

File No: STD/1652, STD/1653 & STD/1654

November 2018

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME  
(NICNAS)**

**PUBLIC REPORT**

**STD/1652: Chemical 1 in Evonik and Redox cleaning products**

**STD/1653: Chemical 2 in Evonik and Redox cleaning products**

**STD/1654: Chemical 3 in Evonik and Redox cleaning products**

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment and Energy.

This Public Report is available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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## 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/1652             | Redox Pty Ltd    | Chemical 1 in Evonik and Redox cleaning products | Yes                | ≤ 80 tonnes per annum | Ingredient in household and personal care products |
| STD/1653             | Evonik Australia | Chemical 2 in Evonik and Redox cleaning products |                    |                       |                                                    |
| STD/1654             |                  | Chemical 3 in Evonik and Redox cleaning products |                    |                       |                                                    |

## CONCLUSIONS AND REGULATORY OBLIGATIONS

### Hazard classification

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

| <i>Hazard classification</i>                     | <i>Hazard statement</i>              |
|--------------------------------------------------|--------------------------------------|
| Serious eye damage /Eye irritation (Category 2A) | H319 – Causes serious eye irritation |

### Human health risk assessment

Provided that the recommended controls are being adhered to, 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, the notified chemicals are not considered to pose an unreasonable risk to the environment.

### Recommendations

#### REGULATORY CONTROLS

##### Hazard Classification and Labelling

- The notified chemicals should be classified as follows:
  - Serious eye damage/eye irritation (Category 2A): H319 – Causes serious eye irritation

#### 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 during reformulation:
  - Enclosed, automated processes, where possible
  - Adequate ventilation
- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemicals during reformulation:

- 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 during reformulation:
  - Protective clothing
  - Impervious gloves
  - Safety glasses
  - Respiratory protection, if inhalation exposure may occur

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

- A copy of the SDS should be easily accessible to employees.
- If products and mixtures containing the notified chemicals are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

#### Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemicals in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

#### 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 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 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
  - the concentration of the notified chemicals (combined) exceeds or is intended to exceed 1.5%
  - The notified chemicals are intended to be used in cosmetic products.or
- (2) Under Section 64(2) of the Act; if
  - the function or use of the chemicals has changed from household and personal care products ingredient, or are likely to change significantly;
  - the amount of chemicals being introduced has 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.

*Safety Data Sheet*

The SDS of the notified chemicals provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

## ASSESSMENT DETAILS

### 1. APPLICANT AND NOTIFICATION DETAILS

#### APPLICANT(S)

Redox Pty Ltd (ABN: 92 000 762 345)  
2 Swettenham Road  
MINTO NSW 2566

Evonik Australia Pty Ltd (ABN: 31 145 739 608)  
1 Ricketts Road  
MOUNT WAVERLY VIC 3149

#### NOTIFICATION CATEGORY

Standard: Chemical other than polymer (more than 1 tonne per year) – Group assessment

#### EXEMPT INFORMATION (SECTION 75 OF THE ACT)

Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, additives/adjuvants, import volume, site of manufacture/reformulation and identity of manufacturer.

#### VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)

Variation to the schedule of data requirements is claimed for all physico-chemical endpoints.

#### PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)

None

#### NOTIFICATION IN OTHER COUNTRIES

STD/1652: EC (2016)

STD/1653: EC (2010)

STD/1654: EC (2010)

### 2. IDENTITY OF CHEMICAL

#### MARKETING NAME(S)

STD/1652: Chemical 1 in Evonik and Redox cleaning products (contains  $\leq 50$  % concentration of Chemical 2 and Chemical 3 together)

STD/1653: Chemical 2 in Evonik and Redox cleaning products

STD/1654: Chemical 3 in Evonik and Redox cleaning products

#### MOLECULAR WEIGHT

STD/1652:  $< 500$  g/mol

STD/1653:  $< 500$  g/mol

STD/1654:  $< 500$  g/mol

#### ANALYTICAL DATA

Reference NMR, IR, HPLC, UV spectra were provided.

### 3. COMPOSITION

#### DEGREE OF PURITY

STD/1652:  $\leq 50$  % (Chemical 2 and Chemical 3 together)

STD/1653: Unknown

STD/1654: Unknown

#### 4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Yellowish liquid (aqueous solution)\*

| Property                                | Value                                   | Data Source/Justification                                                                                                                    |
|-----------------------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Melting Point/Freezing Point            | -50 °C to - 20 °C                       | Analogue B data                                                                                                                              |
| Boiling Point                           | Aqueous Solution ~105 °C*               | SDS*<br>Analogue B data (boiling of analogue B was not observed below the temperature at which reaction and/or decomposition started 250 °C) |
| Density                                 | 1,070-1,090 kg/m <sup>3</sup> at 20 °C* | SDS*                                                                                                                                         |
|                                         | 1,140 kg/m <sup>3</sup> at 20 °C        | Analogue B data                                                                                                                              |
| Vapour Pressure                         | 2.758 kPa at 25 °C (or 20 °C)           | Analogue B data                                                                                                                              |
| Water Solubility                        | 4.9 g/L at 20 °C                        | Measured*                                                                                                                                    |
| Hydrolysis as a Function of pH          | Not determined                          | Contains hydrolysable functionalities but significant hydrolysis is not expected in the environmental pH range of 4-9.                       |
| Partition Coefficient (n-octanol/water) | log P <sub>ow</sub> = -3.3 at 20 °C     | Analogue A data                                                                                                                              |
| Surface Tension                         | 26.32-42.82 mN/m at 20 °C               | Measured*                                                                                                                                    |
| Adsorption/Desorption                   | Not determined                          | Could bind to soil and sediments through hydrophobic and ion exchange mechanisms.                                                            |
| Dissociation Constant                   | Not determined                          | Contains ionisable functionalities which are likely to be ionised in the environmental pH range of 4-9.                                      |
| Particle Size                           | Not determined                          | Introduced in aqueous solution                                                                                                               |
| Flash Point                             | 108 °C at 101.5 kPa                     | Analogue B data                                                                                                                              |
| Flammability                            | Not flammable                           | Analogue B estimate                                                                                                                          |
| Pyrophoric Properties                   | Not pyrophoric                          | Analogue B estimate                                                                                                                          |
| Autoignition Temperature                | 425 °C                                  | Analogue B data                                                                                                                              |
| Explosive Properties                    | Not explosive                           | Analogue B data (additionally the notified chemicals contain no functional groups that imply explosive properties)                           |
| Oxidising Properties                    | Not oxidising                           | Analogue B data (additionally the notified chemicals contain no functional groups that imply oxidising properties)                           |

\* Chemical 1 in Evonik and Redox cleaning products (STD/1652)

#### DISCUSSION OF PROPERTIES

For full details of tests on physical and chemicals properties, refer to Appendix A.

#### Reactivity

The notified chemicals are 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 chemicals are not recommended for physical hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*, as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

#### 5. INTRODUCTION AND USE INFORMATION

##### MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

The notified chemicals will not be manufactured in Australia. The notified chemicals will be imported into Australia at ≤ 50% concentration.

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

| <i>Year</i>   | <i>1</i> | <i>2</i> | <i>3</i> | <i>4</i> | <i>5</i> |
|---------------|----------|----------|----------|----------|----------|
| <i>Tonnes</i> | ≤ 80     | ≤ 80     | ≤ 80     | ≤ 80     | ≤ 80     |

## PORT OF ENTRY

Throughout Australia

## TRANSPORTATION AND PACKAGING

The imported products containing the notified chemicals at ≤ 50% concentration in 220 kg plastic drums or 1,000 kg Intermediate Bulk Containers (IBC) will be transported by road.

## USE

The notified chemicals will be used as surfactants ingredients in household and personal care products, such as laundry detergents, glass cleaners and bathroom and all-purpose cleaners and facial wash, shampoos, shower and bath preparations, and hygiene washes. The concentration of the notified chemicals in end-use cleaning products will be ≤ 1.5%.

