File No: STD/1460

April 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Uniquat GNS-TMA

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and 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/1460	Arch Wood Protection (Aust) Pty Ltd	Chemical in Uniquat GNS-TMA	Yes	≤ 100 tonnes per annum	Production chemical in the oil and gas 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 3) (Oral)	H301 - Toxic if swallowed
Acute Toxicity (Category 3) (Dermal)	H311 - Toxic in contact with skin
Skin Corrosion/Irritation (Sub-category 1C)	H314 – Causes severe skin burns and eye damage
Eye Damage/Irritation (Category 1)	H318 - Cause serious eye damage

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 phrases:

R22: Harmful if swallowed
R21: Harmful in contact with skin
R34: Causes burns
R41: Risk of serious eye damage

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 Category 1	H400 – Very toxic to aquatic life
Not classified for long term 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 PEC/PNEC ratio and the assessed 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 3) (Oral): H301 -Toxic if swallowed
  - Acute Toxicity (Category 3) (Dermal): H311 - Toxic in contact with skin
  - Skin Corrosion/Irritation (Sub-category 1C): H314 – Causes serious skin burns and eye damage
  - Eye Damage/Irritation (Category 1): H318 - Cause serious eye damage

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.

(Material) Safety Data Sheet

- The (M)SDS provided by the notifier should be amended to reflect the hazard classification stated above.

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:
  - Use of enclosed, automated processes, where possible
  - Ventilation system including local exhaust 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 skin and eye contact
  - Avoid generation and inhalation of aerosols
  - A shower and eyewash station should be available

- 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:
  - Impervious rubber gloves
  - Protective clothing
  - Chemical goggles
  - Face shields (if necessary)
  - Respiratory protection when aerosols may be generated

  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

- The notified chemical should be disposed of to landfill.

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 production chemical in the oil and gas sector, 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.

No additional secondary notification conditions are stipulated.

(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)
Arch Wood Protection (Aust) Pty Ltd (ABN: 95 003 780 872)
1 Helium Street
Narangba QLD 4504

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: chemical name, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, use details, import volume and site of reformulation.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physico-chemical endpoints and all toxicological endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Uniquat GNS-TMA (contains the notified chemical at < 40% concentration)

MOLECULAR WEIGHT
< 500 Da

ANALYTICAL DATA
Reference HPLC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 95%

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless clear liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Decomposes at 189 °C (at 101.3 kPa)	Analogue data
Boiling Point	Decomposes at 189 °C (at 101.3 kPa)	Analogue data
Density	935 kg/m^3 at 20 °C	Analogue data
Vapour Pressure	3.1 x 10^{-9} kPa at 25 °C; 1.8 x 10^{-9} kPa at 20 °C	Analogue data
Water Solubility	358 g/L at 20 °C	Measured
Hydrolysis as a Function of	Hydrolytically stable	Measured

pH		
Partition Coefficient (n-octanol/water)	Not determined	Expected to partition to phase boundaries based on its surface activity
Adsorption/Desorption	log K_{oc} = 5.99 at 25 °C	Analogue data
Dissociation Constant	Not determined	The notified chemical is a salt and is ionised in this form
Flash Point	Not determined	-
Flammability	Not highly flammable	Analogue data
Autoignition Temperature	> 400 °C	Analogue data
Explosive Properties	Not determined	Not expected to be explosive based on structure
Oxidising Properties	Not determined	Not expected to be oxidising based on structure

DISCUSSION OF PROPERTIES

Reactivity
The notified chemical reacts with oxidising agents to form oxides of carbon and nitrogen, smoke and other toxic fumes. However it 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 for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported at < 40% concentration as a component of an aqueous product.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 100	< 100	< 100	< 100	< 100

PORT OF ENTRY
Fremantle, WA

IDENTITY OF MANUFACTURER/RECIPIENTS
Arch Wood Protection (Aust) Pty Ltd

TRANSPORTATION AND PACKAGING
The product containing the notified chemical at < 40% concentration will be imported in 1000 L intermediate bulk containers (IBCs) and will be transported to the customer's location for repacking and relabelling or reformulation. The reformulated product containing the notified chemical at < 30% concentration will then be transported to oil/gas wells on land by truck and to oil/gas rigs offshore by boat.

USE
The notified chemical will be imported for use as a down-hole production chemical for onshore and offshore applications in the oil and gas industry.

OPERATION DESCRIPTION
Repackaging and Relabelling
The notified chemical will be repackaged and relabelled prior to use in oil and gas production. Repackaging will involve the transfer of the product containing the notified chemical at < 40% concentration from IBCs to end-use containers using flexible transfer hoses and pumping equipment. This operation will take place in a bunded area. Once repackaged, the product containing the notified chemical at < 40% concentration will be relabelled into a different product.

Reformulation
The product containing the notified chemical will be reformulated prior to use in oil and gas production. Reformulation will involve typical liquid blending methods where the notified chemical (at < 40% concentration) is transferred from the IBC to a blending tank using flexible transfer hoses and pumping equipment. The final concentration after reformulation will be < 30%. The tank is sealed until filling. Filling is via a filling machine into 1000 L IBCs or 205L drums. This operation will be conducted in a bunded area with local exhaust ventilation.

End-use
After transport of the product containing the notified chemical at < 30% concentration to gas wells and/or oil rigs via road and/or sea, the required amount of product will be dosed from the storage containers either by batch treatment or continuous injection to maintain approximately 10 ppm of the notified chemical in the pipeline flow. The notified chemical is expected to be contained in the aqueous phase when discharged from the well for disposal.

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	0.5	25
Reformulation	0.5	25
Warehouse	0.5	25
Field operation	1	300

EXPOSURE DETAILS
Storage and transport
Exposure of workers to the notified chemical at up to 40% concentration during transport and storage will only occur in the event of an accidental release.

Repackaging and reformulation
Dermal and ocular exposure to the notified chemical at up to 40% concentration may occur during reformulation and repackaging when charging blending vessels, connecting pump lines, sampling for quality control, packaging off, and during maintenance and cleaning. Dermal and ocular exposure is expected to be limited by the stated use of personal protective equipment (PPE) including gloves, protective clothing and goggles or a face shield. Given the low vapour pressure of the notified chemical at ambient temperatures, inhalation exposure is not expected unless aerosols are formed.

End-use
Dermal and ocular exposure to the notified chemical at < 30% concentration may occur when connecting pump lines for dosing, and during maintenance and cleaning of pumping and dosing equipment. Dermal and ocular exposure is expected to be limited by the stated use of personal protective equipment (PPE) including gloves, protective clothing and goggles or a face shield.

6.1.2. Public Exposure
The notified chemical is intended only for use in the oil and gas industry, hence public exposure to the notified chemical is not expected.

6.2. Human Health Effects Assessment
The results from toxicological investigations conducted on acceptable analogues of the notified chemical are summarised in the table below. For full details of the studies, refer to Appendix B.

