File No.: STD/1735

October 2020

AUSTRALIAN INDUSTRIAL CHEMICALS INTRODUCTION SCHEME (AICIS)

PUBLIC REPORT

Aldirez A

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals Act 2019* (the IC Act) and *Industrial Chemicals (General) Rules 2019* (the IC Rules) by following the *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Act 2019* (the Transitional Act) and *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Rules 2019* (the Transitional Rules). The legislations are Acts of the Commonwealth of Australia. The Australian Industrial Chemicals Introduction Scheme (AICIS) is administered by the Department of Health, and conducts the risk assessment for human health. The assessment of environmental risk is conducted by the Department of Agriculture, Water and the Environment.

This Public Report is available for viewing and downloading from the AICIS website. For enquiries please contact AICIS at:

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Executive Director
AICIS

TABLE OF CONTENTS

SUMMARY

The following details will be published on the AICIS website:

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1735	Chemicalia Pty Ltd. Era Polymers Pty Ltd.	Aldirez A	Yes	≤ 100 tonnes per annum	Accelerator, cross-linker, moisture scavenger and latent curing agent for industrial surface coatings, sealants and adhesives

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard Classification	*Hazard Statement*
Sensitisation, Skin (Category 1)	H317 – May cause an allergic skin reaction
Skin corrosion/Irritation (Category 1C)	H314 – Causes severe skin burns and eye damage
Flammable liquid (Category 4)	H227 – Combustible liquid

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

Hazard classification	*Hazard statement*
Acute (Category 3)	H402 - Harmful to aquatic life

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

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

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

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The assessed chemical should be classified as follows:
  - Sensitisation, Skin (Category 1): H317 – May cause an allergic skin reaction
  - Skin Corrosion/Irritation (Category 1C): H314 – Causes severe skin burns and eye damage
  - Flammable liquid (Category 4): H227 – Combustible liquid

The above should be used for products/mixtures containing the assessed chemical, if applicable, based on the concentration of the assessed chemical present.

Health Surveillance

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

CONTROL MEASURES

Occupational Health and Safety

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

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the assessed chemical:
  - Avoid contact with skin and eyes
  - Avoid inhalation of aerosols
  - Remove all sources of ignition

- 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 assessed chemical:
  - Impervious gloves
  - Safety glasses or goggles
  - Respiratory protection if inhalation exposure may occur
  - Protective clothing
  - Chemical resistant boots

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

- Spray applications should be carried out in accordance with the Safe Work Australia Code of Practice for *Spray Painting and Powder Coating* (SWA, 2015) or relevant State or Territory Code of Practice.

- A copy of the SDS should be easily accessible to employees.

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

Transport and Packaging

- Due to the combustibility of the assessed chemical, introducers of the chemical should consider their obligations under *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG code) (NTC, 2018).

Storage

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

Emergency procedures

- Spills or accidental release of the assessed chemical should be handled by physical containment, collection and subsequent safe disposal.

Disposal

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

Regulatory Obligations

Specific Requirements to Provide Information
This risk assessment is based on the information available at the time of the application. The Executive Director may initiate an evaluation of the chemical based on changes in certain circumstances. Under Section 101 of the IC Act the applicant of the assessed chemical has post-assessment regulatory obligations to provide information to AICIS when any of these circumstances change. These obligations apply even when the assessed chemical is listed on the Australian Inventory of Industrial Chemicals (the Inventory).

Therefore, the Executive Director of AICIS must be notified in writing within 20 working days by the applicant or other introducers if:

- the function or use of the chemical has changed from accelerator, cross-linker, moisture scavenger and latent curing agent for industrial surface coatings, sealants and adhesives, or is likely to change significantly;
- finished products containing the chemical have become available to the public for end use;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on human health, or the environment.

The Executive Director will then decide whether an evaluation of the introduction is required.

Safety Data Sheet
The SDS of the assessed chemical and products containing the assessed chemical provided by the applicant were reviewed by AICIS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND APPLICATION DETAILS

APPLICANT(S)
Chemicalia Pty Ltd (ABN: 17 100 190 270)
7 Cremin Court
MOUNT WAVERLEY VIC 3149

Era Polymers Pty Ltd (ABN: 14 003 055 936)
25-27 Green Street
EAST BOTANY NSW 2019

APPLICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year)

PROTECTED INFORMATION (SECTION 38 OF THE TRANSITIONAL ACT)
Data items and details taken to be protected information include: chemical name, specific other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, import volume, and identity of recipients.

VARIATION OF DATA REQUIREMENTS (SECTION 6 OF THE TRANSITIONAL RULES)
Schedule data requirements are varied for acute inhalation toxicity, eye irritation, genotoxic damage *in vivo* and bioaccumulation.