## OPERATION DESCRIPTION

The notified chemicals will not be manufactured within Australia.

*Reformulation*

Where imported as a blended bulk raw material (≤ 50% concentration) for reformulation, the notified chemicals will be transferred into the blending tank using metering pumps where it will be mixed with additional additives to form the finished household products. The notifier states that the mixing facilities are expected to be highly automated occurring within fully enclosed systems. After being reformulated, the finished products containing the notified chemicals will be transferred into end-use containers of various sizes suitable for retail packaging.

*End-Use*

The finished household and personal care products containing the notified chemicals (at ≤ 1.5% concentration) may be used by consumers and professionals, such as workers in home and industrial settings. Application of products could be by hand, spray or through the use of an applicator.

**6. HUMAN HEALTH IMPLICATIONS****6.1. Exposure Assessment****6.1.1. Occupational Exposure**

## CATEGORY OF WORKERS

| <i>Category of Worker</i> | <i>Exposure Duration (hours/day)</i> | <i>Exposure Frequency (days/year)</i> |
|---------------------------|--------------------------------------|---------------------------------------|
| Warehouse                 | 1.5                                  | 17                                    |
| Raw incoming sampling     | 0.5                                  | 4                                     |
| Lab Analyst               | 0.25                                 | 4                                     |
| Operators                 | 0.25                                 | 4                                     |
| Compounder                | 0.5                                  | 6                                     |

## EXPOSURE DETAILS

*Transport and storage*

Transport and storage workers are expected to only come into contact with the notified chemicals (at ≤ 50% concentration) in the unlikely event of an accident. In case of such accidental exposure, the main routes of exposure would be dermal and ocular.

*Reformulation*

Workers may be exposed to the notified chemicals during collection of samples, formulation of products, filling and packaging of the products into end-use containers and during cleaning and maintenance of the equipment.



Dermal and ocular exposure to the notified chemicals is expected. Such exposure will be minimised by the use of safe work practices and wearing personal protective equipment (PPE) including impervious gloves, coveralls and goggles. Inhalation exposure to the notified chemicals is not expected to occur due to the use of closed formulation process systems.

#### *End-Use by Professional Cleaners*

Exposure to the notified chemicals in end-use products (at  $\leq 1.5\%$  concentration) may occur in work areas where the service provided involves the use of cleaning products in the cleaning industry and personal care products in hair salon. The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible. Such professionals may use some PPE to minimise repeated exposure. However, good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemicals.

#### **6.1.2. Public Exposure**

The notified chemicals will be sold to the general public only in the form of finished products (containing the notified chemicals at  $\leq 1.5\%$  concentration). Dermal and accidental ocular and inhalation exposure to the notified chemicals may occur during application of the household and personal care product. The exposure frequency and duration are expected to be low due to the expected infrequent use of cleaning products.

#### **6.2. Human Health Effects Assessment**

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

| <i>Endpoint</i>                                                                                                              | <i>Result and Assessment Conclusion</i> |
|------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Rat, acute oral toxicity*                                                                                                    | LD50 > 2000 mg/kg bw; low toxicity      |
| Rat, acute dermal toxicity*                                                                                                  | LD50 > 2000 mg/kg bw; low toxicity      |
| Rabbit, skin irritation*                                                                                                     | slightly irritating                     |
| Eye irritation ( <i>in vitro</i> -Isolated Chicken Eye Method)**                                                             | irritating                              |
| Guinea pig, skin sensitisation – Magnusson and Kligman Test*.                                                                | no evidence of sensitisation            |
| Guinea pig, skin sensitisation – Magnusson and Kligman Test#                                                                 | no evidence of sensitisation            |
| Guinea pig, skin sensitisation – Delayed Contact Hypersensitivity Test#.                                                     | no evidence of sensitisation            |
| Mouse, skin sensitisation –Hypersensitivity test                                                                             | no evidence of sensitisation            |
| Rat, repeat dose oral toxicity –**                                                                                           | NOAEL = 500 mg/kg bw/day                |
| Mutagenicity – bacterial reverse mutation**                                                                                  | non mutagenic                           |
| Genotoxicity – <i>in vitro</i> Mammalian Chromosome Aberration*                                                              | non genotoxic                           |
| Genotoxicity – <i>in vivo</i> Cell Mutation at the Thymidine Kinase Locus (TK <sup>+/-</sup> in Mouse Lymphoma L5178Y Cells+ | non mutagenic                           |

\*Analogue B

\*\*Chemical 1 in Evonik and Redox cleaning products

+Analogue D

#Analogue C

#### *Toxicokinetics, metabolism and distribution*

No toxicokinetics data for the notified chemicals or analogues were provided. For dermal absorption, molecular weights below 100 g/mol. are favourable for absorption and molecular weights above 500 g/mol. do not favour absorption (ECHA, 2017). Dermal uptake is likely to be moderate to high if the water solubility is between 100-10,000 mg/L (ECHA, 2017). In addition evidence of skin sensitisation or irritation increase the probability of dermal absorption occurring (ECHA, 2017). Based on the low molecular weights (< 500 g/mol) and moderate water solubility (4.9 g/L at 20 °C) of the notified chemicals passage across biological membranes is expected to occur.

#### *Acute toxicity*

No acute oral, dermal or inhalation toxicity data for the notified chemicals were provided. Analogue B was found to be of low acute oral and dermal toxicity with LD50s > 2,000 mg/kg bw.

*Irritation and sensitisation*

The notified chemical (chemical 1 in Evonik and Redox cleaning products) was found to be an eye irritant in an evaluation of an *in vitro* eye irritation study using isolated chicken eye test.

In an acute skin irritation / corrosion study on analogue B (38.2%) on New Zealand White rabbits the analogue test substance was classified as mildly irritating.

No evidence of skin sensitisation was found in Magnusson and Kligman skin sensitisation tests performed on analogues B and C.

*Repeated dose toxicity*

In a four week oral toxicity repeated dose study in rats followed by two week recovery period test, the No Observed Adverse Effect Level (NOAEL) of chemical 1 was established to be the highest dose tested 500 mg/kg bw/day.

*Mutagenicity/Genotoxicity*

The bacterial reverse mutation test (Ames test) assessed the mutagenic potential of chemical 1 in Evonik and Redox cleaning products in several bacterial strains. Based on the results obtained in this study, it can be concluded that the test item does not induce point mutations or frame-shifts in the genome of the bacterial strains used with or without metabolic activation regardless of the procedure. Data provided for analogue B and E showed them to be non-genotoxic in an *in vitro* Mammalian Chromosome Aberration test or in an *in vitro* Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y cells mutation test respectively.

**Health hazard classification**

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

| <i>Hazard classification</i>                     | <i>Hazard statement</i>              |
|--------------------------------------------------|--------------------------------------|
| Serious eye damage /Eye irritation (Category 2A) | H319 – Causes serious eye irritation |

**6.3. Human Health Risk Characterisation****6.3.1. Occupational Health and Safety**

The notified chemicals are expected to be irritating to the eye and slight skin irritants. There is potential for dermal and ocular exposure of workers to the notified chemicals (at  $\leq 50\%$  concentration) during reformulation processes. Exposure should be minimised through the stated use of enclosed, automated processes, local exhaust ventilation and PPE.

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

**6.3.2. Public Health**

The public may have dermal or ocular exposure to the notified chemicals (at  $\leq 1.5\%$  concentration) through the use of household and general personal care products. The risk of irritant effects from the notified chemicals at these concentrations is considered to be low.

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

## 7. ENVIRONMENTAL IMPLICATIONS

### 7.1. Environmental Exposure & Fate Assessment

#### 7.1.1. Environmental Exposure

##### RELEASE OF CHEMICAL AT SITE

The notified chemicals will be imported as a blended bulk raw material for reformulation into the end-use household and industrial cleaning products. The reformulation processes are expected to involve automated blending operation in an enclosed environment, followed by automated filling of the finished products into end-use containers. Wastes containing the notified chemicals generated during reformulation are expected to be disposed of in accordance with local government regulations. Release of the notified chemicals in the event of accidental spills or leaks during import, reformulation, storage and transport are also expected to be collected for disposal, in accordance with local government regulations.