Endpoint	*Test Substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Analogue 1 (33% active)	*LD50 = 226 mg/kg bw; toxic
Rabbit, acute dermal toxicity	Analogue 1 (33% active)	*LD50 = 528 mg/kg bw; toxic
Rabbit, skin irritation	Analogue 1 (40% active)	corrosive

	Analogue 1 (33% active)	moderately to severely irritating
Rabbit, eye irritation	Analogue 1 (33% active)	corrosive
Guinea pig, skin sensitisation – non-adjuvant test	Analogue 1	no evidence of sensitisation
Rat, repeat dose oral toxicity – 90 days	Analogue 1	NOAEL = 113 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	Analogue 1	non mutagenic
Genotoxicity – in vitro mammalian chromosomal aberration test (human lymphoma)	Analogue 1	non genotoxic
Genotoxicity – in vitro mammalian cell gene mutation test (mouse lymphoma)	Analogue 1	non genotoxic
Genotoxicity – in vivo mammalian bone marrow chromosomal aberration test	Analogue 2	non genotoxic

* LD50 adjusted for concentration of analogue chemical in test substance

Toxicokinetics.
The notified chemical is of low molecular weight (< 500 Da) and is corrosive hence passage across biological membranes is expected. This is supported by systemic effects noted in the acute dermal toxicity and repeated dose oral toxicity studies (see below) with Analogue 1. Given its low vapour pressure, exposure by inhalation is not expected, unless aerosols/mists are formed.

Acute toxicity.
Analogue 1 tested as a 33% aqueous solution was found to be toxic via the oral route in rats (LD50 = 226 mg/kg bw (adjusted for concentration of analogue chemical)) and toxic by the dermal route in rabbits (LD50 = 528 mg/kg bw (adjusted for concentration of analogue chemical)).

In the acute oral toxicity study, mortality in rats was observed from 620 mg/kg bodyweight (low mid dose) and treatment related changes among rats that died included enlarged and/or reddened adrenal glands, meningeal haemorrhage or dilated meningeal vessels in the brain, dark purple liver, reddened cortico-medullary junction in the kidney, reddened and/or distended stomach and reddened intestines. Treatment related systemic toxicity included diarrhoea, respiratory distress, ataxia, lethargy and salivation.

In the acute dermal toxicity study, mortality in rabbits was observed from 1020 mg/kg bodyweight (mid dose). Moderate to severe erythema and oedema with necrosis, desquamation and scabbing were noted on essentially all application sites. Eschar, exfoliation, fissuring and blanching were also observed in some rabbits. Other treatment related findings included lethargy and ataxia, body cool to touch, decreased respiratory rate, laboured respiration, clear and purulent nasal discharge, decreased defecation, emaciation, wet red staining and clear wet matting around the mouth, clear wet ventral abdominal matting, diarrhoea, scabbing on the right hind leg, hair loss and desquamation in the urogenital area. Treatment related abnormalities observed in the nine animals that died included haemorrhagic thymus, red foci or dark red areas of the stomach, brain haemorrhage and soft and/or pale liver.

Irritation and sensitisation.
Analogue 1 tested as a 33% aqueous solution was found to be moderately to severely irritating to rabbit skin and corrosive when tested as a 40% aqueous solution. Analogue 1 was found to be corrosive to the rabbit eye when tested as a 33% aqueous solution.

A non-OECD study on Analogue 1 found no evidence of sensitisation in the guinea pig.

Repeated dose toxicity.
In a 90-day repeated dose oral toxicity study in rats, Analogue 1 was found to have a No Observed Effect Level (NOEL) of 22 mg/kg bw/day based on marginal treatment related effects at the 113 mg/kg bw/day dose level. These effects were considered to be minor so that the 113 mg/kg bw/day dose level is considered the No Observed Adverse Effect Level (NOAEL).

Clinical signs in high dose animals from day 7 included hunched posture, pilo-erection, tiptoe gait, diarrhoea and red/brown staining of the body surface (consequently the dose level was reduced to 50% of the original value from day 29). High dose females also exhibited increase in startle reflex. A reduced bodyweight gain was

detected in high dose animals before the reduction in dose. The elevated relative organ weights of high dose animals (brain, epididymides, kidneys, spleen, testes and ovaries) were attributed to their reduced terminal bodyweights.

Mutagenicity/Genotoxicity.
Analogue 1 was negative in a bacterial reverse mutation assay, negative in an *in vitro* mouse lymphoma gene mutation test and negative in an *in vitro* mammalian chromosome aberration test. Analogue 2 was negative in an *in vivo* bone marrow cytogenetic test.

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 3) (Oral)	H301 - Toxic if swallowed
Acute Toxicity (Category 3) (Dermal)	H311 - Toxic in contact with skin
Skin Corrosion/Irritation (Category 1C)	H314 - Causes severe skin burns and eye damage
Eye Damage/Irritation (Category 1)	H318 - Cause serious eye damage

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):

R22: Harmful if swallowed
R21: Harmful in contact with skin
R34: Causes burns
R41: Risk of serious eye damage

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on studies conducted on acceptable analogue chemicals, the notified chemical under the GHS classification is expected to be toxic by the oral route, toxic by the dermal route and corrosive to eyes and skin. Based on a NOAEL of 113 mg/kg bw/day for Analogue 1, long-term exposure from the notified chemical is potentially of concern. The notified chemical is however not expected to be genotoxic or a skin sensitiser. Due to both the likely local and systemic toxicity of the notified chemical, its use is only considered to be reasonable when appropriate engineering controls, safe work practices and personal protective equipment (PPE) are used to greatly reduce the potential for exposure.

During repackaging, reformulation and end-use, dermal and ocular exposure to the notified chemical at up to 40% concentration is possible. Exposure is expected to be limited by the largely automated and enclosed processes and the expected use of PPE including gloves, protective clothing and goggles or a face shield. Inhalation exposure by workers to the notified chemical is not expected as the vapour pressure of the notified chemical at ambient temperatures is predicted to be low and the largely enclosed processes reduce the potential for exposure to aerosols. Provided that adequate PPE is used and engineering controls are in place to limit exposure, the risk to the health of workers is not considered to be unreasonable.

6.3.2. Public Health
The public is not expected to be exposed to the notified chemical except in the event of an accident; hence, the risk to public health 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 imported notified chemical in aqueous solution will be transported to the customer's site/s for reformulation into final products. Environmental release at this stage is expected to be limited to accidental spills and leaks during reformulation and repackaging (up to 1% of the total imported volume), residual notified chemical in import containers and washings from equipment cleaning. Accidental spills are expected to be handled in accordance with the emergency procedures. Residual notified chemical contained in import and transport containers is expected to be removed during drum reconditioning, and the drums will be reused. Washings from equipment cleaning are expected to be recovered and either re-used in subsequent batches or be disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The products containing the notified chemical will be used as production chemical for onshore (30% of the total import volume) and offshore (70%) in the oil and gas industry. In the oilfield, the formulated product containing the notified chemical will be applied either as a batch treatment or continuous injection. The notified chemical will be injected into the systems at the dose rates of 5 - 30 mg/L for continuous injection and 25 - 125 mg/L for batch treatment, respectively. Products containing the notified chemical are expected to coat on the walls of the installations as it passes through the pipeline. Excess product is removed downstream and captured for re-use or if excessively contaminated, for disposal. Notified chemical that coats the walls of the installations is expected to be desorbed from the walls overtime and be eventually released with the produced fluids. The produced fluids, including water and oil/gas, will be treated at the processing facilities. The notified chemical contained in the produced fluids is expected to primarily partition to the produced water.

