File No: STD/1513 and STD1392 and STD1393

September 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

STD/1513: Glutamic acid, N,N-bis(carboxymethyl)-

STD/1392: Glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (1:1)

STD/1393: Glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (1:2)

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

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1513, STD/1392 and STD/1393	STD/1513: Akzo Nobel Pty Ltd STD/1392 and STD/1393: Akzo Nobel Pty Ltd and M-I Australia Pty Ltd	STD/1513: L-Glutamic acid, N,N-bis(carboxymethyl)- STD/1392: L-Glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (1:1) STD/1393: L-Glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (1:2)	ND*	STD/1513: ≤ 50 tonnes per annum STD/1392: < 20 tonnes per annum STD/1393: < 20 tonnes per annum	Components of water-based drilling fluids in offshore oil and gas production

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemicals are not recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemicals are not considered to pose an unreasonable risk to the health of workers.

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

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the reported use pattern, the notified chemicals are not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemicals:
  - Automated and enclosed processes, where possible

- 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 chemicals:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemicals:
  - Impermeable gloves

- Goggles
- Protective clothing
- Protective footwear

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 chemicals 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

- In the absence of an on-shore waste treatment plant as a disposal option, the notified chemicals should be disposed of to landfill.

Emergency procedures

- Spills or accidental release of the notified chemicals 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 chemicals 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 chemicals, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemicals are listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- products or fluids containing the notified chemicals are to be released directly to surface waters.

(2) Under Section 64(2) of the Act; if
- the function or use of the chemicals has changed from components of water based drilling fluids in offshore oil and gas production, or is likely to change significantly;
- the amounts of chemicals being introduced have increased, or is likely to increase, significantly;
- the chemicals have begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemicals 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 (STD/1513) (and products containing the notified chemicals (STD/1392 and STD/1393) provided by the notifier were reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

This notification has been conducted under the cooperative arrangement with Canada. The health and environmental hazard assessment components of the Canadian report were provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS and the Department of the Environment.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
STD/1513 and STD/1392 and STD/1393
Akzo Nobel Pty Ltd (ABN: 59 000 119 424)
8 Kellaway Place
WETHERILL PARK NSW 2164

STD/1392 and STD/1393
M-I Australia Pty Ltd (ABN: 67 009 214 162)
Level 11, 251 Adelaide Terrace
PERTH WA 6000

NOTIFICATION CATEGORY
STD/1513: Standard: Chemical other than polymer (more than 1 tonne per year) – Group Assessment.
STD/1392: Standard: Chemical other than polymer (more than 1 tonne per year) – Group Assessment.
STD/1393: Standard: Chemical other than polymer (more than 1 tonne per year) – Group Assessment.

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
STD/1513
EU REACH (2013)
Canada (2010)

STD/1392 and STD/1393
EU REACH (pre-registered in 2009)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Dissolvine GLZ-S (solid contains 89-92% STD/1513)
Dissolvine GZ-30-S (aqueous solution contains 28-32% STD/1513)
Dissolvine GZ-30-XL (aqueous solution contains 28-32% STD/1513)
Dissolvine GL-NA-36-S (aqueous solution contains 23-27% STD/1513)
Dissolvine StimWell HTF (aqueous solution contains 23-27% STD/1513)
Dissolvine GL-NA-33 (aqueous solution contains 30-50% STD1392 and STD1393)
Dissolvine GL-NA-40S (aqueous solution contains 40% STD1392 and STD1393)

CAS NUMBER
STD/1513: 58976-65-1
STD/1392: 282524-66-7
STD/1393: 65345-21-3

CHEMICAL NAME
STD/1513: L-Glutamic acid, N,N-bis(carboxymethyl)-
STD/1392: L-Glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (1:1)
STD/1393: L-Glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (1:2)

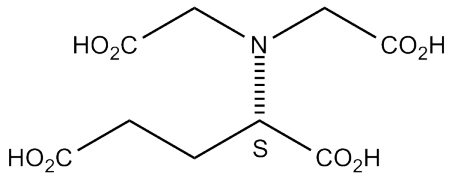
OTHER NAME(S)
STD1513
N,N-bis(carboxymethyl)-L-glutamic acid
Dicarboxymethyl-L-glutamic acid
GLDA
Glutamic acid, N,N-bis(carboxymethyl)-, L-
Glutamic acid-N,N-diacetic acid
L-Glutamic acid-N,N-di(acetic acid)
N,N-Bis(carboxymethyl) L-glutamic acid