##### RELEASE OF CHEMICAL FROM USE

The majority of the notified chemicals are expected to be released to sewers across Australia as a result of their uses in cleaning products.

##### RELEASE OF CHEMICAL FROM DISPOSAL

Residues of the notified chemicals in empty import and end-use containers are likely to either share the fate of the containers and be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

#### 7.1.2. Environmental Fate

Following their uses in cleaning products, the majority of the notified chemicals are expected to enter sewers across Australia. The ready biodegradation test conducted on Chemical 1 shows that it is readily biodegradable (90% degradation over 28 days in OECD 301B test). Therefore, the notified chemicals are expected to be removed effectively by biodegradation at sewage treatment plants (STPs) before potential release to surface waters nationwide. For details of the biodegradability study, refer to Appendix C. A very minor proportion of the notified chemicals may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. As the notified chemicals contain ionic functionalities and are surface active, they could bind to soil through hydrophobic and ion exchange mechanisms. The notified chemicals are not expected to be bioaccumulative in the environment due to their ready biodegradability. In the aquatic and soil compartments, the notified chemicals are expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon and nitrogen.

#### 7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume the worst case scenario with 100% release of the notified chemicals into sewer systems nationwide over 365 days per annum. It is also assumed under the worst-case scenario that there is no removal of the notified chemicals during sewage treatment processes. The resultant PEC in sewage effluent on a nationwide basis is estimated as follows:

---

##### Predicted Environmental Concentration (PEC) for the Aquatic Compartment

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|                                               |        |              |
|-----------------------------------------------|--------|--------------|
| Total Annual Import/Manufactured Volume       | 80,000 | kg/year      |
| Proportion expected to be released to sewer   | 100    | %            |
| Annual quantity of chemical released to sewer | 80,000 | kg/year      |
| Days per year where release occurs            | 365    | days/year    |
| Daily chemical release:                       | 219.18 | kg/day       |
| Water use                                     | 200    | L/person/day |
| Population of Australia (Millions)            | 24.386 | million      |
| Removal within STP                            | 0      | %            |
| Daily effluent production:                    | 4,877  | ML           |
| Dilution Factor - River                       | 1      |              |
| Dilution Factor - Ocean                       | 10     |              |
| PEC - River:                                  | 44.9   | µg/L         |
| PEC - Ocean:                                  | 4.49   | µg/L         |

---

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m<sup>2</sup>/year (10 ML/ha/year). The notified chemicals in this volume are assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m<sup>3</sup>). Using these assumptions, irrigation with a concentration of 44.9 µg/L may potentially result in a soil concentration of approximately 0.3 mg/kg. Due to the notified chemicals ready biodegradability, annual accumulation is not expected.

## 7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on Chemical 1 and Analog C are summarised in the table below. Details of these studies can be found in Appendix C.

| <i>Endpoint</i>              | <i>Result</i>         | <i>Assessment Conclusion</i>   |
|------------------------------|-----------------------|--------------------------------|
| Fish Toxicity of Chemical 1  | 96 h LC50 > 289 mg/L  | Not harmful to fish            |
| Daphnia Toxicity of Analog C | 48 h EC50 = 7.8 mg/L  | Toxic to aquatic invertebrates |
| Algal Toxicity of Analog C   | 72 h EC50 = 17.2 mg/L | Harmful to Algae               |

The above ecotoxicological endpoints of Analog C indicate that the notified chemicals could be toxic to aquatic invertebrates. Therefore, the notified chemicals are provisional classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) as “Acute Category 2; Toxic to aquatic life” (United Nations, 2009).

### 7.2.1. Predicted No-Effect Concentration

The most sensitive endpoint from the above ecotoxicity tests is 48 h EC50 for Daphnia, and this was selected for the calculation of the predicted no-effect concentration (PNEC). An assessment factor of 100 was used in this case given acute endpoints for three trophic levels are available as a general indication of potential toxicity.

| Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment |          |
|----------------------------------------------------------------------|----------|
| 48 h EC50 for Daphnia                                                | 7.8 mg/L |
| Assessment Factor                                                    | 100      |
| Mitigation Factor                                                    | 1        |
| PNEC:                                                                | 78 µg/L  |

## 7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the PEC and PNEC:

| Risk Assessment | PEC µg/L | PNEC µg/L | Q            |
|-----------------|----------|-----------|--------------|
| Q - River       | 44.9     | 78        | <b>0.58</b>  |
| Q - Ocean       | 4.49     | 78        | <b>0.058</b> |

The conservative risk quotients (Q = PEC/PNEC) have been calculated to be less than 1 for both the riverine and marine compartments, indicating that the notified chemicals are unlikely to reach ecotoxicologically significant concentrations in the aquatic environment based on its maximum annual importation quantity and the assessed use pattern. Therefore, based on the calculated risk quotient, the notified chemicals are not expected to pose an unreasonable risk to the aquatic environment.

**APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES**

|                                                |                                                                                                                                                                                                                                                                                                                                                   |
|------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Melting Point/Freezing Point</b>            | -50 °C to - 20 °C                                                                                                                                                                                                                                                                                                                                 |
| Method                                         | OECD TG 102 Melting Point/Melting Range<br>European Economic Community (EEC), EEC-Directive 92/69 EEC, Part A, Methods for the determination of physico-chemical properties, A.1 Melting/Freezing Temperature                                                                                                                                     |
| Remarks                                        | The test was performed to analogue B at 40.1% concentration using Q100 differential scanning calorimeter (DSC).                                                                                                                                                                                                                                   |
| Test Facility                                  | Notox B.V. (2006a)                                                                                                                                                                                                                                                                                                                                |
| <b>Boiling Point</b>                           | Not determined                                                                                                                                                                                                                                                                                                                                    |
| Method                                         | OECD TG 103 Boiling Point<br>European Economic Community (EEC), EEC-Directive 92/69 EEC, Part A, Methods for the determination of physico-chemical properties, A.2 Boiling temperature                                                                                                                                                            |
| Remarks                                        | Evaporation of water from the test substance (analogue B at 40.1% concentration) was observed between approximately 25°C and 175°C and reaction and/or decomposition of this test substance was observed above approximately 250 °C: boiling of analogue B was not observed below the temperature at which reaction and/or decomposition started. |
| Test Facility                                  | Notox B.V. (2006a)                                                                                                                                                                                                                                                                                                                                |
| <b>Density</b>                                 | 1,140 kg/m3 at 20 °C                                                                                                                                                                                                                                                                                                                              |
| Method                                         | OECD TG 109 Density of Liquids and Solids<br>European Economic Community (EEC), EEC-Directive 92/69 EEC, A.3 Relative Density                                                                                                                                                                                                                     |
| Remarks                                        | A glass pycnometer with a nominal volume of 10 ml was used for analogue B at 40.1% concentration. The temperature of measurement was 20.0 °C.                                                                                                                                                                                                     |
| Test Facility                                  | Notox B.V. (2006b)                                                                                                                                                                                                                                                                                                                                |
| <b>Vapour Pressure</b>                         | 2.758 kPa at 20 °C                                                                                                                                                                                                                                                                                                                                |
| Method                                         | OECD TG 104 Vapour Pressure<br>European Economic Community (EEC), EEC-Directive 92/69 EEC, Part A, Methods for the determination of physico-chemical properties, A.4 Vapour Pressure                                                                                                                                                              |
| Remarks                                        | Static technique method for analogue B at 40.1% concentration                                                                                                                                                                                                                                                                                     |
| Test Facility                                  | Notox B.V. (2006c)                                                                                                                                                                                                                                                                                                                                |
| <b>Water Solubility</b>                        | 4.9 g/L at 20 °C                                                                                                                                                                                                                                                                                                                                  |
| Method                                         | OECD TG 115 Surface Tension of Aqueous Solutions<br>EC Council Regulation No 440/2008 A.5 Surface Tension                                                                                                                                                                                                                                         |
| Remarks                                        | Test concentration of 0.5 g/L to 50 g/L. The water solubility expressed by the critical micelle concentration.                                                                                                                                                                                                                                    |
| Test Facility                                  | Dr U Noack-Laboratorien (2015a)                                                                                                                                                                                                                                                                                                                   |
| <b>Partition Coefficient (n-octanol/water)</b> | $\log P_{ow} = -3.3$ at 20 °C and pH = 7.1                                                                                                                                                                                                                                                                                                        |
| Method                                         | OECD TG 107 Partition Coefficient (n-octanol/water).<br>EEC directive 92/69 A.8 Partition Coefficient.                                                                                                                                                                                                                                            |
| Remarks                                        | Flask Method                                                                                                                                                                                                                                                                                                                                      |
| Test Facility                                  | NOTOX B.V. (2006d)                                                                                                                                                                                                                                                                                                                                |
| <b>Surface Tension</b>                         | 26.32 to 42.82 mN/m at 20 °C                                                                                                                                                                                                                                                                                                                      |
| Method                                         | OECD TG 115 Surface Tension of Aqueous Solutions<br>EC Council Regulation No 440/2008 A.5 Surface Tension                                                                                                                                                                                                                                         |
| Remarks                                        | Concentration: 1.11 g/L                                                                                                                                                                                                                                                                                                                           |
| Test Facility                                  | Dr U Noack-Laboratorien (2015a)                                                                                                                                                                                                                                                                                                                   |