PREVIOUS APPLICATION IN AUSTRALIA BY APPLICANT(S)
None

APPLICATION IN OTHER COUNTRIES
EU REACH (2018)
New Zealand (2010)
Switzerland (2014)
USA (2009)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Aldirez A

MOLECULAR WEIGHT
< 1000 g/mol

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

3. COMPOSITION

DEGREE OF PURITY
> 95%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless to yellowish liquid

Property	*Value*	*Data Source/Justification*
Melting Range	-66.0 to -62.2 °C	Measured
Boiling Point	232.4 °C	Measured
Density	833 kg/m^3 at 20 °C	Measured
Vapour Pressure	0.063 kPa at 25 °C	Measured
Water Solubility	Not determined	Hydrolytically unstable

Property	*Value*	*Data Source/Justification*
Hydrolysis as a Function of pH	$t_{1/2}$ < 5 minutes at pH 4, 7 and 9 at 25°C	Measured
Partition Coefficient (n-octanol/water)	Not determined	Hydrolytically unstable
Surface Tension	48.07 nM/m at 20 °C (surface active)	Measured
Adsorption/Desorption	Not determined	Hydrolytically unstable
Dissociation Constant	Not determined	Has no dissociable functionality, but rapidly hydrolyses to form degradation products that have cationic functionality
Flash Point	81.5 °C (closed cup)	Measured
Flammability	Category 4 combustible liquid	Based on measured flash point
Autoignition Temperature	239 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

DISCUSSION OF PROPERTIES
For details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The assessed chemical hydrolyses quickly in contact with water or moisture in the air, releasing isobutyraldehyde (CAS No. 78-84-4) and hazardous amine type compounds. During the end use of the products containing the assessed chemical, the released amines are expected to be cross-linked into the polymer matrix and the aldehyde is likely to evaporate into the air.

The assessed chemical is expected to be stable under normal conditions of use.

Physical Hazard Classification
Based on the submitted physico-chemical data depicted in the above table, the assessed chemical is 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.

Hazard Classification	*Hazard Statement*
Flammable Liquids (Category 4)	H227 – Combustible liquid

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF ASSESSED CHEMICAL (100%) OVER NEXT 5 YEARS
The assessed chemical will not be manufactured in Australia. It will be imported as Aldirez A (neat form of the assessed chemical) in 25 L steel pails or 200 L steel drums.

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

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

PORT OF ENTRY
Sydney, Melbourne, Brisbane, Adelaide or Perth

TRANSPORTATION AND PACKAGING
The product containing the neat form of the assessed chemical will be imported into Australia by sea in 25 L steel pails or 200 L steel drums and stored on pallets containing up to 800 kg product. It will be transported by road, using registered carriers for dangerous goods, to contracted third party warehouses. It will be distributed from these premises by road to a number of surface coatings, adhesives and sealants manufacturers.

USE
The assessed chemical will be used as an accelerator, cross-linker and moisture scavenger in the manufacture of 2-component polyurethane and polyaspartic surface coatings, adhesives and sealants at concentration up to 100%, and as a latent curing agent in 1-component epoxy resin surface coatings, adhesives and sealants at concentration up to 25%.

OPERATION DESCRIPTION
The product containing the assessed chemical will be distributed to formulators for reformulation into polyurethane, polyaspartic and epoxy resin surface coatings, adhesives and sealants.

At the reformulation sites, the product containing the assessed chemical will be pumped by an operator into closed mixing vessels where it will be blended with other raw materials. During mixing, quality assurance (QA) chemists will take aliquots of samples for testing. Once blending is complete, Part A of 2-component polyurethane and polyaspartic coatings and sealants/adhesives (containing the assessed chemical at 3% to 100% concentration) and 1-component epoxy resins (containing the assessed chemical at 1% to 25% concentration) will be packed in a variety of packages ranging from 0.025 L cartridges or cans to 200 L drums.

End-users in industrial coatings, adhesive and sealant application industries will apply the 2-component polyurethane and polyaspartic coatings/sealants/adhesives (following combination with the Part B curing agent containing polyisocyanates) or 1-component epoxy resins by spray, roller, trowel or similar methods onto fabricated steel products, concrete floors, and metal or concrete joints. During curing at ambient temperature, the assessed chemical will react with water present in the coating or air. No assessed chemical is expected to remain in the final dry formulations.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Stevedores	3	10-15
Transport workers	6	260
Distribution workers	4	260
Warehouse staff	6	260
Production operators	6	260
Quality control technicians	6	260
Cleaning and maintenance workers	4	260
Surface coatings applicators	6	260
Adhesive/sealants applicators	6	240

EXPOSURE DETAILS

Transport and storage
Exposure of transport and storage workers to the assessed chemical is not expected, except in the event of accidental spill or breach of container.

Reformulation
Dermal and ocular exposure to the assessed chemical at concentrations ranging from 3% to 100% are likely to be the main routes of potential exposure that may occur during manual weighing, connecting and disconnecting spear pumps, charging the blending vessels, blending, sampling from the blending vessel and routine cleaning and maintenance of equipment. Given that the assessed chemical has relatively low vapour pressure, significant inhalation exposure is not expected, unless aerosols or mists are formed during the mixing processes.

The applicant states that exposure to the assessed chemical is expected to be minimised through the use of engineering controls such as local exhaust ventilation, and suitable personal protective equipment (PPE) capable of protecting workers from exposure to the assessed chemical including safety googles, gloves, protective clothing and footwear.