STD/1392
L-Glutamic acid, N,N-bis(carboxymethyl)-, monosodium salt

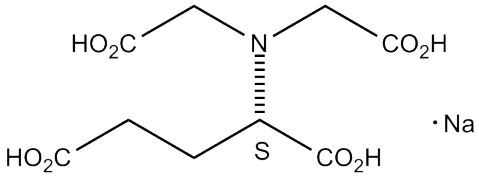
STD/1393
Glutamic acid, N,N-bis(carboxymethyl)-, disodium salt, L-
L-Glutamic acid, N,N-bis(carboxymethyl)-, disodium salt
L-Glutamic acid-N,N-di(acetic acid) disodium salt

MOLECULAR FORMULA
STD/1513: $C_9H_{13}NO_8$
STD/1392: $C_9H_{13}NO_8.Na$
STD/1393: $C_9H_{13}NO_8.2Na$

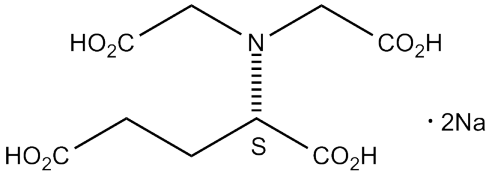
STRUCTURAL FORMULA
STD/1513:



STD/1392:



STD/1393:



MOLECULAR WEIGHT
STD/1513: 263.20 Da
STD/1392: 285.18 Da
STD/1393: 307.17 Da

ANALYTICAL DATA
Reference NMR, IR, HPLC spectra were provided for Analogue 1 (L-Glutamic acid, N,N-bis(carboxymethyl)-, tetra sodium salt, CAS No. 51981-21-6) (STD/1316, 2009).

3. COMPOSITION

DEGREE OF PURITY
STD/1513: 89-92%
STD/1392 and STD/1393: 90%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS

STD/1513

Chemical Name	Formic acid		
CAS No.	64-18-6	*Weight %*	1-2
Hazardous Properties	Conc. ≥ 90%: C; R35 10% ≤ Conc. < 90%: C; R34 2% ≤ Conc. < 10%: Xi; R36/38		

Chemical Name	Acetic acid, 2-hydroxy-		
CAS No.	79-14-1	*Weight %*	1-2
Hazardous Properties	Conc. ≥ 25%: C; R34; R20/22; R41; R37 20% ≤ Conc. < 25%: Xi; R36/37/38 10% ≤ Conc. < 20%: Xi; R36/38		

STD/1392 and STD/1393

Chemical Name	Sodium hydroxide		
CAS No.	1310-73-2	*Weight %*	0-1.9
Hazardous Properties	Conc. ≥ 5%: C; R35 2% ≤ Conc. < 5%: C; R34 0.5% ≤ Conc. < 2%: Xi; R36/38		

Chemical Name	Glycine, N,N-bis(carboxymethyl)- (or sodium salts)		
CAS No.[1]	139-13-9 (acid) 5064-31-3 (trisodium salt)	*Weight %*	1-3
Hazardous Properties[2]	Conc. ≥ 25%: Xn; R40; R22; R36 ≥ 20% Conc. < 25%: Xn; R40; R36 ≥ 5% Conc. < 20%: Xn; R40		

[1]Other CAS numbers for the salts include: 15467-20-6, 18994-66-6, 10042-84-9 or (for hydrates) 23255-03-0 or 18662-53-8.
[2]HSIS for the trisodium salt (5064-31-3). IARC (vol. 73; 1999) evaluation of nitrilotriacetic acid and its salts was that i) there is inadequate evidence in humans for the carcinogenicity of nitrilotriacetic acid and its salts; and ii) there is sufficient evidence in experimental animals for the carcinogenicity of nitrilotriacetic acid and its salts; with the overall evaluation that nitrilotriacetic acid and its salts are possibly carcinogenic to humans (Group 2B).

Chemical Name	Acetic acid, 2-hydroxy (or sodium salt)		
CAS No.	79-14-1 (acid) 2836-32-0 (salt)	*Weight %*	3-5
Hazardous Properties[1]	Conc. ≥ 25%: C; R34; R20/22; R41; R37 20% ≤ Conc. < 25%: Xi; R36/37/38 10% ≤ Conc. < 20%: Xi; R36/38		

[1]HSIS for Acetic acid, 2-hydroxy (79-14-1).

Chemical Name	Formic acid (or sodium salt)		
CAS No.	64-18-6 (acid) 141-53-7 (salt)	*Weight %*	0.5-1
Hazardous Properties[1]	Conc. ≥ 90%: C; R35 ≥ 10% Conc. < 90%: C; R34 ≥ 2% Conc. < 10%: Xi; R36/38		

[1]HSIS for Formic acid (64-18-6).