|                                 |                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Flash Point</b>              | > 108 °C at 101.5 kPa                                                                                                                                                                                                                                                                                                              |
| Method                          | European Economic Community (EEC), EEC-Directive 92/69 EEC, A.9 Flash Point                                                                                                                                                                                                                                                        |
| Remarks                         | A Pensky-Martens Closed Cup automatic flash-point tester was used for analogue B at 40.1% concentration.<br>No flammable vapour/air mixture was produced up to the point where the test substance started to boil at 108 °C.                                                                                                       |
| Test Facility                   | Notox B.V. (2006e)                                                                                                                                                                                                                                                                                                                 |
| <b>Flammability</b>             | Not flammable                                                                                                                                                                                                                                                                                                                      |
| Method                          | European Economic Community (EEC), EEC directive 92/69 EEC, Part A, Methods for the determination of physico-chemical properties, A.12 "Flammability (contact with water)                                                                                                                                                          |
| Remarks                         | Based on the composition of the test substance (analogue B at 40.1% concentration), the molecular structure of the main component and the presence of water (50%) in the test substance. It was concluded that analogue B is incapable of developing a dangerous amount of (flammable) gas in contact with air, damp air or water. |
| Test Facility                   | Notox B.V. (2006f)                                                                                                                                                                                                                                                                                                                 |
| <b>Pyrophoric Properties</b>    | Not pyrophoric                                                                                                                                                                                                                                                                                                                     |
| Method                          | European Economic Community (EEC), EEC directive 92/69 EEC, A.13 Pyrophoric properties of solids and liquids.                                                                                                                                                                                                                      |
| Remarks                         | Based on the structure, experience in handling and the presence of water in the test substance the study authors determined that analogue B is not pyrophoric.                                                                                                                                                                     |
| Test Facility                   | Notox B.V. (2006g)                                                                                                                                                                                                                                                                                                                 |
| <b>Autoignition Temperature</b> | 425 °C                                                                                                                                                                                                                                                                                                                             |
| Method                          | European Economic Community (EEC), EEC directive 92/69 EEC, A.15 Auto-Ignition Temperature (Liquids and Gases)                                                                                                                                                                                                                     |
| Remarks                         | The temperature in the test vessel containing analogue B at 40.1% concentration was lowered gradually from a sufficiently high temperature until a temperature at which there was no more ignition occurred.                                                                                                                       |
| Test Facility                   | Notox B.V. (2006h)                                                                                                                                                                                                                                                                                                                 |
| <b>Explosive Properties</b>     | Not explosive                                                                                                                                                                                                                                                                                                                      |
| Method                          | European Economic Community (EEC), EEC-Directive 92/69 EEC, Part A, Methods for the determination of physico-chemical properties, A.14 Explosive Properties.                                                                                                                                                                       |
| Remarks                         | Based on the composition of the test substance analogue B (40.1%), the molecular structure of the major component and the presence of water (56.1%), it was concluded that the substance is not explosive                                                                                                                          |
| Test Facility                   | Notox B.V. (2006i)                                                                                                                                                                                                                                                                                                                 |
| <b>Oxidizing Properties</b>     | Not oxidising                                                                                                                                                                                                                                                                                                                      |
| Method                          | European Community (EC), Commission directive 2004/73/EC, Part A, Methods for the determination of physico-chemical properties, A.21: "Oxidizing properties (liquids)"                                                                                                                                                             |
| Remarks                         | Based on the composition of the test substance analogue B at 40.1% concentration and the molecular structures of both the major component and the presence of water (56.1%), it was concluded that the test substance has no oxidising properties.                                                                                 |
| Test Facility                   | Notox B.V. (2006j)                                                                                                                                                                                                                                                                                                                 |

**APPENDIX B: TOXICOLOGICAL INVESTIGATIONS****B.1. Acute toxicity – oral**

|                  |                                                                                                                                                         |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE   | Analogue B (38.2%)                                                                                                                                      |
| METHOD           | OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method<br>EC Council Regulation No 440/2008 B.1 tris Acute Oral Toxicity – Acute Toxic Class Method |
| Species/Strain   | Rat/White Wistar                                                                                                                                        |
| Vehicle          | The test substance administered as supplied /tap water                                                                                                  |
| Remarks - Method | No significant protocol deviations                                                                                                                      |

## RESULTS

| <i>Group</i> | <i>Number and Sex of Animals</i> | <i>Dose (mg/kg bw)</i> | <i>Mortality</i> |
|--------------|----------------------------------|------------------------|------------------|
| 1            | 6F                               | 300                    | 0/6              |
| 2            | 6F                               | 2000                   | 0/6              |

|                   |                                                                                                                                                |
|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| LD50              | > 2000 mg/kg bw                                                                                                                                |
| Signs of Toxicity | No acute oral toxicity was observed after administration of 300 and 2000 mg/kg bw of the test substance                                        |
| Effects in Organs | The necropsy results showed no treatment related morphological pathological findings. Average body weight gain in both animal groups was 19.6% |
| Remarks - Results | No death was observed in both animal groups                                                                                                    |

CONCLUSION The test substance is of low acute toxicity via the oral route.

TEST FACILITY Stockhausen (2005a)

**B.2. Acute toxicity – dermal**

|                  |                                                                                                                                                                    |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE   | Analogue B (40.1%)                                                                                                                                                 |
| METHOD           | OECD TG 402 Acute Dermal Toxicity<br>EC, Council Directive 67/548/EEC, Annex V, B.3 (1992) "Acute Toxicity (Dermal)"                                               |
| Species/Strain   | Rat/Wistar CrI:WI                                                                                                                                                  |
| Vehicle          | None                                                                                                                                                               |
| Type of dressing | Occlusive                                                                                                                                                          |
| Remarks - Method | No significant protocol deviations. The test substance was administered to each animal of both sexes by a single dermal application at 2000 mg/kg bw for 24 hours. |

## RESULTS

| <i>Group</i> | <i>Number and Sex of Animals</i> | <i>Dose (mg/kg bw)</i> | <i>Mortality</i> |
|--------------|----------------------------------|------------------------|------------------|
| 1            | 5F                               | 2000                   | 0/5              |
| 2            | 5M                               | 2000                   | 0/5              |

|                              |                                                                                                                                                                                                                                                             |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LD50                         | > 2000 mg/kg bw                                                                                                                                                                                                                                             |
| Signs of Toxicity - Local    | No abnormalities were found at macroscopic post mortem examination of the animals. However, chromodacryorrhea (bloody tears) was noted among four animals on days 1 and 2. Scales were seen in the treated skin-area of four animals between days 3 and 12. |
| Signs of Toxicity - Systemic | No sign of systemic toxicity effects was observed.                                                                                                                                                                                                          |
| Effects in Organs            | The body weights gain was within the range expected for rats used in this type of study during the observation period.                                                                                                                                      |
| Remarks - Results            | No death was observed in both animal groups                                                                                                                                                                                                                 |

CONCLUSION The test substance is of low acute toxicity via the dermal route.