Produced water, containing the notified chemical, is expected to be either reinjected into wells or further treated before disposed of as waste water. Notified chemical within the oil phase will either share the same end-use fate as the oil or be removed during oil refining, in which case it will remain in the distillation residues/tar fraction. Environmental release of the notified chemical in oil pipelines is expected to be limited.

For offshore application, the majority of the produced water is expected to be discharged directly to the ocean (Cobby, 2002). Up to 70% of the notified chemical may be discharged to the ocean as the notified chemical is expected to be slowly desorbed from the walls of the installations and be released with the produced water over time.

For onshore applications, the notifier indicates that the produced water will be discharged to holding ponds for evaporation. Therefore, the notified chemical is not expected to be released significantly to surface waters from onshore applications.

RELEASE OF CHEMICAL FROM DISPOSAL

The empty drums and tanks will be sent to reconditioners where the residual notified chemical may be washed with water during recycling/cleaning and disposed of to sewer, or to landfill with the containers.

7.1.2. Environmental Fate

Environmental fate data were not submitted for the notified chemical itself. However, the biodegradability of Analogue 1 was determined to be 75% (35% water solution) and 97% (33% water solution) over 28 days. Analogue 1 is structurally similar to the notified chemical. They are expected to have similar chemical-physical properties and environmental fate profiles. Therefore, it is scientifically reasonable to use the analogue data to predict the environmental fate for the notified chemical. Based on these analogue data, the notified chemical is considered to have a potential to be readily biodegradable. For the details of the environmental fate studies for the analogue chemical, please refer to Appendix C.

After injection into the system, most of the notified chemical is expected to coat on the walls of the installations as it passes through the pipeline. Excess product is removed downstream and captured for re-use or if excessively contaminated, for disposal as waste water. Notified chemical that coats the walls of the installations is expected to be desorbed from the walls overtime and be eventually released with the produced fluids. Notified chemical contained in the produced fluids, including water and oil/gas, is expected to share the fate of the produced water and oil/gas.

For offshore application, the majority of the produced water is expected to be discharged directly to the ocean. In the marine environment, the notified chemical has potential to adsorb to sediment and any suspended particulate matter, based on the soil/water adsorption coefficient for Analogue 2 (Log K_{oc} = 5.99), in addition to the surface activity and cationic properties of the notified chemical. The notified chemical is expected to readily biodegrade based on the results of laboratory tests for Analogue 1. The notified chemical is not expected to bioaccumulate in aquatic organisms based on its surface activity, high water solubility, the presence of cationic functional groups and the low measured bioaccumulation factor for Analogue 2 (BCF ≤ 140).

For onshore application, the produced water will be either re-injected into wells or discharged to holding ponds, where the notified chemical is expected to rapidly biodegrade and/or partition to sludge sediment due to its surface activity and cationic functionalities. The notified chemical is expected to be immobile in sediment or soil based on the high soil/water adsorption coefficient for Analogue 2. Therefore, very little, if any, of the notified chemical is expected to be released to surface waters from onshore applications.

In water, landfill and soil, the notified chemical is expected to degrade via abiotic or biotic pathways forming water and oxides of carbon and nitrogen.

Small amounts of the notified chemical contained in the oil phase are expected to be sent to oil refineries in the oil phase. It may either be removed during oil refining and remain in the distillation residues/tar fraction that will be most likely used as road base, or share the fate of the oil product. The notified chemical contained in oil products is expected to be eventually thermally decomposed during use to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

Offshore release

Assuming for the worst case scenario that all the produced water will be directly discharged into the ocean, the Predicted Environmental Concentration (PEC) of the notified chemical in marine water has been calculated based on the CHARM method (Thatcher M. et al., 2005).

The concentration of the notified chemical in produced water has been calculated by equation 1:

$$C_{pws} = C_{pw} = \frac{f_r \times C_i \times F_i}{F_{pw}}$$

in which:

C_{pw} = Concentration of the chemical in produced water (mg/L),

f_r = Fraction released (for injection chemicals f_r = 0.01).

C_i = Concentration of the chemical in the injection fluid or total fluid (mg/L),

F_i = Fluid injected or total fluid production (m^3/day),

F_{pw} = Volume of produced water discharged per day (m^3/day)

It is indicated by the notifier that the notified chemical will be injected into the system at the dose rate of 25 - 125 mg/L for batch treatment. Total fluid production and volume of produced water discharged per day were each estimated by the notifier to be 20 to 40 m^3/day. For the worst case scenario, it is assumed the dose rate is 125 mg/L, total fluid production is 40 m^3/day and volume of produced water discharged per day is 20 m^3/day. Therefore, the calculated C_{pw} is:

$$C_{pws} = \frac{0.01 \times 125 \times 40}{20} = 2.5 \text{ mg/L}$$

The PEC can be calculated using equation 2:

$$PEC = C_{pws} \times D_{distance\ x}$$

in which:
PEC = Predicted Environmental Concentration of a chemical at a certain distance from the platform (mg/L),

$D_{distance\ x}$ = Dilution factor at distance x from the platform (0-1). The dilution factor at a distance of x = 500 m is set to a realistic worst case default value of 0.001.

$$PEC = 2.5 \text{ mg/L} \times 0.001 = 2.5 \text{ µg/L}$$

Onshore release

It is indicated that 30% of the total import volume of the notified chemical will be used for onshore applications. The notifier indicated that the produced water containing the notified chemical will be discharged into holding ponds for evaporation. The release of the notified chemical to the aquatic environment from onshore application

is not expected to reach ecotoxicologically significant concentrations. Therefore, the PEC for the notified chemical released from the onshore applications was not calculated.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical or analogue chemical are summarised in the table below. The algal toxicity study was conducted on the notified chemical. Respiration effects on bacterial and toxicity effects on fish and daphnia were conducted on Analogue 1. Details of these studies can be found in Appendix C.

Endpoint	*Result (mg/L)*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 0.77	Expected to be very toxic to fish
Daphnia Toxicity	48 h EC50 = 0.09	Expected to be very toxic to aquatic invertebrates
Algal Toxicity	72 h E_rC50 = 0.11 72 h NOE_rC = 0.011	Very toxic to algae
Inhibition of Bacterial Respiration	3 h EC50 = 12.2	Expected to be inhibitory to microbial activity

The notified chemical and the analogue chemical contain the same functional groups and belong to the same chemical class. They are expected to have similar ecotoxicity effects on aquatic life. Therefore, it is reasonable to use the analogue chemical as read-across to predict environmental effects for the notified chemical.