End-use in 2-component polyurethane and polyaspartic coatings and sealants/adhesives
Dermal, ocular and inhalation exposure to the assessed chemical at concentrations ranging from 3% to 100% are expected to be the main routes of potential exposure that may occur when manually connecting the product containers to the 2-component mixer and application equipment, and during routine cleaning and maintenance of application equipment. When coatings containing the assessed chemical are applied by spray, respirable aerosols or mists are likely to form.

The applicant states that exposure of operators to the assessed chemical is expected to be minimised through the use of engineering controls such as local exhaust ventilation, and suitable PPE including protective breathing apparatus, googles, clothing, gloves and footwear. Inhalation exposure during application will be minimised by conducting spray and similar operations within application booths with local exhaust ventilation/extraction. Should personnel be required to work within the booths they will wear a full body suit equipped with an air makeup hood.

Following curing at ambient temperature, the assessed chemical will react with water present in the products or air typically within 1 hour. Isobutyraldehyde may be released into the air during curing period. No assessed chemical is expected to remain in the final dry formulations.

End-use in 1-component epoxy resins
Dermal, ocular and inhalation exposure to the assessed chemical at concentrations ranging from 1% to 25% are expected to be the main routes of potential exposure that may occur when manually connecting the product containers to the application equipment, and during routine cleaning and maintenance. When coatings containing the assessed chemical are applied by spray, respirable aerosols and mists may form.

The applicant states that dermal and ocular exposure of operators to the assessed chemicals will be reduced through the use of engineering controls such as local exhaust ventilation in application areas, and the use of suitable PPE including protective googles, clothing, gloves and footwear. Inhalation exposure during spray application will be minimised by operating within application booths with local exhaust ventilation/extraction. Should personnel be required to work within the booths they will wear a full body suit equipped with an air makeup hood.

Following curing at ambient temperature, the assessed chemical will react with water present in the products or air typically within 8 hours. Isobutyraldehye may be released into the air during the curing period. No assessed chemical is expected to remain in the final dry formulations.

6.1.2. Public Exposure
The assessed chemical will be for industrial use only and will not be made available to the public. Surface coatings and adhesives/sealants containing the assessed chemical are not expected to be available to the general public for any DIY application.

The public may come into contact with finished articles to which surface coatings, adhesives and sealants have been applied; however, once the end use product has cured, no assessed chemical is expected to remain within the final dry formulation.

6.2. Human Health Effects Assessment
The results from toxicological investigations conducted on the assessed chemical are summarised in the following table. Since the assessed chemical hydrolyses rapidly in contact with water, under the conditions of the studies the reported toxicity effects were likely caused by the degradants of the chemical. For details of the studies, refer to Appendix B.

Endpoint	***Result and Assessment Conclusion***
Acute oral toxicity – rat	LD50 > 2000 mg/kg bw; low toxicity
Acute dermal toxicity – rat	LD50 > 2000 mg/kg bw; low toxicity
Skin irritation – *in vitro* EpiDerm™	corrosive or irritating
Skin irritation – rabbit	corrosive
Skin sensitisation – mouse local lymph node assay	evidence of sensitisation
Repeat dose oral toxicity – rat, 28 days	NOAEL = 609 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	equivocal
Genotoxicity – *in vitro* mammalian chromosome aberration test	non genotoxic
Genotoxicity – *in vitro* mammalian cell gene mutation assay	non genotoxic
Reproductive and developmental toxicity – rat	NOAEL = 750 mg/kg bw/day

Toxicokinetics, Metabolism and Distribution
In contact with body fluids or moisture, the assessed chemical is expected to release isobutyaldehyde and amine compounds. Results from sub-acute oral toxicity studies showed changes to haematology parameters demonstrating possibility of absorption via the oral route. Disregarding hydrolysis of the chemical, absorption via the respiratory route is considered less likely due to low vapour pressure and water solubility, limiting concentration in the mucus lining of the respiratory tract. Dermal absorption is also not considered likely based on high log Pow and low water solubility. This is supported by results from acute dermal toxicity studies, in which no signs of systemic toxicity were reported.

Acute Toxicity
Based on studies in rats, the assessed chemical may be of low acute toxicity via the oral and dermal routes. However, diarrhoea and diuresis may occur if the chemical is ingested. Local irritation effects, including erythema and oedema, may also precede if the chemical comes into contact with skin.

No acute inhalation toxicity data are available for the assessed chemical.

Irritation and Sensitisation
According to the results of a skin irritation/corrosion assay in rabbits, the assessed chemical is considered corrosive to skin requiring hazard classification. This is supported by an *in vitro* EpiDerm reconstructed human epidermis assay, and local irritation/corrosion effects observed in acute dermal toxicity and skin sensitisation assays.

Testing for eye irritation was not carried out for animal welfare reasons. The chemical is considered to cause severe eye damage based on the skin corrosive characteristics.

There was clear evidence of sensitisation to the assessed chemical in a local lymph node assay (LLNA) using mice, requiring hazard classification.