TEST FACILITY NOTOX (2006k)

### B.3. Irritation – skin

TEST SUBSTANCE Analogue B (38.2%)

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion  
EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation)  
EC Directive 2004/10/EC B.4 Acute Toxicity (Skin Irritation)

Species/Strain Rabbit/New Zealand White  
Number of Animals 1Male & 2Females  
Vehicle None  
Observation Period 7 days  
Type of Dressing Semi-occlusive  
Remarks - Method No significant protocol deviations.

#### RESULTS

| Lesion          | Mean Score* |   |   | Maximum Value | Maximum Duration of Any Effect | Maximum Value at End of Observation Period |
|-----------------|-------------|---|---|---------------|--------------------------------|--------------------------------------------|
|                 | 1           | 2 | 3 |               |                                |                                            |
| Erythema/Eschar | 0           | 0 | 0 | 1             | < 24h                          | 0                                          |
| Oedema          | 0           | 0 | 0 | 0             | 7days                          | 0                                          |

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

Remarks - Results Slight erythema but no oedema was observed in one animal 1 h after removal of the test substance. No erythema and oedema were observed between 24 and 72 hours.

No systemic toxicity was observed during the study.

Body weight gain was positive and within the normal range.

CONCLUSION The test substance is slightly irritating to the skin.

TEST FACILITY Stockhausen (2005b)

### B.4. Irritation – eye (*in vitro*) ( Isolated Chicken Eye Test)

TEST SUBSTANCE Chemical 1 in Evonik and Redox cleaning products

METHOD Isolated Chicken Eye Test Method for Identifying Ocular Corrosives and Severe Irritants OECD TG 438 (ICE) Test

Vehicle Saline  
Remarks - Method Three main parameters were measured to disclose possible adverse effects: corneal thickness (expressed as corneal swelling relative to control values), corneal opacity and fluorescein retention of damaged epithelial cells. In addition, histopathology of the corneas was performed.

#### RESULTS

| Test material    | Mean Corneal Thickness Swelling % (Time in min) | Mean Corneal opacity (min)                     | Mean Fluorescein Retention (min) |
|------------------|-------------------------------------------------|------------------------------------------------|----------------------------------|
| Negative control | 0                                               | 0(30), 0(75), 0(120), 0(180), 0(240)           | 0(30)                            |
| Test substance   | 6(30), 9(75), 9(120), 10(180), 14(240)          | 1.8(30), 2.0(75), 2.0(120), 2.3(180), 2.3(240) | 2.2(30)                          |



|                         |                                              |                                                   |       |
|-------------------------|----------------------------------------------|---------------------------------------------------|-------|
| <i>Positive control</i> | 41(30), 43(75), 46(120),<br>47(180), 47(240) | 4.0(30), 4.0(75), 4.0(120), 4.0(180),<br>4.0(240) | 3(30) |
|-------------------------|----------------------------------------------|---------------------------------------------------|-------|

OD = optical density

#### Remarks - Results

After administration of the test substance to isolated chicken eyes, a small lump of the test substance adhered to the cornea of one eye. After approximately 5 minutes, the eye was rinsed with saline. Mean percentage of corneal swelling was calculated for all observation time points. The test substance caused:

- a slight corneal swelling (14%);
- moderate to severe opacity (2.3); and
- moderate or moderate to severe fluorescein retention (2.2)

Based on the highest mean score of 14% ICE class II is applicable for the test substance.

Based on the highest mean score for corneal opacity (2.3) and fluorescein retention (2.2), ICE class III is applicable for the test substance.

The prolonged exposure to the test substance showed severe opacity and moderate to severe fluorescein retention.

Based on 2 ICE class scores of III and ICE class score of II, the eye irritation hazard classification for the test substance cannot be predicted according to the Test Guideline (TG). However, it is not a Cat. 1 eye irritant or a non-irritant.

Negative control eye did not show any corneal effects demonstrating that the general conditions during the test were adequate.

The positive control (NaOH) caused severe corneal effects demonstrating the ICE test valid to detect severe eye irritants.

Microscopic examination of the treated cornea with the test substance showed very slight erosion of the epithelium. The treated cornea with negative control showed no abnormalities and the treated cornea with the positive control caused severe erosion of the epithelium, severe necrosis of the stroma and necrosis of the endothelium.

#### CONCLUSION

The test substance was considered to be irritating to the eye under the conditions of the test.

#### TEST FACILITY

TNO Triskelion (2014)

### B.5. Skin sensitisation - Magnusson and Kligman Test

#### TEST SUBSTANCE

Analogue B (38.2%)

#### METHOD

OECD TG 406 Skin Sensitisation - Magnusson and Kligman test

EC Directive 2004/10/EC Skin Sensitisation

#### Species/Strain

Guinea pig/ Pirbright White, BOR DHPW

#### PRELIMINARY STUDY

Maximum Non-irritating Concentration: 70% (w/w)

intradermal: 0.5% of 2% (no skin reaction); 3.5% and 5% (elicited a slight reaction).

topical: 50% provoked a slight reaction and 30% showed no reaction

#### MAIN STUDY

##### Number of Animals

Test Group: 10

Control Group: 5

##### Vehicle

0.9% NaCl solution

##### Positive control

Conducted in parallel with the test substance

|                              |                                                                                                                                                                                                 |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| INDUCTION PHASE              | Induction Concentration:<br>intradermal: 0.1 mL of 3.5% (w/w)<br>topical: 30%                                                                                                                   |
| Signs of Irritation          | Intradermal application of the 3.5 % caused slight to moderate erythema and oedema formation. The topical application of 50% of the test substance caused slight erythema and oedema formation. |
| CHALLENGE PHASE<br>challenge | topical: 30% (The challenge application was carried out on control and test group animals 21 days after the dermal application).                                                                |
| Remarks - Method             | No significant protocol deviations.                                                                                                                                                             |

## RESULTS

| <i>Animal</i>        | <i>Challenge Concentration</i> | <i>Number of Animals Showing Skin Reactions after:<br/>challenge</i> |             |
|----------------------|--------------------------------|----------------------------------------------------------------------|-------------|
|                      |                                | <i>24 h</i>                                                          | <i>48 h</i> |
| <i>Test Group</i>    |                                |                                                                      |             |
| <i>10 F</i>          | 30%                            | 0/10                                                                 | 0/10        |
| <i>Control Group</i> |                                |                                                                      |             |
| <i>5F</i>            | Nil                            | 0/5                                                                  | 0/5         |

|                   |                                                                                                                                                                                                                                                         |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Remarks - Results | The challenge application of the test substance at a concentration of 30% did not cause any irritation in test animals.<br><br>A formation of crusts at the injection sites of the test substance was observed from the intradermal application (3.5%). |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|            |                                                                                                                             |
|------------|-----------------------------------------------------------------------------------------------------------------------------|
| CONCLUSION | There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test. |
|------------|-----------------------------------------------------------------------------------------------------------------------------|

|               |                     |
|---------------|---------------------|
| TEST FACILITY | Stockhausen (2005c) |
|---------------|---------------------|