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)
STD/1513

Chemical Name	Water		
CAS No.	7732-18-5	*Weight %*	0-10

STD/1392 and STD/1393

Chemical Name	L-Glutamic acid, N-carboxymethyl-, sodium salt		
CAS No.	-	*Weight %*	1-2

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: white free-flowing crystals

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	Decomposes at ~ 140-190 °C prior to melting analogue data[1]
Boiling Point	Not determined	Decomposes at ~ 140-190 °C prior to boiling - analogue data[1]
Density	~1,350 kg/m^3 at 20 °C	Analogue data[1]
Vapour Pressure	0.08 kPa at 20 °C	Analogue data[2]
Water Solubility	~ 500 g/L at 20°C	Analogue data[2]
Hydrolysis as a Function of pH	Stable at pH 4, 7 and 9	The notified chemicals contain no readily hydrolysable functionality
Partition Coefficient (n-octanol/water)	log Pow = - 12 at 20°C	Estimated for the analogue[2]. The negative value reflects the high water solubility and low solubility in lipids (< 0.1%).
Adsorption/Desorption	Not determined	The notified chemicals may associate to soil via chelating to divalent metal ions despite of the hydrophilicity.
Dissociation Constant	pKa = 9.36, 5.03, 3.49 and 2.56	Analogue data[2]. The notified chemicals are expected to be ionised in the environmental pH range of 4-9.
Particle Size	≤ 400 µm *Particle size distribution:* ≤ 240 µm: 90% ≤ 142 µm: 50% ≤ 68 µm: 10%	Analogue data[2]
Flash Point	Not determined	Expected to be high based on the predicted low vapour pressure and high melting points
Autoignition Temperature	> 600 °C	Analogue data[2]
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidative properties

[1] Read-cross data from Analogue 1, L-Glutamic acid, N, N-bis(carboxymethyl)-, sodium salt (CAS No. 302337-35-5) (Canadian report)
[2] Read-cross data from Analogue 1, L-Glutamic acid, N, N-bis(carboxymethyl)-, tetrasodium salt (CAS No. 51981-21-6) (STD/1316, 2009)

DISCUSSION OF PROPERTIES

Reactivity
The notified chemicals are expected to be stable under normal conditions of use. Avoid contact with strong oxidisers, aluminium, nickel, zinc, copper alloys and store in PVC, PE, stainless steel or bituminised tanks.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemicals are 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
STD/1513
The notified chemical will be imported as a component of an aqueous formulation at a concentration of up to 35%, contained in 250 kg plastic drums or 1100 kg (net) intermediate bulk containers (IBC).

STD/1392 and STD/1393
The notified chemicals will be imported as components of an aqueous formulation at a concentration of up to 50%, contained in 250 kg plastic drums or 1100 kg (net) IBC.

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

	Year	*1*	*2*	*3*	*4*	*5*
STD/1513	*Tonnes*	5-50	5-50	5-50	5-50	5-50
STD/1392	*Tonnes*	< 20	< 20	< 20	< 20	< 20
STD/1393	*Tonnes*	< 20	< 20	< 20	< 20	< 20

PORT OF ENTRY
Perth, Darwin, Brisbane, Sydney, Melbourne and Hobart

IDENTITY OF RECIPIENTS
STD/1513: Akzo Nobel Pty Ltd
STD/1392 and STD/1393: Akzo Nobel Pty Ltd and M-I Australia Pty Ltd

TRANSPORTATION AND PACKAGING
STD/1513
The notified chemical will be imported in products with dangerous goods classification of Class 8, UN3265 Corrosive liquid, acidic, organic, n.o.s. Therefore, the products will be transported and stored in accordance with Australian Code for the Transport of Dangerous Goods (NTC, 2007). The notified chemical will be imported in 250 kg plastic drums or 1,100 kg (net) IBC. The notified chemical will be transported to the offshore platforms by boat/barge in the original containers.

STD/1392 and STD/1393
The notified chemicals will be imported in products in 250 kg plastic drums or 1,100 kg (net) IBC. The imported product is not classified as Dangerous Goods.

USE
The notified chemicals will be used as components in water-based drilling fluids in offshore oil and gas production.

OPERATION DESCRIPTION
The notified chemicals will not be manufactured, reformulated or repacked in Australia. At end-use sites (offshore drilling platforms), the products containing the notified chemicals will be weighed and transferred manually or pumped directly into the tanks through enclosed piping to a hopper where they will be mixed with other components to achieve a concentration of up to 2% for any of the notified chemicals. The notifier has stated that the operation area is expected to be ventilated. The resulting breaker fluid will then be pumped into the well through enclosed pipes. Spent, unused and wash fluids will be transferred to enclosed tanks for proper 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 and warehouse	2-8	20
Rig operators/chemical handling	2	200

EXPOSURE DETAILS

Transport and storage workers may come into contact with the notified chemicals only in the event of accidental rupture of packaging.

