Monitoring: Validated Atomic Absorption Spectrometric (AAS) method
- Remarks – Method: No significant protocol deviations. GLP Certificate.

RESULTS

Concentration mg/L	*Number of Fish*	*Mortality*				
Nominal		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0	0

0	7	0	0	0	0	0
100	7	0	0	0	0	0

LC_{50}	> 100 mg/L at 96 hours.
NOEC (or LOEC)	100 mg/L at 96 hours.
Remarks – Results	All validity criteria were within acceptable limits, no mortality was observed and therefore the study was considered valid. At the beginning and at the end of the test, the content of the notified chemical in the test solutions was determined by measurement of Nickel as a component of the notified chemical using Mass Spectroscopy (MS). Recovery after 96 hours was 100% of the starting concentration and the correlation between nominal and measured concentration was very good (92%). Therefore, the determination of the results was based on the nominal concentration.
CONCLUSION	The notified chemical is not harmful to fish
TEST FACILITY	LAUS GmbH (2011a)

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	250 mg $CaCO_3$/L
Analytical Monitoring	Validated Atomic Absorption Spectrometric (AAS) method.
Remarks - Method	No significant protocol deviations. GLP Certificate. At the start and at the end of the test, the content of the test item in the test solutions was determined by measurement of Nickel as component of the test item using AAS. The analytical determinations of the test item showed acceptable correlation between nominal and measured concentrations and good recovery rates. Therefore, the test item can be stated as stable under the test conditions. The determination of the results was based on the geometric means of the measured concentrations.

RESULTS

Concentration mg/L Nominal	*Number of D. magna*	*Number Immobilised (%)*	
		24 h	*48 h*
Control	20	0	0
0	20	0	0
10	20	0	0
22	20	0	25
46	20	15	80
100	20	60	100

LC_{50}	25 mg/L at 48 hours
NOEC	8.3 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. For the estimation of the EC50s of test item and positive control, the fits showed sufficient statistical correspondence of the data with the dose-response- equation.
CONCLUSION	The notified chemical is harmful to aquatic invertebrates
TEST FACILITY	LAUS GmbH (2011b)

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: 0.1, 0.32, 1.0, 3.2 and 10 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	Validated Atomic Absorption Spectrometric (AAS) method.
Remarks - Method	No significant protocol deviations. GLP Certificate.

RESULTS

Biomass		*Growth*	
$< E_yC_{50}>$ *mg/L at 72h*	NOE_yC *mg/L at 72h*	$< E_rC_{50}>$ *mg/L at 72 h*	NOE_rC *mg/L at 72h*
0.48	0.07	1.4	0.07
95%-confidence-interval			

Remarks - Results	All validity criteria for the test were satisfied. At the start and at the end of the test, the content of the test item in the test solutions was determined by measurement of Ni as component of the test item using MS. The recovery after 72 hours ranged from 76% to 91% of the start concentration, the correlation between nominal and measured concentration was acceptable (81% -92% at the beginning and 64% - 83% at the end of the experiment). The lower measured test item concentrations at the end of the study might cause by assimilation of Nickel by the algal cells. Therefore, the determination of the results was based on the geometric means of the measured concentrations.
CONCLUSION	The notified chemical is very toxic to algae.
TEST FACILITY	LAUS GmbH (2011c)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated Sludge
Exposure Period	3 hours
Concentration Range	Nominal: 1, 10, 100 and 1,000 mg/L
Remarks – Method	No significant protocol deviations. GLP Certificate. Activated sewage sludge was exposed to a dispersion of the test item at a loading rate of 10, 100 and 1,000 mg/L for a period of 3 hours.
RESULTS	
IC_{50}	191 mg/L
NOEC	10 mg/L
Remarks – Results	All validity criteria for the test were satisfied.
CONCLUSION	The notified chemical is not expected to inhibit microbial respiration

TEST FACILITY	LAUS GmbH (2009j)

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