**B.6. Skin sensitisation - Magnusson and Kligman Test**

|                              |                                                                                                                     |
|------------------------------|---------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE               | Analogue C                                                                                                          |
| METHOD                       | OECD TG 406 Skin Sensitisation - Magnusson and Kligman Test                                                         |
| Species/Strain               | Guinea pig/ Pirbright White Bor: DHPW (SPF)                                                                         |
| PRELIMINARY STUDY            | Maximum Non-irritating Concentration:<br>intradermal: 1%<br>topical: 30%                                            |
| MAIN STUDY                   |                                                                                                                     |
| Number of Animals            | Test Group: 20                      Control Group: 20                                                               |
| Vehicle                      | Water                                                                                                               |
| Positive control             | Conducted in parallel with the test substance                                                                       |
| INDUCTION PHASE              | Induction Concentration:<br>intradermal: Not specified<br>topical: Saturated solution in Freund's complete adjuvant |
| Signs of Irritation          | No record of effects following induction were included in the study report.                                         |
| CHALLENGE PHASE<br>challenge | topical: 30%                                                                                                        |
| Remarks - Method             | No significant protocol deviations.                                                                                 |

## RESULTS

| <i>Animal</i>     | <i>Challenge Concentration</i> | <i>Number of Animals Showing Skin Reactions after:<br/>challenge</i> |             |
|-------------------|--------------------------------|----------------------------------------------------------------------|-------------|
|                   |                                | <i>24 h</i>                                                          | <i>48 h</i> |
| <i>Test Group</i> |                                |                                                                      |             |
| <i>10M, 10F</i>   | 30%                            | 0/20                                                                 | 4/20        |

|                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                   |      |      |
|-----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|------|
| <i>Control Group</i><br><i>10M, 10F</i> | 30%                                                                                                                                                                                                                                                                                                                                                                                                                               | 0/20 | 5/20 |
| Remarks - Results                       | Preliminary Study (range finding test):<br>intradermal: 0.1, 0.5% (no skin reaction), 1% (immoderate erythema), and 5% (elicited a black discolouration of the injection sites).<br>topical: 5% did not produce a skin reaction or excessive inflammation (Occlusive patch).<br>Main study:<br>At the 48 hour observation 4 female animals in the test group, and 5 female animals in the control group showed slight irritation. |      |      |
| CONCLUSION                              | There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.                                                                                                                                                                                                                                                                                                       |      |      |
| TEST FACILITY                           | IBR (1990)                                                                                                                                                                                                                                                                                                                                                                                                                        |      |      |

### B.7. Skin sensitisation – Magnusson and Kligman Test

|                           |                                                                                                                              |                  |  |
|---------------------------|------------------------------------------------------------------------------------------------------------------------------|------------------|--|
| TEST SUBSTANCE            | Analogue C                                                                                                                   |                  |  |
| METHOD                    | Similar to OECD TG 406 Skin Sensitisation - Magnusson and Kligman Test                                                       |                  |  |
| Species/Strain            | Guinea-Pig/ Pirbright white                                                                                                  |                  |  |
| PRELIMINARY STUDY         | Maximum Non-irritating Concentration: Not reported                                                                           |                  |  |
| MAIN STUDY                |                                                                                                                              |                  |  |
| Number of Animals         | Test Group: 15                                                                                                               | Control Group: 5 |  |
| Vehicle                   | Water                                                                                                                        |                  |  |
| Positive control          | Not conducted in parallel with the test substance.                                                                           |                  |  |
| INDUCTION PHASE           | Induction Concentration:<br>intradermal: 0.5%<br>topical: 60%                                                                |                  |  |
| Signs of Irritation       | Temporary and slight dermal irritation was observed following both the intradermal and topical applications.                 |                  |  |
| CHALLENGE PHASE           |                                                                                                                              |                  |  |
| 1 <sup>st</sup> challenge | topical: 10%                                                                                                                 |                  |  |
| Remarks - Method          | The control animals were inducted similarly to the test animals omitting the intradermal injections and topical application. |                  |  |

| <i>Animal</i>        | <i>Challenge Concentration</i> | <i>Number of Animals Showing Skin Reactions after:</i> |             |             |
|----------------------|--------------------------------|--------------------------------------------------------|-------------|-------------|
|                      |                                | <i>24 h</i>                                            | <i>48 h</i> | <i>72 h</i> |
| <i>Test Group</i>    |                                |                                                        |             |             |
| <i>15M</i>           | 10%                            | 2/15                                                   | 0/15        | 0/15        |
| <i>Control Group</i> |                                |                                                        |             |             |
| <i>5M</i>            | 10%                            | 0/5                                                    | 0/5         | 0/5         |

|                   |                                                                                                                                                                                                                                               |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Remarks - Results | Dermal reactions were observed in two treated animals after 24h hour observation after challenge. Dryness and sloughing of the epidermis was observed in two control animals and one test animal after 72 hours of the challenge application. |
| CONCLUSION        | There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.                                                                                                                   |
| TEST FACILITY     | HRC (1980)                                                                                                                                                                                                                                    |



**B.9. Genotoxicity – Bacterial Reverse Mutation Test**

|                                  |                                                                                                                                                                                                                           |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE                   | Chemical 1 in Evonik and Redox cleaning products                                                                                                                                                                          |
| METHOD                           | OECD TG 471 Bacterial Reverse Mutation Test<br>Council Regulation (EC) No 440/2008 B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria<br>Plate incorporation procedure and Pre incubation procedure              |
| Species/Strain                   | <i>Salmonella typhimurium</i> : TA1535, TA1537, TA98, TA100, and<br><i>Escherichia coli</i> : WP2uvrA                                                                                                                     |
| Metabolic Activation System      | S9 fraction from Phenobarbital/ $\beta$ -Naphthoflavone induced rat liver.                                                                                                                                                |
| Concentration Range in Main Test | a) With metabolic activation: 3-5,000 $\mu$ g/plate<br>b) Without metabolic activation: 3-5,000 $\mu$ g/plate                                                                                                             |
| Vehicle                          | Deionised water                                                                                                                                                                                                           |
| Remarks - Method                 | No significant deviations from the OECD guidelines. The pre-experiment is reported as main experiment 1, since the criteria are met (Evaluable plates (> 0 colonies) at five concentrations or more in all strains used). |

## RESULTS

| Metabolic Activation | Test Substance Concentration ( $\mu$ g/plate) Resulting in: |                           |               |                  |
|----------------------|-------------------------------------------------------------|---------------------------|---------------|------------------|
|                      | Cytotoxicity in Preliminary Test                            | Cytotoxicity in Main Test | Precipitation | Genotoxic Effect |
| <i>Absent</i>        | > 5000 (except TA100 $\geq$ 5000)                           |                           |               |                  |
| Test 1               |                                                             | $\geq$ 5000               | > 5000        | Negative         |
| Test 2               |                                                             | $\geq$ 5000)              | > 5000        | Negative         |
| <i>Present</i>       | > 5000                                                      |                           |               |                  |
| Test 1               |                                                             | > 5000                    | > 5000        | Negative         |
| Test 2               |                                                             | $\geq$ 5000)              | > 5000        | Negative         |

|                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Remarks - Results | <p>The plates incubated with the test item showed normal background growth up to 5000 <math>\mu</math>g/plate with or without S9 mix in all strains tested.</p> <p>Toxic effects, as a reduction in the number of revertants (below the indication factor of 0.5), were absent in nearly all strains, except in strain TA 100 where toxic effects were observed at 5000 <math>\mu</math>g/plate without S9 mix in experiment 1 and with or without S9 mix in experiment 2</p> <p>No precipitation of the test item occurred up to the highest investigated dose.</p> <p>No substantial increase in revertant colony numbers of any of the five tester strains was observed following treatment with the test substance at any dose level, neither in the presence nor absence of metabolic activation (S9 mix). There was also no tendency of higher mutation rates with increasing concentrations in the range below the generally acknowledged border of biological relevance.</p> <p>The positive controls showed a significant increase of induced revertant colonies, thus confirming the integrity of S9-mix and the test system.</p> |
| CONCLUSION        | The notified chemical (Chemical 1) was not mutagenic to bacteria under the conditions of the test.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| TEST FACILITY     | Harlan (2014)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