During mixing of the product into breaker fluids, workers will manually weigh and transfer the products containing the notified chemicals at up to 35% concentration (STD1315) or at 30-50% concentration (STD1392 and STD1393) to the hopper, or transfer it using pumping equipment. Mixing may lead to dermal and ocular exposure. Inhalation exposure is not expected, given the predicted low vapour pressure of the notified chemicals. The notifier states in the notification dossier that workers will wear appropriate personal protective equipment (PPE) such as impermeable gloves, eye protection and coats to minimise dermal and ocular exposure.

Workers may also encounter dermal and ocular exposure to the notified chemicals at up to 2% each in breaker fluids, when they are returned to the surface. The notifier states in the notification dossier that such exposure will be minimised by the use of PPE such as impermeable gloves, eye protection and overalls.

6.1.2. Public Exposure

The notified chemicals will be used in industrial settings only and will not be sold to the public. Therefore, public exposure to the notified chemicals is not expected.

6.2. Human Health Effects Assessment

The majority of the toxicological data were provided for an acceptable analogue of the notified chemicals (Analogue 1), L-Glutamic acid, N,N-bis(carboxymethyl)-, tetrasodium salt (CAS No. 51981-21-6). The data were previously assessed by NICNAS as STD/1316. The abovementioned toxicological data on the tetrasodium salt is also discussed in the Canadian assessment for L-glutamic acid, N,N-bis(carboxymethyl)-, sodium salt (CAS No. 302337-35-5, NSN 15812).

Additional studies on Analogue 1 were also provided in the submission of the notified chemicals. For full details of the studies, refer to Appendix A.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity[1]	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute dermal toxicity[2]	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute inhalation toxicity[2]	LC50 > 4.2 mg/L/4 hours; low toxicity
Rabbit, skin irritation[1]	slightly irritating
Rabbit, eye irritation[1]	slightly irritating
Guinea pig, skin sensitisation – adjuvant test[1]	no evidence of sensitisation
Rat, repeat dose oral toxicity – 90 days[1]	NOAEL = 300 mg/kg/day
Mutagenicity – bacterial reverse mutation[1]	non mutagenic
Genotoxicity – *in vitro* mammalian cell gene mutation test[1]	non genotoxic
Genotoxicity – *in vitro* mammalian chromosome aberration test[1]	weakly genotoxic/equivocal at high doses
Genotoxicity – *in vivo*, micronucleus test[1]	non genotoxic
Rabbit, oral prenatal developmental toxicity[2]	maternal NOAEL = 30 mg/kg/day developmental NOAEL = 300 mg/kg/day

Rat, oral two-generation reproduction toxicity[2]	NOAEL > 908 – 1141 mg/kg/day(males) NOAEL > 1230 – 2668 mg/kg/day(females)

[1] Read-cross data from L-Glutamic acid, N, N-bis(carboxymethyl)-, tetrasodium salt (CAS No. 51981-21-6) (Canadian report) (STD/1316, 2009)
[2] Read-cross data from L-Glutamic acid, N, N-bis(carboxymethyl)-, tetrasodium salt (CAS No. 51981-21-6) (Appendix A)

Toxicokinetics, metabolism and distribution.
No data on toxicokinetics for the notified chemicals were provided. Based on the low molecular weights (< 500 Da), the notified chemicals have a potential to be dermally absorbed after exposure. However, the potential may be reduced to some extent given the estimated low partition coefficients of the notified chemicals (log Pow = -12 at 20 °C for Analogue 1).

Acute toxicity.
No acute toxicity data for the notified chemicals were submitted. Analogue 1 was found to be of low acute oral toxicity in rats (LD50 > 2000 mg/kg bw) and of low acute dermal toxicity in rats (LD50 > 2000 mg/kg bw). Analogue 1 was found to be of low acute inhalation toxicity in rats (LC50 > 4.2 mg/L/4 hours).

Irritation and sensitisation.
No irritation or sensitisation data for the notified chemicals were submitted. Analogue 1 was found to be slightly irritating to eyes and skin but not a sensitiser.

Analogue 1 is a tetrasodium salt of STD/1513 which is an acid. STD/1513 may cause a greater degree of irritation than its sodium salt. In addition, the impurities (acetic acid, 2-hydroxy- and formic acid) are classified as irritants. Indeed, the MSDS of STD/1513 states that the notified chemical may cause skin, eye and respiratory tract irritation. The degrees of irritation of STD/1392 and STD/1393 are expected to be between those of Analogue 1 and STD1513.

Repeated dose toxicity.
No repeated dose toxicity data for the notified chemicals were submitted. In a 90-day repeated dose oral toxicity study in rats for Analogue 1, the No Observed Adverse Effect Level (NOAEL) was established to be 300 mg/kg bw/day.

Mutagenicity/Genotoxicity.
No mutagenicity/genotoxicity data for the notified chemicals were submitted. Analogue 1 was negative in a bacterial reverse mutation assay, in an *in vitro* mammalian gene forward mutation test in Chinese hamster ovary (CHO) cells, and in an *in vivo* micronucleus test using mice bone marrow. Analogue 1 showed a small but statistically significant increase in aberrant cells at the highest doses (1825 and 3650 μg/ml) in an *in vitro* mammalian chromosome aberration test on Chinese hamster lung (CHL) cells.