Repeated Dose Toxicity
The oral No Observed Adverse Effect Level (NOAEL) was established by the study authors as 609 mg/kg bw/day in a 28 day repeat dose study in rats, based on the absence of observed adverse effects at this dose level in the study. The assessed chemical was tested at actual 39, 210 and 937 mg/kg bw/day in the animals. The high dose caused one male and one female deaths in a group of 5 males and 5 females, and was reduced to 609 mg/kg bw/day on Day 16. Clinical signs observed in the high dose group before dose reduction included decreased activity, salivation, Straub-tail, nuzzling of bedding and vocalisation. Decreased activity and Straub-tail ceased after the dose reduction. Body weight of the high dose group was reduced, correlating with the food consumption reduction. Other laboratory findings, including clinical chemistry, haematology and organ observations in the test, were considered by the study authors either to be adaption reactions or not to be treatment related.

In a reproductive/developmental toxicity study (according to OECD TG 421), the assessed chemical was tested via oral gavage at 50, 250 and 750 mg/kg bw/day for 40 days in rats. A NOAEL of 250 mg/kg bw/day was established by the study authors for the systemic toxicity in the parental generation of the males and females based on changes in clinical signs, body weight and food consumptions. Clinical signs observed were similar to those noted in the 28-day repeat dose oral toxicity study from the high dose group.

Mutagenicity/Genotoxicity
The assessed chemical was found to be equivocal in a bacterial reverse mutation assay compliant with OECD TG 471. Some bacterial strains showed increased revertant colony numbers, although some of these increases were within the historical control ranges and there was no clear dose response. However, substantially increased revertant colony numbers above historical control data ranges were observed in the plate incorporation test with *S. typhimurium* TA 98 at 5000 µg/plate without metabolic activation, and in *E. coli* WP2 uvrA at 5000 µg/plate with metabolic activation and 1581 µg/plate without metabolic activation. Substantial increases above historical control data ranges were also observed in the pre-incubation test in *E. coli* WP2 uvrA at 500 µg/plate without metabolic activation and 1581 µg/plate with metabolic activation. Therefore, the potential of the assessed chemical to cause point mutations cannot be ruled out.

Negative results were observed in an *in vitro* mammalian chromosome aberration test (OECD TG 473) using Chinese hamster V79 (fibroblast) cells and an *in vitro* mammalian cell gene mutation test (OECD TG 476) using Chinse hamster ovary (CHO) cells.

Toxicity for Reproduction
In the reproductive/development toxicity study mentioned above, the NOAEL was established as 750 mg/kg bw/day, based on the absence of observed adverse effects to reproductive performance in the parental animals and to the development in the offspring, noting that the NOAEL for the systemic toxicity to the parental animals was established at 250 mg/kg bw/day in the same study.

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

Hazard Classification	*Hazard Statement*
Sensitisation, Skin (Category 1)	H317 – May cause an allergic skin reaction
Skin Corrosion/Irritation (Category 1C)	H314 – Causes severe skin burns and eye damage

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available information, the assessed chemical is expected to present a concern for a number of health effects including skin sensitisation, and severe skin/eye irritation.

During reformulation and end-use, exposure of workers to the assessed chemical is expected to be limited given the use of engineering controls (such as enclosed and automated systems, and sufficient ventilation) and PPE (including protective clothing, impervious gloves, safety glasses and respirators). Once the final product (surface coatings, adhesive and sealant) is cured, no assessed chemical is expected to remain in the final dry formulations.

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

6.3.2. Public Health
The assessed chemical is intended for industrial use only and will not be made available to the public. Members of the public may come into contact with cured coatings, adhesives and sealants. However, no assessed chemical is expected to remain in the final dry formulations when the finished products containing the chemical are cured.

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

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The assessed chemical is imported in a neat form. It will be reformulated into either a 2-component polyurethane and polyaspartic (part A) or a 1-component epoxy resin surface coating, adhesives or sealant. The reformulation process includes blending operation in closed systems followed by packing of the reformulated products into end-use packages. Waste generated during the reformulation process and accidental spills containing the assessed chemical are expected to be collected and disposed of in accordance with state and local government regulations.

RELEASE OF CHEMICAL FROM USE
The coatings, adhesives and sealants containing the assessed chemical, either as a 2-component (part A) or 1-component product will be applied by spray, roller, trowel or similar methods onto fabricated steel products, concrete floors, and metal or concrete joints. The majority of the coatings, adhesives and sealants containing the assessed chemical are expected to be cured with no significant amount of the assessed chemical remaining on the applied surface. It is expected that some of the coatings will be in the form of overspray during spraying operations, and will typically entail disposal to landfill after being collected and cured. The liquid waste from cleaning of the application equipment is expected to be collected by an approved waste contractor, and be disposed of safely.

During use, the assessed chemical may also be released to the environment as accidental spills. These releases are expected to be collected and disposed of to landfill in accordance with local government regulations.

RELEASE OF CHEMICAL FROM DISPOSAL

Most of the assessed chemical is expected to cure and no significant amount of assessed chemical is expected to remain in the final dry coatings, adhesives or sealants. These dried coatings, adhesives or sealants will share the fate of the articles to which they have been applied, to be either recycled for metal reclamation or disposed of to landfill at the end of their useful life. Empty import and end use packages containing residues of the assessed chemical will be collected by an approved waste contractor for safe disposal.