Under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS; United Nations, 2009) the notified chemical is considered to be very toxic to fish, aquatic invertebrates and algae. Based on its toxicity to alga, the notified chemical is formally classified under the GHS as "Acute category 1; Very Toxic to aquatic life". Based on analogue data, the notified chemical has potential to be readily biodegradable and is not expected to be bioaccumulative (BCF ≤ 140). Thus, the notified chemical is not formally classified for its chronic hazard under the GHS.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) has been calculated based on the endpoint for marine alga (72 h E_rC50 = 0.11 mg/L) as it reflects a more realistic situation. Although the most sensitive aquatic species is freshwater daphnia (48 h EC50 = 0.092 mg/L), the majority of the notified chemical is expected to be released to the ocean based on its use pattern. A safety factor of 100 is used since ecotoxicity data for three trophical levels of aquatic organisms are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
ErC50 (alga)	0.11	mg/L
Assessment Factor	100	
PNEC:	1.1	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - Ocean	2.5	1.1	**2.3**

The Risk Quotient (Q = PEC/PNEC) for onshore application was not calculated as the PEC for this release scenario was not calculated.

The Q of the notified chemical for off-shore applications has been calculated to be > 1. The calculated risk quotient Q indicates the notified chemical may cause a risk to the aquatic environment based on the above worst scenario. However, the above Q value is based on the worst case calculations for the PEC.

The worst case PEC was calculated based on the maximum dose rate of 125 mg/L for the notified chemical to be injected into the system. However, the average dose rate is most likely to be less than 125 mg/L since the dose rate was indicated to be 25 - 125 mg/L in the application dossier. If using an average dose rate of 75 mg/L for the PEC calculation, the Q will drop to 1.4.

Additionally, the PNEC used for the Q calculation was based on the E_rC50 for algae, which was determined by incubating the algal cells in the test media for 72 hours. However, algae cells are unlikely to be exposed to the notified chemical contaminated water for 72 hours when the notified chemical is discharged to the marine

environment by batchwise release. After discharge, the ocean currents will continue to dilute the notified chemical contaminated waters so that the worst case concentration of the notified chemical are not expected to remain for extended periods. Furthermore, the bioavailability and ecotoxicity of the notified chemical to aquatic organisms is likely to be further reduced due to sorption of the notified chemical to sediment and suspended particulate matters. In addition, the notified chemical is expected to have the potential for biodegradation, thus it is unlikely to persist in surface waters or soils. The notified chemical is considered to have low potential for bioaccumulation. Therefore, the notified chemical is unlikely to remain at ecotoxicologically significant concentrations in the aquatic environment.

Based on the consideration of the mitigation factors, the PEC/PNEC ratio for marine water is expected to be acceptable for the worst case scenario of batchwise release. Therefore, on the basis of the PEC/PNEC ratio and the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment for both offshore and onshore oil and gas applications.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point Decomposes at 189 °C (at 101.3 kPa)

Method	OECD TG 102 Melting Point/Melting Range. EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature.
Remarks	The test was conducted on Analogue 1 (98.2%). The result was based on both visual observation and differential scanning calorimetry (DSC) – glass crucible (closed and open). The DSC result corresponded with the observed behaviour of the test substance in the melting device which leads to the conclusion that the test substance has no melting or boiling point.
Test Facility	AllessaChemie (2002a)

Boiling Point Decomposes at 189 °C (at 101.3 kPa)

Method	OECD TG 102 Melting Point/Melting Range. EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature.
Remarks	The test was conducted on Analogue 1 (98.2%). The result was based on both visual observation and differential scanning calorimetry (DSC) – glass crucible (closed and open). The DSC result corresponded with the observed behaviour of the test substance in the melting device which leads to the conclusion that the test substance has no melting or boiling point.
Test Facility	AllessaChemie (2002a)

Density 935 kg/m^3 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids. EC Council Regulation No 440/2008 A.3 Relative Density.
Remarks	The test was conducted on Analogue 1 (98.2%). The pycnometer method was used.
Test Facility	AllessaChemie (2002b)

Vapour Pressure 3.1×10^{-9} kPa at 25 °C; 1.8×10^{-9} kPa at 20 °C

Method	OECD TG 104 Vapour Pressure. EC Council Regulation No 440/2008 A.4 Vapour Pressure.
Remarks	The test was conducted on Analogue 1 (98.2%). Thermal stability was conducted via DSC according to OECD TG 113. Vapour pressure was measured using the effusion method. Thermal stability results showed two temperature ranges that displayed endothermic effects: 30-85 °C and 185-250 °C. The calculated vapour pressure values were extrapolated from measured pressure data.
Test Facility	Siemens (2002)

Water Solubility 358 g/L in water,
300 g/L in buffer pH 5,
346 g/L in buffer pH 7,
373 g/L in buffer pH 9 at 20 °C

Method	Based on OECD TG 105 Water Solubility.
Remarks	Modified Flask Method. Conducted on Analogue 1 (98.2%). Water was added in small quantities to an amount of test substance in a graduated cylinder until full dissolution occurred. The mixture was shaken for sufficient period of time. The solution was cooled down to 20 °C to check if the test substance was still soluble at test temperature. At the point where all test substance dissolved in water, the total volume of the solution was measured and the water solubility of the test substance was calculated.
Test Facility	AllessaChemie (2002c)

Hydrolysis as a Function of pH Hydrolytically stable

Method	40 CFR 158 130: Hydrolysis as a Function of pH.

pH	*T (°C)*	*$t_{½}$ (days)*
5	25	> 30
7	25	> 30
9	25	> 30

Remarks The test was conducted on product containing 33% of Analogue 1. The test substance was incubated in unbuffered and buffered solution, pH 5, 7 and 9, under dark conditions at 25 °C. Less than 10% hydrolysis occurred after 33 days, as determined by colorimetric analysis. The test substance is considered hydrolytically stable according to the criterion in data reporting guidelines for hydrolysis studies according to this test.
Test Facility Akzo (1989a)

Adsorption/Desorption – main test log K_{oc} = 5.99 at 25 °C

Method US EPA-FIFRA N-163-1 40 CFR 158.130 and 158.50, Soil-/Sediment Adsorption - Desorption.

Soil Type	*Organic Carbon Content (%)*	*pH*	*K_{oc}*	*Log K_{oc}*
#1 Sand	0.25	7.4	4.38×10^5	5.64
#2 Sandy Loam	0.90	6.3	9.09×10^5	5.96
#3 Silty Clay Loam	2.05	7.9	1.60×10^6	6.20
#4 Silt Loam	2.1	7.4	1.47×10^6	6.17

Remarks The test was conducted on Analogue 2 (98.2%). Aqueous solutions of the test substance were equilibrated with four soil types and the adsorption and desorption coefficients and constants were determined. The concentration of the test substance remaining in the aqueous phase was determined by liquid scintillation counting analysis. The amount of the test substance adsorbed on the soils was determined by extraction and/or combustion followed with radioanalysis.
The mean of the logarithmic adsorption coefficient (log K_{oc} = 5.99) was reported for the test substance, indicating that the test substance was immobile in the soils tested.