Toxicity for reproduction.
No reproduction toxicity data for the notified chemicals were submitted. The NOAEL for maternal toxicity for Analogue 1 was established to be 30 mg/kg bw/day, based on the occurrence of mortalities, clinical signs and reduced body weights and food consumption. The NOAEL for developmental effects was established to be 300 mg/kg bw/day, based on the absence of fetal malformations or developmental variations.

Toxicity for development.
No developmental toxicity data for the notified chemicals were submitted. A preliminary NOAEL for parental toxicity for Analogue 1 was established to be > 908-1141 mg/kg bw/day for males and 1230-2668 mg/kg bw/day for females, based on the interim findings in P-generation and F1-generation. A preliminary NOAEL for prenatal development toxicity for Analogue 1 was established to be > 908-1141 mg/kg bw/day for males and 1230-2668 mg/kg bw/day for females, based on the interim findings in P-generation and F1-generation.

Health hazard classification
Based on the available information, the notified chemicals are not recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on the read-across data the notified chemicals are expected to be of low acute toxicity, non-sensitising and are not expected to be genotoxic or reproductive and developmental toxicants. However, the notified chemicals may be irritating to the eye and skin.

During mixing of the product into breaker fluids, exposure of workers to the products containing the notified chemicals is expected to be limited, due to the largely enclosed/automated production processes. There is a greater potential for dermal and ocular exposure to the notified chemicals at up to 35% concentration (STD1315) or at 30-50% concentration (STD1392 and STD1393) when manually weighing and transferring the products containing the notified chemicals to the hopper. The notifier stated use of appropriate personal protective equipment (PPE) such as impermeable gloves, eye protection and protective clothing and footwear should minimise such exposure.

Exposure (dermal and ocular) of workers to the notified chemicals at up to 2% each when handling breaker fluids returned to the surface is expected to be mitigated by the notifier stated use of PPE such as impermeable gloves, eye protection and coveralls.

Given the stated controls in place and the use of PPE to minimise 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 chemicals as they are used in industrial settings only. Therefore, the risk to health of the public 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 chemicals will be imported as a component of end products for water-based drilling fluids in offshore oil and gas production. No further reformulation of the notified chemicals is expected to occur in Australia. Significant release of the notified chemicals to the environment is not expected to occur from storage and transportation.

RELEASE OF CHEMICAL FROM USE

According to the notifier, all of the notified chemicals will be used on offshore rigs typically for production facilities. At offshore drilling platforms, the products containing the notified chemicals will be weighed and transferred manually or pumped directly into the tanks through enclosed piping to a hopper. In this process the chemicals will be mixed with other components. Approximately 2 tonnes of the notified chemicals may be used during a single operation in a liquid formulation at concentrations < 5%. The resulting breaker fluid will then be pumped into the well through enclosed pipes. The notified chemicals react with the $CaCO_3$ in the filter cake which are dissolved in this way. The residual and spent notified chemicals may reside in the aqueous phase in the well for a temporary period. Subsequently, the chemicals may flow back to the surface with produced fluids and solids. The solids are most likely to be treated via gravity type separation equipment for onsite disposal to the ocean. It is estimated by the notifier that of the > 95% notified chemicals recovered from the wells, about 50% of the spent chemicals will remain on-board and be reused in grey water. The remaining 50% will be taken on-shore and put through a waste water treatment plant (WWTP).

RELEASE OF CHEMICAL FROM DISPOSAL

The notifier advised that the spent, unused and wash fluids containing the notified chemicals will be transferred to enclosed tanks for proper disposal to landfill or, in the worst case, to a WWTP.

7.1.2. Environmental Fate

The notified chemicals are readily biodegradable. For the details of the environmental fate studies please refer to STD/1316. They are not expected to have bioaccumulation potential given their high water solubility.

A small portion (< 5%) of the notified chemicals may associate to the solids (produced from wells) via chelating and are expected to be disposed of to the ocean sediment. About 50% of the chemicals recovered from each application are expected to remain in grey water for reuse and 50% will be treated onshore in WWTPs. A small amount of the chemicals may be collected as spills and residues and also be disposed of to a WWTP, in the worst case scenario. In the WWTP, some of the chemicals may chelate with the metal cations and form insoluble precipitates that will settle out into sludge, which is expected to be sent to landfill.