7.1.2. Environmental Fate

The biodegradability study conducted on the assessed chemical show that it is not readily biodegradable (5.9% degraded over 28 days in OECD 301D test); however, the assessed chemical hydrolyses rapidly ($t_{1/2} < 5$ min) in contact with water. For details of the biodegradability study, see Appendix C. As a result of its use pattern, the majority assessed chemical is expected to react and form a final dry coating, adhesive or sealant with no significant amount of assessed chemical remaining. These dried coatings, adhesives or sealants will be either thermally decomposed during metal reclamation or eventually degrade via biotic or abiotic processes. As it rapidly hydrolyses in contact with water, the assessed chemical is not expected to be bioaccumulative. In landfill, the assessed chemical collected from waste and spills is expected to hydrolyse with moisture in the air and eventually further degrade via 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 not been calculated as release of the assessed chemical to the aquatic environment will be limited based on its reported use pattern.

7.2. Environmental Effects Assessment

The assessed chemical is hydrolytically unstable, and the reported toxicity is likely caused by the degradants of the assessed chemical. The results from ecotoxicological investigations conducted on the assessed chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 27.79 mg/L	Harmful to fish
Daphnia Toxicity	48 h EC50 = 68.79 mg/L	Harmful to aquatic invertebrates
Algal Toxicity	72 h EC50 = 14.8 mg/L NOEC = 6.13 mg/L	Harmful to algae
Inhibition of Bacterial Respiration	3 h IC50 = 375.38 mg/L	Not inhibitory to bacterial respiration

Based on the above ecotoxicological endpoints, the assessed chemical and its degradants are harmful to aquatic life. Therefore, the assessed chemical is classified as 'Acute Category 3: Harmful to aquatic life' according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) (United Nations, 2009). Based on its rapid hydrolytic degradability, the assessed chemical is not formally classified for chronic toxicity under the GHS.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) has not been calculated since no significant release of the assessed chemical to the aquatic environment is expected from the proposed use pattern.

7.3. Environmental Risk Assessment

The risk quotient (Q = PEC/PNEC) for the assessed chemical has not been calculated as release to the aquatic environment in ecotoxicologically significant quantities is not expected based on its reported use pattern as a component of industrial coatings. The majority of the assessed chemical is expected to cure with no significant amount of assessed chemical in the final dry coatings, adhesives or sealants. These coatings, adhesives or sealants will share the fate of the articles to which they have been applied, to be either recycled for metal reclamation or disposed of to landfill at the end of their useful life. Therefore, on the basis of the assessed use pattern, the assessed chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Range -66.0 to -62.2 °C

Method OECD TG 102 Melting Point/Melting Range
Remarks Determined using the capillary method
Test Facility LAUS GmbH (2011a)

Boiling Point 232.4 °C

Method OECD TG 103 Boiling Point
EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks Siwoboloff method with automatic photo-electrical detection
Test Facility TOXI-COOP ZRT (2011a)

Density 833 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids
EC Council Regulation No 440/2008 A.3 Relative Density
Remarks Gas pycnometer method
Test Facility TOXI-COOP ZRT (2011b)

Vapour Pressure 0.063 kPa at 25 °C

Method OECD TG 104 Vapour Pressure
Remarks Static method
Test Facility LAUS GmbH (2011b)

Hydrolysis as a Function of pH $t_{1/2}$ < 5 minutes at pH 4, 7 and 9 at 25°C

Method OECD TG 111 Hydrolysis as a Function of pH
EC Council Regulation No 440/2008 C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH

pH	*T (°C)*	*$t_{½}$ (minutes)*
4	25	< 5
7	25	< 5
9	25	< 5

Remarks After 5 minutes hydrolysis at room temperature (25 ºC) the test item could not be detected ($t_{1/2}$ < 5 minutes). Therefore, based on the above-mentioned influence of the temperature on the velocity of chemical reactions, the $t_{1/2}$ value is expected to be also very small in a lower temperature range (10 – 25 ºC). Consequently, it was also not feasible to measure the concentration of the test item to obtain more information on the stability under these conditions. HPLC was used for analysis.
Test Facility TOXI-COOP ZRT (2012)

Surface Tension 48.07 mN/m at 20 °C (surface active)

Method OECD TG 115 Surface Tension of Aqueous Solutions
EC Council Regulation No 440/2008 A.5 Surface Tension
Remarks Concentration: 1 mg/mL
Test Facility LAUS GmbH (2011c)

Flash Point 81.5 °C (closed cup)

Method EC Council Regulation No 440/2008 A.9 Flash Point
Remarks Determined using the equilibrium method with closed cup and electrical ignitions
Test Facility LAUS GmbH (2011d)

Autoignition Temperature 239 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Remarks	Smoke and sound observed during test
Test Facility	TOXI-COOP ZRT (2011c)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method EC Council Regulation No 440/2008 B.1 tris Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain	Rat/Crl(WI)Br
Vehicle	Concentration of the assessed chemical in sunflower seed oil (Helianthi Annui Oleum Raffinatum) was adjusted to maintain a treatment volume of 10 mg/kg bw.
Remarks – Method	GLP compliant No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	3F	2000	0/3
2	3F	2000	0/3