The analogue chemical was demonstrated to be immobile in the soils tested. Therefore, the notified chemical is expected to be immobile in soils.
Test Facility ABC (1989)

Solid Flammability Not highly flammable

Method EC Council Regulation No 440/2008 A.10 Flammability (Solids).
Remarks The test was conducted on Analogue 1 (98.2%). The test substance ignited, melted and burned with a yellow flame and black smoke. The six replicates of the definitive test burned between 118-142 seconds.
Test Facility Huntingdon Life Sciences (2004a)

Autoignition Temperature > 400 °C

Method EC Council Regulation No 440/2008 A.16 Relative Self-Ignition Temperature for Solids.
Remarks The test was conducted on Analogue 1 (98.2%). There was no exothermic reaction of the test substance indicating that it does not self-ignite below 400 °C.
Test Facility Huntingdon Life Sciences (2004b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Analogue 1 (33% aqueous solution)

METHOD: OECD TG 401 Acute Oral Toxicity.

Species/Strain: Rat/Sprague-Dawley COBS CD

Vehicle: None

Remarks - Method: A range-finding study was conducted on 2 rats/dose (1/sex) at 500, 1000, 1500 and 2000 mg/kg bw. The rats dosed at 500 mg/kg bw survived while the rats at the higher dosage levels died. On this basis dosage levels of 512, 620, 750 and 908 mg/kg bw were selected for the main study. The control group was dosed with deionised water at a dose volume equal to that used for administration of the test material to the 750 mg/kg bw dosage group.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
Control	5/sex	0	None
Low dose	5/sex	512	None
Low mid dose	5/sex	620	1 male, 2 females
High mid dose	5/sex	750	2 males, 5 females
High dose	5 males	908	5 males

LD50 (95% confidence limits in parentheses): 684 (629-743) mg/kg bw; Males: 732 (616-869), Females: 626 (598-656) mg/kg bw

Signs of Toxicity: Clinical observations that were considered to be directly related to treatment in the low mid, high mid and high dosage groups included diarrhoea, respiratory distress (exhibited as respiratory rales and/or bradypnoea – slow breathing), ataxia, lethargy and salivation. No changes were observed in bodyweights during the 14-day study period.

Effects in Organs: Treatment-related changes among rats that died were enlarged and/or reddened adrenal glands, meningeal haemorrhage or dilated meningeal vessels in the brain, dark purple liver, reddened cortico-medullary junction in the kidney, reddened and/or distended stomach and reddened intestines.

CONCLUSION: The test substance is harmful via the oral route.

TEST FACILITY: WIL Research Laboratories (1987)

B.2. Acute toxicity – dermal

TEST SUBSTANCE: Analogue 1 (33% aqueous solution)

METHOD: In general accordance with the EPA Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Section 81-2.

Species/Strain: Rabbit/New Zealand White

Vehicle: Not stated but assumed to be deionised water if used.

Type of dressing: Semi-occlusive.

Remarks - Method: The test material was applied to approximately 20% of the body surface area for 24 hours prior to application of a gauze binder. Control animals received deionised water.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
Control	3/sex	0	None
Low dose	5/sex	520	None
Mid dose	5/sex	1020	2 males
High dose	5/sex	2000	4 males, 3 females

LD50 (95% confidence limits in parentheses)	1600 (1200-2100) mg/kg bw; Males: 1300 (800-1900); Females: 1900 (1500-2400) mg/kg bw
Signs of Toxicity - Local	Moderate to severe erythema and oedema with necrosis, desquamation and scabbing were noted on essentially all application sites. Eschar, exfoliation and fissuring were noted on more than 50% of the sites. Blanching was observed in 5 mid dose rabbits and 1 high dose rabbit.
Signs of Toxicity - Systemic	Of the 9 deaths, eight rabbits were found dead on day 1 and one rabbit found dead on day 2. A range of clinical findings related to treatment included lethargy and ataxia. Other findings were body cool to touch, decreased respiratory rate, laboured respiration, clear and purulent nasal discharge, decreased defecation, emaciation, wet red staining and clear wet matting around the mouth, clear wet ventral abdominal matting, diarrhoea, scabbing on the right hind leg, hair loss and desquamation in the urogenital area. Body weight losses were observed for ten rabbits, two of which occurred over the 14-day period, a mid-dose male and a high-dose female. For the remaining 8 rabbits, body weight losses occurred from days 0 to 7 with recovery during days 7 to 14 and net gains over the observation period.
Effects in Organs	Abnormalities observed in the 9 animals that died included: haemorrhagic thymus (6 rabbits), red foci or dark red areas of the stomach (3 rabbits), brain haemorrhage (3 rabbits), soft and/or pale liver (2 rabbits). One high-dose female had soft spongy kidneys with dark red cortices (however this was not attributed to the test material since kidney abnormalities were observed in 5/21 treated rabbits and one female from the control group [with no other changes seen in the control group]).

CONCLUSION The test substance is harmful via the dermal route.

TEST FACILITY WIL Research Laboratories (1988a)

B.3. Irritation – skin

TEST SUBSTANCE Analogue 1 (40% aqueous solution)

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.

Species/Strain	Rabbit/New Zealand White
Number of Animals	6
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	2.6	3	14 days	1
Oedema	1.7	3	7 to < 14 days	0

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

Remarks - Results	Distinct oedema and moderate to severe erythema were observed in all animals which partly resulted in distinct eschar formation after 48 hours. After 7 days the treated skin of all animals was hardened. At 7 days large and small detachments of skin were observed in some animals and scar formation was observed in 4 of 6 animals after detachment of eschar. The test substance was judged to be corrosive on the basis of severe skin lesions - scar formation.
CONCLUSION	The test substance is corrosive to the skin.
TEST FACILITY	Hoechst (1982)

B.4. Irritation – skin

TEST SUBSTANCE	Analogue 1 (33% aqueous solution)
METHOD	In general accordance with the EPA Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Section 81-2.
Species/Strain	Rabbit/New Zealand White
Number of Animals	6
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive
Remarks - Method	1 animal was sacrificed *in extremis* on day 3 due to a broken back.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	2.9	3	14 days	2
Oedema	2.7	4	14 days	1

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

Remarks - Results	The test substance induced moderate erythema and moderate to severe oedema on all sites. In general, the highest levels of irritation occurred two to three days after dosing and irritation subsequently decreased although moderate reactions persisted in one animal through study day 1. Desquamation was noted for all surviving animals late in the observation period and fissuring was noted in two animals.
CONCLUSION	The test substance is moderately to severely irritating to the skin.
TEST FACILITY	WIL Research Laboratories (1988b)

B.5. Irritation – eye

TEST SUBSTANCE	Analogue 1 (33% aqueous solution)
METHOD	In general accordance with the EPA Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Section 81-2.
Species/Strain	Rabbit/New Zealand White
Number of Animals	Unwashed eyes (6) and washed (3)
Observation Period	21 days

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	2.1	3	21 days	3
Conjunctiva: chemosis	4	4	21 days	3
Conjunctiva: discharge	2.7	3	21 days	2
Corneal opacity	2.8	4	21 days	4
Iridial inflammation	1.1	2	21 days	2

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

Remarks - Results: Corneal epithelial damage was observed over the entire observation period with petite haemorrhage being common. Washing resulted in slight alleviation of effects.