**B.10. Genotoxicity – *in vitro* - Mammalian Chromosome Aberration**

|                             |                                                                                                                                                                                                                                                            |
|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE              | Analogue B (38.2%)                                                                                                                                                                                                                                         |
| METHOD                      | OECD TG 473 <i>In vitro</i> Mammalian Chromosome Aberration Test<br>EC Directive 2000/32/EC B.10 Mutagenicity - <i>In vitro</i> Mammalian Chromosome Aberration Test                                                                                       |
| Species/Strain              | Chinese hamster                                                                                                                                                                                                                                            |
| Cell Type/Cell Line         | V79 cells                                                                                                                                                                                                                                                  |
| Metabolic Activation System | S9 fraction from Phenobarbital/ $\beta$ -Naphthoflavone induced rat liver.                                                                                                                                                                                 |
| Vehicle                     | Cell culture medium                                                                                                                                                                                                                                        |
| Remarks - Method            | No significant deviations from the OECD guidelines were noted. The treatment interval was 4 hours with and without metabolic activation. Two parallel cultures were set up. 100 metaphases per culture were scored for structural chromosomal aberrations. |

| <i>Metabolic Activation</i> | <i>Test Substance Concentration (<math>\mu\text{g/mL}</math>)</i> | <i>Exposure Period</i> | <i>Harvest Time</i> |
|-----------------------------|-------------------------------------------------------------------|------------------------|---------------------|
| <i>Absent</i>               |                                                                   |                        |                     |
| Test 1                      | 0*, 250, 500, 1000*, 2500*, 5000*                                 | 4 h                    | 20 h                |
| Test 2                      | 0*, 125, 250, 500, 1000*, 2500*, 5000*                            | 4 h                    | 20 h                |
| <i>Present</i>              |                                                                   |                        |                     |
| Test 1                      | 0*, 250, 500, 1000*, 2500*, 5000*                                 | 4 h                    | 20 h                |
| Test 2                      | 0*, 1000*, 2000*, 3000*, 4000*, 5000*                             | 4 h                    | 20 h                |

\*Cultures selected for metaphase analysis.

**RESULTS**

| <i>Metabolic Activation</i> | <i>Test Substance Concentration (<math>\mu\text{g/mL}</math>) Resulting in:</i> |                                  |                      |                         |
|-----------------------------|---------------------------------------------------------------------------------|----------------------------------|----------------------|-------------------------|
|                             | <i>Cytotoxicity in Preliminary Test</i>                                         | <i>Cytotoxicity in Main Test</i> | <i>Precipitation</i> | <i>Genotoxic Effect</i> |
| <i>Absent</i>               |                                                                                 |                                  |                      |                         |
| Test 1                      | > 5000                                                                          | > 5000                           | > 5000               | Negative                |
| Test 2                      |                                                                                 | > 5000                           | > 5000               | Negative                |
| <i>Present</i>              |                                                                                 |                                  |                      |                         |
| Test 1                      | > 5000                                                                          | > 5000                           | > 5000               | Negative                |
| Test 2                      |                                                                                 | > 5000                           | > 5000               | Negative                |

**Remarks - Results**

In experiment 1 and 2 no precipitate of the test item was noted in all dose group and no toxic effects of the test item were noted up to the highest dose group.

No biologically significant decrease of mitotic cells (relative mitotic index below 70%) was noted in all dose groups evaluated with and without metabolic activation compared to the vehicle control. No increase in the frequencies of polyploid cells was found after treatment with the test item as compared to the control groups.

The positive controls showed a significant increase in number of chromosome aberrations confirming the integrity of S9-mix and the test system.

**CONCLUSION**

The test substance was not clastogenic to Chinese hamster V79 cells treated *in vitro* under the conditions of the test.

**TEST FACILITY**

BSL BIOSERVICE (2005)

### B.11. Genotoxicity – *in vitro* Cell Mutation Test at the Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y Cells

|                             |                                                                                                                                                                                                                                                                      |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE              | Analogue D                                                                                                                                                                                                                                                           |
| METHOD                      | OECD TG 476 <i>In vitro</i> Mammalian Cell Gene Mutation Test<br>EC Directive No. 440/2008 B.17: Mutagenicity – <i>In vitro</i> Mammalian Cell Gene Mutation Test                                                                                                    |
| Species/Strain              | Mouse Lymphoma L5178Y Cells                                                                                                                                                                                                                                          |
| Metabolic Activation System | S9 fraction from Phenobarbital/ $\beta$ -Naphthoflavone induced rat liver.                                                                                                                                                                                           |
| Vehicle                     | Deionised water                                                                                                                                                                                                                                                      |
| Remarks - Method            | No significant deviations from protocols. A test item is classified as mutagenic if the induced mutation frequency reproducibly exceeds a threshold of 126 colonies per 10 <sup>6</sup> cells above the corresponding solvent control.                               |
|                             | Experiment 1 was performed with and without liver microsomal activation and a treatment period of 4 h.<br>Experiment 2 was performed with a treatment period of 24 hours in the absence of metabolic activation and 4 hours in the presence of metabolic activation. |
|                             | The highest applied concentration in the pre-experiment (5000 $\mu$ g/mL) was limited by the solubility properties of the test item in aqueous medium. The concentration range of the main experiments was limited by the cytotoxic potential of the test item.      |

| Metabolic Activation | Test Substance Concentration ( $\mu$ g/mL)    | Exposure Period | Expression Time | Selection Time |
|----------------------|-----------------------------------------------|-----------------|-----------------|----------------|
| <i>Absent</i>        |                                               |                 |                 |                |
| Test 1               | 2.4*; 4.9*; 9.8*; 19.5*; 39.0*, 58.5, 78.0    | 4 h             | 48 h            | 52 h           |
| Test 2               | 2.5, 5.0, 10*; 20*; 40*; 50*; and 60*         | 24 h            | 48 h            | 72 h           |
| <i>Present</i>       |                                               |                 |                 |                |
| Test 1               | 4.9*; 9.8*; 19.5*; 39.0*; 78.0*, 117.0, 156.0 | 4 h             | 48 h            | 52 h           |
| Test 2               | 10, 20, 40*; 80*; 100*; 110*; and 120*        | 4 h             | 48 h            | 52 h           |

\*Cultures selected for metaphase analysis.

#### RESULTS

| Metabolic Activation | Test Substance Concentration ( $\mu$ g/mL) Resulting in: |                           |               |                  |
|----------------------|----------------------------------------------------------|---------------------------|---------------|------------------|
|                      | Cytotoxicity in Preliminary Test                         | Cytotoxicity in Main Test | Precipitation | Genotoxic Effect |
| <i>Absent</i>        |                                                          |                           |               |                  |
| Test 1               | $\geq 78.1$                                              | $\geq 19.5$               | > 5000        | Negative         |
| Test 2               | $\geq 39.1$                                              | $\geq 40$                 | > 5000        | Negative         |
| <i>Present</i>       |                                                          |                           |               |                  |
| Test 1               | $\geq 312.5$                                             | $\geq 117.0$              | > 5000        | Negative         |
| Test 2               |                                                          | $\geq 40$                 | > 5000        | Negative         |

RESULTS No substantial and reproducible dose dependent increase in mutant colony numbers was observed in both experiments 1 and 2.

#### Doses Producing Toxicity

The positive controls showed a significant increase in number of chromosome aberrations confirming the integrity of S9-mix and the test system.