LD50	> 2000 mg/kg bw
Signs of Toxicity	In treatment group 1, diarrhoea and diuresis occurred in 2 separate animals. The animals were symptoms free 30 minutes after treatment and between observation days 2 to 14. All animals made the expected body weight gains.
Effects in Organs	No macroscopic pathological findings related to the test item were observed at the necropsy.
CONCLUSION	The assessed chemical is of low acute toxicity via the oral route.
TEST FACILITY	TOXI-COOP ZRT (2010)

B.2. Acute Dermal Toxicity – Rat

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test EC Council Regulation No 440/2008 B.3 Acute Toxicity (Dermal) – Limit Test
Species/Strain	Rat/Crl:(WI)BR
Vehicle	Test substance administered as supplied
Type of dressing	Semi-occlusive
Remarks – Method	GLP compliant No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5/sex	2000	0/10

LD50	> 2000 mg/kg bw
Signs of Toxicity – Local	Symptoms of local irritation including erythema (All animals of both sex; score +1 to +4; Day 1 to Day 14), oedema (2 Males, score +1; Day 1 to Day 7) and other signs including dry skin surface (All Males Day 2 to Day 14, and 4 Females Day 1 to Day 14), wounds (3 Males and 3 Females) crusting (All Males and 4 Females) were reported at the treatment site.
Signs of Toxicity – Systemic	There were no deaths or test-substance related clinical signs. A slight body weight loss (4%) was evident in one female between Day 0 and Day 7. All

	other animals achieved satisfactory bodyweight gains throughout the study.
Effects in Organs	No macroscopic pathological findings related to the systemic toxic effects of the test item were observed at the necropsy.
CONCLUSION	The assessed chemical is of low acute toxicity via the dermal route.
TEST FACILITY	TOXI-COOP ZRT (2011i)

B.3. Skin Irritation – *In Vitro* EpiDerm™ Reconstructed Human Epidermis Model

TEST SUBSTANCE	Assessed Chemical
METHOD	EC Council Regulation No 440/2008 B.46. *In vitro* Skin Irritation – Reconstructed Human Epidermis Model Test
Vehicle	Test substance administered as supplied using a nylon mesh
Remarks – Method	GLP compliant The protocol was conducted according to a draft OECD guideline (*In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method, (version 7.6) equivalent to OECD TG 439 Negative Control: Dulbecco's Phosphate Buffered Saline (DPBS) Positive Control: 5% sodium dodecyl sulphate (SDS) in deionised water

RESULTS

Test Material	*Mean OD_{570} of Triplicate Tissues*	*Relative Mean Viability (%)*	*SD of Relative Mean Viability*
Negative control	2.045	100	6.4
Test substance	0.129	6.3	10.9
Positive control	0.130	6.4	3.6

OD = optical density; SD = standard deviation

Remarks – Results	The test substance was shown not to directly reduce MTT. The value for the negative control was within the historical data range of the test facility. The value for the positive control was below the historical data range of the test facility. However, the experiment was considered valid as variation of biological systems within this order of magnitude are not unusual.
CONCLUSION	Based on the mean tissue viability of ≤ 50%, the assessed chemical should be classified for skin irritation according to the GHS criteria.
TEST FACILITY	LAUS GmbH (2011e)

B.4. Skin Irritation – Rabbit

TEST SUBSTANCE	Assessed Chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation)
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	Test substance administered as supplied
Observation Period	The animals were examined at 1, 24, 48 and 72 hours, then one and two weeks after patch removal
Type of Dressing	Semi-occlusive
Remarks – Method	GLP compliant

No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	3.00	3.33	2.00	4	< 14 days	0
Oedema	1.66	2.66	0.66	3	< 14 days	0

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

Remarks – Results: Slight to well defined erythema was seen in two animals (score of 1 and 2, respectively) 1 hour after patch removal. Slight to well defined erythema was reported in 2 animals; and moderate to severe erythema with slight oedema in 1 animal at 24 hours. At 48 hours, dry skin, wounds and bleeding were reported in 2 animals. At 72 hours dry skin, wounds, bleeding and bloody scabs were reported in 2 animals and scabs and crusting in 1 animal. Wounds and crusting were reported in all animals after 1 week. All signs of irritation were reversible within the 14 day study period. There were no deaths or test substance-related clinical signs or remarkable body weight changes during the study period.

CONCLUSION: The assessed chemical is corrosive to the skin.

TEST FACILITY: TOXI-COOP ZRT (2011j)

B.5. Skin Sensitisation – LLNA

TEST SUBSTANCE: Assessed chemical

METHOD: OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)

Species/Strain: Mouse/CBA/Ca
Vehicle: Acetone/Olive oil 4:1 (v/v)
Preliminary study: Yes
Positive control: α-Hexylcinnamaldehyde (HCA) at concentrations of 50% or 25%
Remarks – Method: GLP compliant
A pre-test with 100%, 50% and 25% showed local irritation effects (irritation and necrosis) and considered unacceptable. A test item concentration of 10% was selected as the highest concentration for use in the main test.