CONCLUSION: The test substance is corrosive to the eye.

TEST FACILITY: WIL Research Laboratories (1988c)

B.6. Skin sensitisation

TEST SUBSTANCE: Analogue 1

METHOD: Identified as Procter and Gamble Standard Procedure No. 4.
Species/Strain: Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal: Not done
topical: 0.1% (w/v)
MAIN STUDY
Number of Animals: Test Group: 20 Control Group: 10
INDUCTION PHASE: Induction Concentration:
topical: 0.1% (w/v)
Signs of Irritation: Not stated
CHALLENGE PHASE
1st challenge: topical: 0.1% (w/v)
2nd challenge: topical: -
Remarks - Method: The test substance was administered in aqueous ethanol for induction and in acetone for challenge. In the range-finding study, 0.4 mL of the test solution was applied for 6 hours under a dressing occluded by elastoplast. Skin reactions were checked after 24 hours. For the main study, treatment was the same as with topical induction at 0, 7 and 14 days. On day 28 a challenge patch was applied in the same way to an untreated site. After 6 hours the patches were removed and the sites scored at 24 and 48 hours.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	0.1% (w/v)	0/20	0/20	-	-
Control Group	0.1% (w/v)	0/10	0/10	-	-

Remarks - Results: Slightly patchy erythema was observed in 2 control and 3 test animals at 24 hours.

CONCLUSION: There was no evidence of reactions indicative of skin sensitisation to the analogue chemical under the conditions of the test.

TEST FACILITY: Hazleton (1978)

B.7. Repeat dose toxicity

TEST SUBSTANCE	Analogue 1 (35.5% aqueous solution)
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents. EC Directive 88/302/EEC B.26 Sub-Chronic Oral Toxicity Test: 90-Day Repeated Oral Dose Study using Rodent Species. The USEPA Health Effects Test Guidelines OPPTS 870.3100 – 90-Day Oral Toxicity in Rodents.
Species/Strain	Rat/Sprague-Dawley Crl:CD (SG) IGS BR
Route of Administration	Oral – diet
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week (dosage adjusted for concentration) Post-exposure observation period: None
Vehicle	None

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10/sex	0	0
low dose	10/sex	22	0
mid dose	10/sex	113	0
high dose	10/sex	273	0

Mortality and Time to Death

There were no unscheduled deaths during the study.

Clinical Observations

High dose animals developed clinical signs from day 7 such that the dose level was reduced to 50% of the original value from Day 29 onwards. The signs included hunched posture, pilo-erection, tiptoe gait, diarrhoea and red/brown staining of the body surface. Clinical signs persisted following dose reduction including two incidences of pallor of the extremities and generalised fur loss. By the end of the study period observations were limited to hunched posture, red/brown staining of the fur and a low incidence of tiptoe gait. Incidental findings of fur staining and hunched posture were observed in the low and mid dose groups.

No treatment-related functional observations were apparent beyond those noted as clinical signs. High dose females exhibited a statistically significant increase in startle reflex compared to controls.

No effect of treatment on bodyweight was observed for low dose animals and mid dose females. Reduced food intake occurred in mid and high dose animals over the study period and a reduction of bodyweight gain to food intake (food efficiency) was observed in the high dose animals over the first 3 weeks of the 13-week study. Bodyweight gain was reduced in high dose animals for the first 5 weeks of the study with mid dose males also affected in weeks 1 and 2. Water consumption was not affected by treatment.

No treatment-related ocular effects were observed.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Albumin/globulin ratio was elevated for high dose males and decreased for mid and high dose females. Plasma albumin was lower for mid and high dose females as was total plasma protein at the mid dose. A clear dose response was not evident and the changes were slight. Alanine aminotransferase and alkaline phosphatase were elevated in high dose males but had no histopathological correlate. A slight reduction in cholesterol for high dose females was attributable to an artificially high control group mean. Elevated chloride concentration was observed for high dose males.

No treatment-related changes in haematological parameters.

No urinalysis was performed.

Effects in Organs

A range of effects on organ weights were attributed to reduced terminal bodyweight. These included reduced absolute weights of heart, kidneys, liver and thymus for high dose males and heart for the mid dose. Elevated relative organ weights attributed to the reduced terminal bodyweights of high dose animals were for the brain, epididymides, kidneys, spleen, testes and ovaries.

No toxicologically significant macroscopic abnormalities were observed.

A higher incidence of haemosiderin accumulation was observed in the kidneys of mid and high dose males. Lower severity of haemosiderin accumulation was observed in the spleen of high dose males compared to controls. As haemolytic anaemia is unlikely on the basis of these results (splenic extramedullary haemopoiesis and splenic haemosiderin accumulation would be expected), it is suggested that metabolism and storage of iron may be affected by the test substance.

CONCLUSION
The NOEL was established as 22 mg/kg bw/day in this study, based on treatment related (marginal) effects at the 113 mg/kg bw/day dose level. These effects were considered to be minor so that the 113 mg/kg bw/day dose level is considered the NO(A)EL.

TEST FACILITY Safepharm Laboratories (2002b)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE Analogue 1 (33% aqueous solution)

METHOD OECD TG 471 Bacterial Reverse Mutation Test (1983).
Plate incorporation procedure
Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100
Metabolic Activation System S9 mix derived from Aroclor 1254 induced rat liver
Concentration Range in Main Test a) With metabolic activation: 0 – 100 µg/plate
b) Without metabolic activation: 0 – 100 µg/plate
Remarks - Method The dose range for the main test was selected based on the results of a preliminary toxicity test in strain TA98. In the preliminary toxicity test the lowest dose causing visible thinning of the background lawn was 250 µg/plate.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 250	100	-	Negative
Test 2		100	-	Negative
Present				
Test 1		100	-	Negative
Test 2		100	-	Negative

Remarks - Results No toxicologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, at any dose of the test substance, either with or without metabolic activation.