In water or soil/sediment environments, the notified chemicals are expected to undergo biodegradation or abiotic degradation, forming water, inorganic salts, and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated as shown below assuming that, per application (2 tonnes), 100% of the used chemicals flow back to surface and 50% of these chemicals is sent back to land for on-shore treatment in a local WWTP. Using a log K_{OW} of 0.0, which is the input minimum value for SimpleTreat model (EC, 2003), a removal of 87% via biodegradation was predicted and used in the following calculations. A flow rate of 40 ML/day was used for a local WWTP according to the notifier's information. It is assumed for the worst case that the waste water for one single operation is treated in one day in a local WWTP.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	2,000	kg/year
Proportion expected to be released to sewer	50%	
Annual quantity of chemical released to sewer	1000	kg/year
Days per year where release occurs	1	days/year
Daily chemical release:	1000	kg/day
Individual Sewage Treatment Plant Average Daily Flow:	40	ML/day
Removal within STP	87%	**Mitigation**
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	3250	µg/L
PEC - Ocean:	325	µg/L

WWTP effluent re-use for irrigation may occur throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 3.25 mg/L may potentially result in a soil concentration of approximately 21.65 mg/kg. Assuming accumulation of the notified chemicals in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemicals in the applied soil in 5 and 10 years may be approximately 108.5 mg/kg and 216.5 mg/kg, respectively.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on an analogue (the notified chemical in STD/1316) are summarised in the table below. Details of these studies can be found in Appendix B and STD/1316. The test chemical is considered to be an acceptable analogue for the notified chemicals.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (*Cyprinodon variegatus* j.)	96 h LC50 > 76 mg/L	Potentially harmful
Fish Toxicity *(Oncorhynchus mykiss)*	96 h LC50 > 70.7 mg/L	Not harmful
Invertebrate Toxicity (*Acartia tonsa*)	48 h LC50 > 170 mg/L	Not harmful
Invertebrate Toxicity *(Daphnia magna)*	48 h LC50 > 70.7 mg/L	Not harmful
	21 d NOEC = 265 mg/L	Not harmful
Algal Toxicity (*Skelelonema costatum*)	72 h ErC50 > 1000 mg/L NOEC = 1000 mg/L	Not harmful
Algal Toxicity (*Scenedesmus subspicatus*)	72 h ErC50 > 100 mg/L	Not harmful
Inhibition of Bacterial Respiration	0.5 h IC50 > 412 mg/L	Not harmful

Dose responses are observed in the test for *Cyprinodon variegatus* j. (20% mortality observed at 76 mg/L) and *Acartia tonsa* (15% immobilised at 170 mg/L). Based on the above data for the acceptable analogue chemical, the notified chemicals are considered to be potentially harmful to aquatic species. Considering the low effects at the top test concentrations, the notified chemicals may be not harmful to aquatic organisms. Therefore, the

notified chemicals are not classified under the Globally Harmonised System of Classification (GHS) and Labelling of Chemicals (United Nations, 2009) on acute and chronic bases.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) for fresh water organisms has not been calculated because the notifier indicated no direct release to surface waters. The PNEC for marine species has been calculated by using the endpoint of 76 mg/L for marine fish. This is considered to be the most sensitive species since dose responses were observed up to the concentration of 76 mg/L. A safety factor of 100 was used since endpoints for three trophic levels were available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish).	> 76	mg/L
Assessment Factor	100	
PNEC:	> 760	µg/L

7.3. Environmental Risk Assessment

The notified chemicals are for offshore application only. In addition, the used notified chemicals are expected to be sent back with grey water to a coastal WWTP for treatment. The effluent after treatment is expected to be discharged directly to the ocean. Additionally, a PNEC for fresh water organisms has not been calculated. Therefore, the risk quotient (Q = PEC/PNEC) has been calculated for treated effluent discharge to marine water only.

Risk Assessment	PEC (µg/L)	PNEC (µg/L)	Q
Q - Ocean:	325	> 760	< 0.43

The risk quotient (Q = PEC/PNEC) in the marine environment is less than 1. This indicates a low risk for marine aquatic organisms from exposure to the waste water treatment plant effluent associated with the waste notified chemicals. The predicted Q value was for conservative scenario since removal of the notified chemicals by associating to waste solids from wells or sludge via chelating to divalent metal ions were not considered.
Based on the assessed use pattern, the notified chemicals are not expected to pose an unreasonable risk to the marine environment.