RESULTS

Concentration (% w/w)	*Number and Sex of Animals*	*Proliferative Response (DPM/lymph node)*	*Stimulation Index (test/control ratio)*
Test Substance			
0 (vehicle control)	5F	1421.4	1.0
2.5	5F	7872.8	5.5
5	5F	12745.1	9.0
10	5F	14987.8	10.5
Positive Control			
25	5F	3383.4	2.4
50	5F	5481.4	3.9

Remarks – Results: No deaths and no signs of systemic toxicity were reported. The stimulation index (SI) for increase in ^{3}H-thymidine incorporation into cells was greater than 3 at all doses, indicating that the assessed chemical

	has sensitisation potential. An EC3 value estimation was not performed as the SI values were greater than 3 at all doses. Acceptance criteria were met confirming the validity of the assay.
CONCLUSION	There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the assessed chemical.
TEST FACILITY	TOXI-COOP ZRT (2011k)

B.6. Repeat Dose Oral Toxicity – Rat (Dose Range Finding)

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral)
Species/Strain	Rat/Hsd.Brl.Han (Wistar rat)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 14 days Dose regimen: 7 days per week Post-exposure observation period: 1 day (dosing was continued up to and including the day before necropsy)
Vehicle	Sunflower oil
Remarks – Method	This study was a dose range finding study for the below 28 day repeat dose oral toxicity study. This study was not GLP compliant. However, GLP principles were followed.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration (mg/kg bw/day)*		*Mortality*
		Nominal	*Actual*	
Control	5/sex	0	0	0/10
Low Dose	5/sex	50	39	0/10
Mid Dose	5/sex	250	212	0/10
High Dose	5/sex	1000	914	0/10

Mortality and Time to Death

No mortality was recorded during the treatment period.

Clinical Observations

All animals in the high dose group showed decreased activity, salivation, and nuzzling up of bedding. Additionally, swollen abdomen, prone position, closed eyes and piloerection were noted in male animals. No clinical signs were reported in the low and mid dose groups. There were no treatment-related changes noted in the functional observation battery. Body weights of male and female animals in the high dose group were reduced during week 1, corresponding to mean daily food consumption reduction.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No test item related alterations in the examined clinical chemistry parameters were reported.

Effects in Organs

Specific macroscopic alterations related to treatment were not noted during the terminal necropsy.

Remarks – Results

No test item related adverse findings were reported at any dose in male and female rats.

CONCLUSION

The doses of 50 (low), 250 (mid) and 1000 (high) mg/kg bw/day were selected for the below 28-day repeat dose oral toxicity study.

TEST FACILITY TOXI-COOP ZRT (2011m)

B.7. Repeat Dose Oral Toxicity – Rat

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral)
Species/Strain	Rat/Hsd.Brl.Han (Wistar rat)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: 1 day (dosing was continued up to and including the day before necropsy)
Vehicle	Sunflower oil
Remarks – Method	GLP compliant Dose setting was based on finding from a 14-day oral gavage dose range finding study. On Day 16 the high dose concentration was reduced from 1000 (actual 937) to 750 (actual 609) mg/kg bw/day for animal welfare reasons. The concentration of the test item in sunflower oil was quantified on Day 4 and 25.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration (mg/kg bw/day)*		*Mortality*
		Nominal	*Actual*	
Control	5/sex	0	0	0/10
Low Dose	5/sex	50	39	0/10
Mid Dose	5/sex	250	210	0/10
High Dose	5/sex	1000/750*	937/609*	1/5 male, 1/5 female

* Due to mortality, the high dose level was reduced on Day 16.

Mortality and Time to Death

The high does at 1000 mg/kg bw/day caused mortality of one male and one female on Day 10 and Day 7, respectively. Following reduction to 750 mg/kg bw/day on Day 16, no further mortality occurred.

Clinical Observations

All animals in the high dose group showed decreased activity, salivation, Straub-tail and nuzzling up of bedding. Additionally, vocalisation was reported in one male and one female. Following dose reduction to 750 mg/kg bw/day (Day 16), Straub tail and decreased activity ceased (Day 18). Salivation was reported in all animals in the mid dose group from Day 7 to Day 28. No clinical signs were reported in the low dose group.

There were no treatment-related changes noted in the functional observation battery. Body weights of males in the high dose group remained below control values for the duration of the study due to significant reductions in body weight gain in Week 1 and Week 2, correlated with significantly reduced mean daily food consumption. Food consumption of females in the high dose group was reduced, but did not reach statistical significance.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

A statistically significant decrease in the activity of alkaline phosphatase (ALP) was reported in high dose and low dose males. Concentration of glucose, sodium, chloride, albumin and total protein were decreased in high dose females. Total bilirubin concentration was statistically reduced in low dose males. These changes were not considered to be treatment related as they were sporadic, within the range of historical controls, without dose-dependent relationships and/or without substantiative correlated histopathological changes.

There was no statistically significant difference in the haematological parameters between male control and treatment groups. In female animals increased white blood cell count (WBC) and percentage of lymphocytes were reported in the high dose group. A decreased percentage of neutrocytes were reported in both the high and mid dose groups. These changes were within the historical control ranges and not considered to be toxicologically significant.

Effects in Organs

No treatment related macroscopic/microscopic changes or changes in absolute organ weights were reported following necropsy of male and female animals.