All the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

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

TEST FACILITY Life Science Research Ltd (1989a)

B.9. Genotoxicity – *in vitro*

TEST SUBSTANCE	Analogue 1 (33% aqueous solution)
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test (1983).
Cell Type/Cell Line	Human peripheral blood lymphocytes
Metabolic Activation System	Rat liver microsomal mix (S9)
Remarks - Method	Three cultures were used at each dosage point in the main test. Cultures without or with S9 mix were incubated with shaking or static, respectively.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0, 0.4, 2.0, 10.0	3 h	24 h
Present			
Test 1	0, 2.0, 10.0, 50.0	3 h	24 h

All cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 8	10	-	Negative
Present				
Test 1	≥ 40	≥ 10	-	Negative

* Indicated by reduction in mitotic index

Remarks - Results	No toxicologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation. All the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.
CONCLUSION	The test substance was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.
TEST FACILITY	Life Science Research Ltd (1989b)

B.10. Genotoxicity – *in vitro*

TEST SUBSTANCE	Analogue 1 (35.5% aqueous solution)
METHOD	OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test. EC Directive 2000/32/EC B.17 Mutagenicity - *In vitro* Mammalian Cell Gene Mutation Test.
Cell Type/Cell Line	Mouse lymphoma L5178 TK+/-
Metabolic Activation System	S9 fraction from phenobarbital/β-naphthoquinone induced rat liver
Remarks - Method	No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	0, 0.625, 1.25, 2.5, 5.0, 10.0, 20.0	3 h	2 d	10 – 14 d

Test 2	0, 0.313, 0.625, 0.938, 1.25, 2.5, 5.0	24 h	2 d	10 – 14 d
Present				
Test 1	0, 0.625, 1.25, 2.5, 5.0, 10.0, 20.0	3 h	2 d	10 – 14 d
Test 2	0, 2.5, 5.0, 10.0, 15.0, 20.0, 30.0	3 h	2 d	10 – 14 d

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 19.53	20	> 20	Negative
Test 2	≥ 1.25	≥ 1.25	> 5	Negative
Present				
Test 1	≥ 19.53	20	> 20	Negative
Test 2		≥ 15	> 30	Negative

Remarks - Results: The test substance did not induce any statistically significant increases in the mutant frequency at any tested concentration in each exposure group with and without metabolic activation.

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

CONCLUSION: The test substance was not mutagenic in mouse lymphoma L5178 TK+/- cells treated *in vitro* under the conditions of the test.

TEST FACILITY: Safepharm Laboratories (2002a)

B.11. Genotoxicity – *in vivo*

TEST SUBSTANCE: Analogue 2 (50% aqueous solution)

METHOD: OECD TG 475 Mammalian Bone Marrow Chromosome Aberration Test. EC Directive 1984 B.12 Mutagenicity – *in vivo* Mammalian Bone Marrow Cytogenetic Test.

Species/Strain: Rat/Sprague-Dawley
Route of Administration: Oral – gavage
Vehicle: Distilled water
Remarks - Method: The maximum tolerable dose for use in the metaphase test was chosen based on the results of a preliminary toxicity test.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5/sex	0	6, 24, 48
II (test substance)	5/sex	600	6, 24, 48
III (positive control, CP)	5/sex	40	24

CP=cyclophosphamide

RESULTS

Doses Producing Toxicity: Clinical signs of toxicity were observed with the test material at and above 600 m/kg bw including hunched posture, pilo-erection, ptosis, diarrhoea and pallor of the extremities.
Genotoxic Effects: None

CONCLUSION: The test substance was not clastogenic under the conditions of this *in vivo* bone marrow cytogenetic test.

TEST FACILITY: Huntingdon Research Centre (1987)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Analogue 1 (33% aqueous solution)
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Activated Sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen electrode to measure the dissolved oxygen
Remarks - Method	The test was conducted in accordance with the test guideline above with no significant deviation from the protocol reported.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation (BOD)*	*Day*	*% Degradation (BOD)*
5	59	5	76
15	74	15	82
28	75	28	82

Remarks - Results	Oxygen depletion was measured to be 2.8 mg/L, exceeding 1.5 mg/L, after 28 days in the inoculums blank. Therefore, the results may not be valid and the results should be treated with caution.
CONCLUSION	The test substance and, by inference, the notified chemical are readily biodegradable.
TEST FACILITY	Akzo (1989b)

C.1.2. Ready biodegradability

TEST SUBSTANCE	Analogue 1 (35% aqueous solution)
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Activated Sludge
Exposure Period	42 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen electrode to measure the dissolved oxygen
Remarks - Method	The test was conducted in accordance with the test guideline above with no significant deviation from the protocol reported.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation (BOD)*	*Day*	*% Degradation (BOD)*
14	90	7	42%
28	97		
42	97		

Remarks - Results	The biodegradability for the reference substance was determined to be 42% after 7 days and no further measurement was performed for longer incubation time period. Therefore, it is not clear whether the reference substance reach the pass level of ≥ 60% within 14 days and the validity for the test results is undetermined. The results should be treated with caution. The test substance was not considered to inhibit the bacterial activity at the

test concentration of 6.1 and 18.3 mg/L as the biodegradability for the toxicity controls was determined to be ≥ 25%.

CONCLUSION The test substance and, by inference, the notified chemical are readily biodegradable.

TEST FACILITY Akzo (1987)

C.1.3. Bioaccumulation

TEST SUBSTANCE Analogue 2 (98.2%)

METHOD Springborn Laboratories, Inc –"Evaluation of [Test substance] in a Dynamic Bioconcentration Study with Bluegill Sunfish, Protocol No. 121588/BG-BIOC.LONZA and protocol amendment #1

Species	Bluegill *(Lepomis macrochirus)*
Exposure Period	Exposure: 28 days Depuration: 18 days
Auxiliary Solvent	None
Concentration Range	Nominal: 59 µg/L Actual: 93 µg/L
Analytical Monitoring	Liquid scintillation spectrometer
Remarks - Method	A group of 40 fish were continuously exposed to the test substance in well water for 28 days. After that, the fish were transferred to uncontaminated water for 18 days for depuration. Samples were taken for analysis at day 0, 3, 4, 10, 11, 17, 24 and 28 for the exposure period and at day 3, 7, 14 and 18 for the depuration period.

RESULTS

Bioconcentration Factor	BCF = 38 in the edible tissue BCF = 140 in the non-edible tissue BCF = 81 in the whole body
CT50	Not determined
Remarks - Results	The concentration of ^{14}C-residues in all selected tissues (edible, non-edible and whole body) reached steady state at day 10 during the exposure period. During the exposure period, 7 and 5 fish were observed to be dead in the control and test, respectively. The mortality of fish for both the control and control exceed 10%. Therefore, the test does not meet the OECD validity criterion of less than 10%. The results should be treated with caution. After 14-day of depuration, the ^{14}C-residues present on the last day of exposure in the edible, non-edible and whole fish tissues had been eliminated by 57%, 71% and 67%, respectively, based on the analysis of the tissue portions of five fish. After 18 days of depuration, the ^{14}C-residues present on the last day of exposure in the edible, non-edible and whole fish tissues had been eliminated by 38%, 66% and 56%, respectively. Of the accumulated ^{14}C-residues in the edible tissue exposed to the test substance for 28 days, 65.5% was extractable with a polar solvent (methanol), 8.1% was extractable with a nonpolar solvent (hexane and 25.9% was not extractable with either solvent. After 28 days exposure, the ^{14}C-residues levels in skin tissue was determined to be higher than those observed for the corresponding edible tissues. These results indicated the test substance significantly bound to the skin and scales of the tested fish.