Relevant cytotoxic effects indicated by a relative total growth of less than 50% in both parallel cultures were observed in the absence of metabolic activation at 39  $\mu$ g/mL in experiment 1 following 4 hour treatment and at 40  $\mu$ g/mL and above in experiment 2 following 24 hours treatment.

|                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Genotoxic Effects | <p>In the presence of metabolic activation: No reproducible cytotoxic effects were noted in experiment 1 and <math>\geq 100</math> <math>\mu\text{g/mL}</math> in experiment 2.</p> <p>The isolated minor reduction of the relative total growth to 43.5 % in the first culture of experiment 1 with metabolic activation was not considered a toxic effect since no comparable reduction was observed in the parallel culture under identical conditions.</p> |
| Remarks - Results | <p>The mutation frequency did not reproducibly reach or exceed the threshold of 126 above the mutation frequency of the corresponding solvent control in any of the experimental parts.</p> <p>The positive controls showed a significant increase in number of mutant colonies confirming the integrity of S9-mix and the test system.</p>                                                                                                                    |
| CONCLUSION        | <p>The test substance was not clastogenic under the conditions of this <i>in vitro</i> Mammalian Cell Gene Mutation Test.</p>                                                                                                                                                                                                                                                                                                                                  |
| TEST FACILITY     | <p>Harlan CCR (2009)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                       |



## APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

### C.1. Environmental Fate

#### C.1.1. Ready biodegradability

|                       |                                                                                                                                                     |
|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE        | Chemical 1                                                                                                                                          |
| METHOD                | OECD TG 301 B Ready Biodegradability: CO <sub>2</sub> Evolution Test                                                                                |
| Inoculum              | Activated sludge from a local STP                                                                                                                   |
| Exposure Period       | 28 days                                                                                                                                             |
| Auxiliary Solvent     | None                                                                                                                                                |
| Analytical Monitoring | CO <sub>2</sub> by titrimetric method                                                                                                               |
| Remarks - Method      | No significant deviations from the test guidelines were reported. The test item was added directly to the test vessels. A toxicity control was run. |

#### RESULTS

| Day | <i>Test substance</i> |               | <i>Sodium acetate</i> |               |
|-----|-----------------------|---------------|-----------------------|---------------|
|     | Day                   | % Degradation | Day                   | % Degradation |
| 6   | 6                     | 35            | 6                     | 47            |
| 14  | 14                    | 68            | 14                    | 68            |
| 21  | 21                    | 86            | 21                    | 74            |
| 28  | 28                    | 90            | 28                    | 90            |

Remarks - Results All validity criteria for the test were satisfied. The percentage degradation of the reference compound, sodium acetate surpassed the threshold level. The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after 28 days was 90%.

CONCLUSION The test substance is readily biodegradable.

TEST FACILITY Dr U Noack-Laboratorien (2005)

### C.2. Ecotoxicological Investigations

#### C.2.1. Acute toxicity to fish

|                       |                                                                                                                                                                      |
|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| TEST SUBSTANCE        | Chemical 1                                                                                                                                                           |
| METHOD                | OECD TG 203 Fish, Acute Toxicity Test – Semi-static                                                                                                                  |
| Species               | <i>Danio rerio</i>                                                                                                                                                   |
| Exposure Period       | 96 hours                                                                                                                                                             |
| Auxiliary Solvent     | None                                                                                                                                                                 |
| Water Hardness        | 231 mg CaCO <sub>3</sub> /L                                                                                                                                          |
| Analytical Monitoring | Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS)                                                                                                            |
| Remarks – Method      | No significant deviations from the test guidelines were reported. The test media was renewed daily. The test concentration was measured at 0 h, 24 h, 72 h and 96 h. |

#### RESULTS

| <i>Concentration mg/L</i> |               | <i>Number of Fish</i> | <i>Mortality 96 h</i> |
|---------------------------|---------------|-----------------------|-----------------------|
| <i>Nominal</i>            | <i>Actual</i> |                       |                       |
| Control                   | < LOQ*        | 7                     | 0                     |
| 289                       | 313           | 7                     | 0                     |

\*LOQ: Limit of Quantification of 100µg/L

LC50 > 289 mg/L at 96 hours  
 Remarks – Results All validity criteria for the test were satisfied. The measured values of the test substance were in the range of 99 to 108% of the nominal values. During the test, the dissolved oxygen was  $\geq$  84%.

CONCLUSION The test substance is not harmful to fish.

TEST FACILITY Dr U Noack-Laboratorien (2015b)

### C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Analogue C

METHOD EC Council Regulation 92/96/EEC C.2 Acute Toxicity for Daphnia - Static

Species *Daphnia magna*

Exposure Period 48 hours

Auxiliary Solvent None

Water Hardness Not provided

Analytical Monitoring Total organic carbon (TOC) was analysed by TOC-500 analyser

Remarks - Method No significant deviations from the test guidelines were reported. The test solutions were prepared from the dilution of a stock solution. A positive control ( $K_2CrO_7$ ) was run less than one month prior to the current study.

#### RESULTS

| Concentration mg/L<br>Nominal | Number of <i>D. magna</i> | Immobilised (%) |      |
|-------------------------------|---------------------------|-----------------|------|
|                               |                           | 24 h            | 48 h |
| Control                       | 19                        | 0               | 0    |
| 3.5                           | 20                        | 15              | 20   |
| 6                             | 20                        | 10              | 20   |
| 10                            | 20                        | 90              | 100  |
| 17                            | 21                        | 67              | 76   |
| 30                            | 20                        | 55              | 75   |

LC50 7.8 mg/L (95% CL: 4.7 – 13 mg/L) at 48 hours (calculated by probit analysis).

Remarks - Results All validity criteria for the test were satisfied. During the test, the dissolved oxygen concentration was  $\geq$  7.4 mg/L at 20 °C ( $\geq$  81 % saturation; USGS 2011). An LC100 of 2 mg/L was calculated for the positive control and this was regarded to sufficiently demonstrate the sensitivity of the test species. The TOC results indicate that the test substance was stable during the test and nominal concentration were used in the endpoint calculation. The increase in percentage immobilisation was not a monotonic response with respect to concentration.

CONCLUSION The test substance is toxic to aquatic invertebrates.

TEST FACILITY Huls (1996)

### C.2.3. Algal growth inhibition test

TEST SUBSTANCE Analogue C

METHOD OECD TG 201 Alga, Growth Inhibition Test  
 EC Council Regulation 92/69/EC C.3 Algal Inhibition Test

Species *Desmodesmus subspicatus*

Exposure Period 72 hours

Concentration Range Nominal: 3.13, 6.25, 12.5, 25, 50, 100 mg/L

|                       |                                                                                                                                                                                     |
|-----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Auxiliary Solvent     | Actual at t = 0 h: 2.51, 5.18, 10.8, 23.8, 44.9, 101 mg/L                                                                                                                           |
| Water Hardness        | None                                                                                                                                                                                |
| Analytical Monitoring | 0.24 mmol Ca+Mg/L                                                                                                                                                                   |
| Remarks - Method      | Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS)<br>No significant deviations from the test guidelines were reported. The test concentration was measured at 0 h and 72 h. |

## RESULTS

| <i>Biomass</i>                     |                            | <i>Growth</i>                      |                            |
|------------------------------------|----------------------------|------------------------------------|----------------------------|
| <i>EC50</i><br><i>mg/L at 72 h</i> | <i>NOEC</i><br><i>mg/L</i> | <i>EC50</i><br><i>mg/L at 72 h</i> | <i>NOEC</i><br><i>mg/L</i> |
| 17.2 (95% CL: 16.4 – 17.9)         | 6.25                       | 31.9 (95% CL: 30.2 – 33.7)         | 12.5                       |

|                   |                                                                                                                                                                                                                                                                                                        |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Remarks - Results | All validity criteria for the test were satisfied. The mean cell density in the control increased by 98 times. At the start of the test, the measured values of the test substance were in the range of 80 to 101% of the nominal values. At the end of the test, they were in the range of 68 to 84%. |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|            |                                        |
|------------|----------------------------------------|
| CONCLUSION | The test substance is harmful to alga. |
|------------|----------------------------------------|

|               |                              |
|---------------|------------------------------|
| TEST FACILITY | Dr U Noack-Labororien (2006) |
|---------------|------------------------------|

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