APPENDIX A: TOXICOLOGICAL INVESTIGATIONS

A.1. Acute toxicity – dermal

TEST SUBSTANCE	Analogue 1
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test. EC Council Regulation No 440/2008 B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	Rat/Wistar Han
Vehicle	Millipore water
Type of dressing	Occlusive
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3F	2000	0/3
2	2F and 5M	2000	0/7

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	Scales and/or scabs were noted on the treated skin area of 4 female animals from Day 3 to Day 9.
Signs of Toxicity - Systemic	Flat and/or hunched posture, piloerection and/or chromodacryorrhea were noted in all animals from Day 1 to Day 4.
Effects in Organs	No abnormalities were found at macroscopic post mortem examination.
CONCLUSION	The test substance is of low toxicity via the dermal route.
TEST FACILITY	Notox (2009a)

A.2. Acute toxicity – inhalation

TEST SUBSTANCE	Analogue 1
METHOD	OECD TG 403 Acute Inhalation Toxicity.
Species/Strain	Rat/Wistar WU
Vehicle	Water
Method of Exposure	Nose-only exposure
Exposure Period	Four hours
Physical Form	Liquid aerosol
Particle Size	2.8 μm (MMAD) with a geometric standard deviation of 2.7
Remarks - Method	No significant protocol deviations. During preliminary experiments it was noted by the study authors that at concentrations greater than 4.3 g/m^3 the particle size increased rapidly and the efficiency of generating the aerosol decreased. The target concentration for the test substance in the study was 5 g/m^3.

RESULTS

Group	*Number and Sex of Animals*	*Concentration g/m^3*		*Mortality*
		Nominal	*Actual*	
1	5 per sex	33.3	4.2	0/10

LC50	> 4.2 mg/L/4 hours
Signs of Toxicity	Shortly after exposure, a slightly or moderately soiled fur of the head, neck, back and/or abdomen was noted in all animals and persisted for 1-4 days. In addition, slight sniffing was noted in 2 male animals and 2 female

	animals. One male animal exhibited a discharge from the eyes on Day 1. All clinical signs were fully reversible within the 14-day observation period.
Effects in Organs	No macroscopic abnormalities were noted at necropsy.
Remarks - Results	The body weights were within the range commonly recorded for this strain and age of rats. Although the target test concentration was not reached this was due to it not being technically feasible to generate respirable particles above 4.3 g/m^3. Therefore, it is unlikely that the test substance would be able to be delivered in an aerosolised form at the target concentration in a way that would be toxic to the test animals.
CONCLUSION	The test substance is of low toxicity via inhalation.
TEST FACILITY	TNO (2009)

A.3. Developmental toxicity

TEST SUBSTANCE	Analogue 1
METHOD	OECD TG 414 Prenatal Developmental Toxicity Study.
Species/Strain	Rabbit/New Zealand White
Route of Administration	Oral – gavage
Exposure Information	Exposure days: 22 days (days 7-28 post-coitum, inclusive) Post-exposure observation period: None
Vehicle	Water
Remarks - Method	The study was designed to evaluate the effects of the test item on embryonic and foetal development. Females were euthanized before delivery, on Day 29 post-coitum. All animals were subjected to a full external and internal examination and any macroscopic abnormalities were recorded. The ovaries and uterine horns were removed and examined for the number of corpora lutea, gravid uterus weight, number and distribution of live and dead foetuses and embryo-fetal deaths, foetal weight, foetal sex and external foetal appearance. External, visceral and skeletal fetal findings were recorded as developmental variations or malformations. Groups 2-4 received the standard diet containing 87.5 mg of zinc/kg diet. The diet of Group 5 animals contained 554 mg of zinc/kg diet. The additional dietary zinc was added to the study to compensate for possible effects due to the chelation of zinc by the test substance.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	24	0 (vehicle control)	0/24
2	24	30	0/24
3	24	100	2/24
4	24	300	3/24
5	24	300 (additional zinc supplementation in diet)	3/24

Mortality and Time to Death

There were no deaths in groups 1 and 2. Two animals (non-pregnant) died in group 3 (100 mg/kg/day) on days 22 and 28 post-coitum, respectively. In Group 4 deaths occurred on days 8 (non-pregnant), 16 (pregnant) and 26 (pregnant-early delivery) post-coitum. In Group 5 deaths occurred on days 17 (non-pregnant), 21 (non-pregnant) and 21 (pregnant) post-coitum.

Effects on Dams

An increase in the incidence of dark faeces and reduced faeces volume were observed in Groups 3-5. Food

consumption was decreased in these groups, but reduced body weight gain was only noted in the 300 mg/kg bw /day groups. Haematology showed evidence of anaemia in group 5 (zinc supplemented).

No treatment-related effects on clinical biochemistry and urinalysis parameters were noted. There were no treatment-related macroscopic findings.

An increase number of non-pregnant females was noted in all treated groups but no dose relationship was noted. Therefore, the higher number of non-pregnant females in the treated groups was not considered by the study authors to have been treatment-related.

Effects on Foetus

No effects were noted on number of corpora lutea, implantation sites, viable or dead foetuses, early or late resorptions, pre- and post-implantation loss, litter size or sex ratio. Fetal body weights were decreased in group 5 (zinc supplemented) and was likely to be due to maternal toxicity in this group. Fetal morphology was unremarkable.