CONCLUSION The test substance and, by inference, the notified chemical have a low potential to bioaccumulate in fish.

TEST FACILITY Springborn (1990)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE Analogue 1 (33% aqueous solution)

METHOD ASTM Standard E729-80, Standard Practice For Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians – Static.

Species	Rainbow trout (*Salmo gairdneri*)
Exposure Period	96 hours
Auxiliary Solvent	none
Water Hardness	34 mg $CaCO_3$/L
Analytical Monitoring	N/A
Remarks – Method	A group of fish were exposed to the test media at different nominal concentrations of the test substance. The test substance was tested as 100% active ingredient. The mortality and physical characteristics of the tested fish were record after 24, 48, 72 and 96 hours exposure period. The temperature and pH of the test media were 12-13 °C and ~7.5. No significant deviation from the protocol was reported.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality (%)*			
Nominal	*Actual*		*24 h*	*48 h*	*72 h*	*96 h*
Control	-	10	0	0	0	0
0.39	-	10	0	0	0	0
0.67	-	10	0	0	0	10
1.09	-	10	0	0	0	0
1.82	-	10	0	0	0	0
3.03	-	10	100	100	100	100

LC50	0.77 mg active ingredient/L at 96 hours (95% confidence limit: 0.59 – 0.99 mg active ingredient/L)
NOEC	0.6 mg active ingredient/L at 96 hours.
Remarks – Results	The test was considered reliable as all validity criteria of the OECD test guideline were satisfied.

The 96 hours LC50 and NOEC were originally reported to be 2.35 and 1.82 mg/L, respectively, in the study. However, the results were based on the nominal concentrations of the test substance, which contained 33% of the active ingredient. The actual results for the LC50 and NOEC of the active ingredient were re-calculated based on the actual concentration of the active ingredient in the test media.

At the nominal test concentration of 0.67 mg/L, one of the surviving fish exhibited darkened pigmentation after 72 hours exposure.

At the nominal test concentration of 1.09 mg/L, one of the surviving fish exhibited darkened pigmentation after 24 and 48 hours exposure; two fish were observed to have darkened pigmentation after 72 hours exposure; one fish exhibited a complete loss of equilibrium and several fish exhibited darkened pigmentation after 96 hour exposure.

At the nominal test concentration of 1.82 mg/L, one of the surviving fish exhibited darkened pigmentation after 48 hours exposure; two fish were observed to have darkened pigmentation after 72 hours exposure; one fish exhibited a complete loss of equilibrium and several fish exhibited

darkened pigmentation after 96 hour exposure.

CONCLUSION The analogue and, by inference, the notified chemical are very toxic to fish.

TEST FACILITY Springborn (1988a)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Analogue 1 (33% aqueous solution)

METHOD ASTM Standard E729-80, Standard Practice For Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians – Static.

Species *Daphnia magna*

Exposure Period 48 hours

Auxiliary Solvent None

Water Hardness 160 mg $CaCO_3$/L

Analytical Monitoring N/A

Remarks - Method Twenty daphnia (5 daphnids per replicates) were exposed to the test media at different nominal concentrations of the test substance. The test substance was tested as 100% active ingredient. The immobilised daphnids were record at time 0, 24 and 48 hours. The temperature and pH of the test media were 20-21 °C and ~8.0. No significant deviation from the protocol was reported.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	0	0
0.236	-	20	0	4
0.394	-	20	1	19
0.667	-	20	17	20
1.09	-	20	20	20
1.82	-	20	20	20
3.03	-	20	20	20

EC50 0.09 mg active ingredient/L at 48 hours (95% confidence limit: 0.08-0.1 mg active ingredient/L)

NOEC < 0.08 mg active ingredient/L at 48 hours

Remarks - Results The test was considered reliable as all validity criteria of the OECD test guideline were satisfied.

The 48 hours EC50 and NOEC were originally reported to be 0.28 and < 0.24 mg/L, respectively, in the study report. However, the results were based on the nominal concentrations of the test substance, which contained 33% of the active ingredient. The actual results for the EC50 and NOEC of the active ingredient were recalculated based on the concentration of the active ingredient in the test media.

Throughout the 48 hours exposure, all daphnids which were not immobilised appeared normal when compared to the control.

CONCLUSION The analogue and, by inference, the notified chemical are very toxic to aquatic invertebrates.

TEST FACILITY Springborn (1988b)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical (35% aqueous solution)
METHOD	SOP104 and ISO10253 (2006) Water Quality - marine algal growth inhibition test
Species	*Skeletonema costatum*
Exposure Period	72 hours
Concentration Range	Nominal: 0.010, 0.032, 0.10, 0.32, 1.0 and 10 mg/L Actual: N/A
Auxiliary Solvent	None
Water Hardness (Salinity)	36‰
Analytical Monitoring	N/A
Remarks - Method	A 1000 mg/L stock solution was prepared in filtered seawater. The resulting mixture was stirred for one hour. The subsequent test concentrations were prepared by serial dilution of this stock solution. The test temperature was 20-21 °C and the pH of the test media was 8.02-8.73. No significant deviation from the protocol was reported.

RESULTS

Biomass		*Growth*	
E_bC50	*NOE_bC*	*E_rC50*	*NOE_rC*
mg/L at 72 h	*mg/Lat 72 h*	*mg/L at 72 h*	*mg/L at 72 h*
-	-	0.105	0.0112

Remarks - Results	All validity criteria for the test were satisfied. The 72 hours E_rC50 and NOE_rC were originally reported to be 0.30 and 0.032 mg/L, respectively, in the study. However, the results were based on the nominal concentrations of the test substance, which contained 35% of the active ingredient. Based on the information provided in the study, it is unclear whether the nominal concentrations were calculated for the test substance or for the active ingredient. Therefore, for the worst case scenario, the results for the E_rC50 and NOE_rC were recalculated assuming the nominal concentrations in the test media were reported for the test substance (35% active ingredient).
CONCLUSION	The notified chemical is very toxic to marine algae.
TEST FACILITY	Opus (2011)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Analogue 1 (35% aqueous solution)
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sludge
Exposure Period	3 hours
Concentration Range	Nominal: 3, 10, 30, 80 and 240 mg active ingredient /L Actual: N/A
Remarks – Method	Following a range finding test, the definitive test was conducted in accordance with the guidelines above. No significant deviations to protocol were reported. A blank control and reference (3,5-dichlorophenol) control were run in parallel.
RESULTS	
IC50	12.2 mg active ingredient/L at 3 hours (95% confidence limit: 10.1-14.4 mg active ingredient/L)
NOEC	Not reported

Remarks – Results	The validation criteria for the control respiration rates and reference material (3,5-dichlorophenol) EC_{50} were satisfied.
CONCLUSION	The analogue and, by inference, the notified chemical are inhibitory to bacterial respiration at concentration > 12.2 mg/L.
TEST FACILITY	Huntingdon Life Sciences (2004c)

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