Remarks - Results

The addition of zinc was not necessary to compensate for possible (repro-)toxic effects due to the chelating (zinc-binding) properties of the test substance.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) for maternal toxicity was established as 30 mg/kg bw/day, based on the occurrence of mortalities, clinical signs and reduced body weights and food consumption.

The NOAEL for developmental effects was established as 300 mg/kg bw/day, based on the absence of fetal malformations or developmental variations.

TEST FACILITY Notox (2009b)

A.4. Toxicity to reproduction – two generation study

TEST SUBSTANCE Analogue 1

METHOD OECD TG 416 Two Generation Reproduction Toxicity Study.

Species/Strain Rat/Wistar Han

Route of Administration Oral – diet

Exposure Information Exposure period - female: 10 weeks prior to mating through to termination
Exposure period - male: 10 weeks prior to mating through to termination

Vehicle Water

Remarks - Method Interim Report – Does not include F1 generation results.

Groups 2-4 of P-generation received the standard diet containing 88.6-93.5 mg of zinc/kg diet. The diet of Group 5 of P-generation contained 605-609 mg zinc/kg diet. The additional dietary zinc was added to the study to compensate for possible effects due to the chelation of zinc by the test substance. The diet of F1-generation did not contain additional zinc.

Generation	*Group*	*Number and Sex of Animals*	*Dose/Concentration <ppm>*
P	1	24 M + 24F	0
	2	24 M + 24F	1,500
	3	24 M + 24F	5,000
	4	24 M + 24F	15,000
	5	24 M + 24F	15000 (additional zinc supplementation in diet)
F1	1	24 M + 24F	0
	2	24 M + 24F	1,500
	3	24 M + 24F	5,000
	4	24 M + 24F	15,000

RESULTS

Mortality and Time to Death

There were no deaths in all the test groups of the P-generation.

Effects on Parental (P) animals:

No treatment-related clinical signs were noted. No adverse effects on body weight, body weight gain, food consumption, haematology, clinical biochemistry and urinalysis parameters, macroscopy or organ weights were noted at all dose levels.

Mating performance, the mean number of implantation sites, duration of gestation and fertility parameters were unaffected by treatment in all of the test groups.

There were no adverse effects on breeding parameters in all of the treatment groups.

Effects on 1st Filial Generation (F1)

There were no treatment-related effects on skeletal morphology at all dose levels.

Remarks – Results

The addition of zinc was not necessary to compensate for possible (repro-)toxic effects due to the chelating (zinc-binding) properties of the test substance.

CONCLUSION

A preliminary NOAEL for parental toxicity was established to be 15,000 ppm (908-1,141 mg/kg bw/day for males and 1,230-2,668 mg/kg bw/day for females), based on the interim findings in P-generation and F1-generation.

A preliminary NOAEL for prenatal development toxicity was established to be 15,000 ppm (908-1,141 mg/kg bw/day for males and 1,230-2,668 mg/kg bw/day for females, based on the interim findings in P-generation and F1-generation.

TEST FACILITY Notox (2009c)

APPENDIX B: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

B.1. Ecotoxicological Investigations

B.1.1. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Analogue Chemical
METHOD	OECD TG 211 *Daphnia magna,* Reproduction Test (1998) – Semi static
Species	*Daphnia magna*
Exposure Period	21 d
Auxiliary Solvent	None
Water Hardness	78.9 – 85.7 mg Ca^{2+}/L
Analytical Monitoring	Concentrations were determined by HPLC with UV detection
Remarks - Method	The test was conducted following the above test guideline and good laboratory practice (GLP). The test solutions were renewed three times each week over the duration of the test. The lowest observed effect concentration (LOEC) was determined using Dunnett's and Bonferroni-t tests, and the no observed effect concentration (NOEC) was determined based on these results.

Nominal concentration, average number of offspring released and standard deviations and mean length of parental daphnids.

	Nominal (mg/L)					
Test Day 21	*Control*	*5.*	*13.5*	*36.5*	*98.4*	*265.7*
Mean number of mobile offspring released (± standard deviation) per survivor	85 (±19)	72 (±10)	78 (±9)	72 (±13)	98 (±15)	125 (±12)
No. of adult *Daphnids* Immobilised	1	0	1	3	2	3
Mean adult daphnid length (mm)	6.4	6.2	6.4	6.2	6.4	6.9

21 day NOEC (reproduction) 265.7 mg/L

Remarks - Results	The test validity criteria wet met. The measured concentrations were determined to be within 80-120% of the nominal values. Therefore, the effects data are based on the nominal concentrations. There were no effects observed on reproduction or parental length in test solutions up to the highest concentration. No EC50 could be calculated because 50% parent mortality was not reached. The test substance is considered as an acceptable analogue for the notified chemicals.
CONCLUSION	The test substance and, by inference, the notified chemicals are not harmful to daphnids on a chronic basis
TEST FACILITY	Akzo Nobel (2009)

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