In the high dose group pinhead sized haemorrhages (1 male) and pale kidneys (1 male were reported). In the mid dose group pale kidneys (1 male), pale liver (1 female) and slight to moderate hydrometra (2 females) were reported. In the low dose group reddish mottled lungs (1 male) and moderate hydrometra (1 female) were reported. In the control group reddish mottled lungs (1 male and 1 female), point sized haemorrhages in the lungs (1 male), alopecia and scar on left shoulder (1 female) and moderate hydrometra (2 females) were reported. No lesions were found in the affected kidneys or liver following microscopic examination. Pulmonary changes occurred at a similar incidence in the control animals and considered to develop during exsanguination. Hydrometra, related to the female sexual cycle, and alopecia were reported as frequent observation in experimental rats.

In the high dose group kidney weights were higher in female rats compared to controls. In the low dose group, adrenal glands were slightly reduced in male rats compared to controls. The increased kidney weights were not accompanied by any microscopic changes and were considered to be an adaption phenomenon.

Remarks – Results

No test item related adverse findings were reported at any dose in male and female rats after the high dose reduction.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established by the study authors as 609 mg/kg bw/day in this study, based on clinical observations, and significant changes to food consumptions and body weight at 937 mg/kg bw/day.

TEST FACILITY	TOXI-COOP ZRT (2011l)

B.8. Genotoxicity – Bacteria

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria Plate incorporation procedure and Pre incubation procedure
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98 and TA100 *Escherichia coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbital/β-naphthoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 15.8-5000 µg/plate b) Without metabolic activation: 15.8-5000 µg/plate
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks – Method	GLP Compliant No significant protocol deviations Positive controls: Without metabolic activation – 4-nitro-1,2-phenylene-diamine (NPD) in DMSO (TA98), Sodium Azide in distilled water (TA100 and TA1535), 9-aminoacridine (9AA) in DMSO (TA1537), methyl-methanesulfonate (MMS) in distilled water (*E. Coli* WP2 *uvrA*). With metabolic activation – 2-aminoantheacene (2AA) in DMSO (all strains) Negative controls – DMSO and distilled water

RESULTS

Test	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Plate incorporation			
With S9 mix	≥ 5000	> 5000	Equivocal
Without S9 mix	≥ 5000	> 5000	Equivocal
Pre-incubation			
With S9 mix	≥ 500	> 5000	Equivocal
Without S9 mix	≥ 5000	> 5000	Equivocal

Remarks – Results

Plate incorporation test
Substantially increased revertant colony numbers (above historical control data ranges) were observed in *S. typhimurium* TA 98 at 5000 µg/plate (without metabolic activation), and in *E. coli* WP2 uvrA at 5000 µg/plate (with metabolic activation) and 1581 µg/plate (without metabolic activation).

Increased revertant colony numbers (within historical control data ranges) were observed in *S. typhimurium* TA 100 at 5000 µg/plate (without metabolic activation), in TA 98 at 158 µg/plate (without metabolic activation), and in *E. coli* WP2 uvrA at 1581 µg/plate (with metabolic activation).

These increases did not show a clear dose response relationship.

Pre-incubation test
Substantially increased revertant colony numbers (above historical control data ranges) were observed in *E. coli* WP2 uvrA at 500 µg/plate (without metabolic activation) and 1581 µg/plate (with metabolic activation).

Increased revertant colony numbers (within historical control data ranges) were observed in *S. typhimurium* TA 98 at 158-1581 µg/plate (without metabolic activation).

These increases did not show a clear dose response relationships.

Vehicle and positive controls performed as expected, confirming the validity of the test system.

CONCLUSION

The assessed chemical was not considered mutagenic to bacteria by the study authors under the conditions of the test.

TEST FACILITY

TOXI-COOP ZRT (2011n)

B.9. Genotoxicity – *In Vitro* Mammalian Chromosome Aberration Test

TEST SUBSTANCE

Assessed Chemical

METHOD

OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test
EC Directive 2000/32/EC B.10 Mutagenicity – *In vitro* Mammalian Chromosome Aberration Test

Cell Type/Cell Line: Chinese Hamster V79 Cells
Metabolic Activation System: S9 fraction from phenobarbital/β-naphthoflavone induced rat liver
Vehicle: Dimethyl Sulfoxide (DMSO)
Remarks – Method: GLP Compliant
No significant protocol deviations

Positive control: Without metabolic activation – Ethylmethane sulphonoate in Dulbecco's Modified Eagle's medium (DMEM), with

metabolic activation – N-nitrodimethylamine in Dulbecco's Modified Eagle's medium (DMEM)
Negative Control: DMSO

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Experiment A	39.1, 78.2, 156.3, 312.5, 625*	3 hr	20 hr
Experiment B	39.1, 78.2, 156.3, 312.5, 625*	20 hr	20 hr
Experiment B	39.1, 78.2, 156.3, 312.5, 625*	20 hr	28 hr
Present			
Experiment A	78.2, 156.3, 312.5, 625*	3 hr	20 hr
Experiment B	78.2, 156.3, 312.5, 625	3 hr	28 hr

*This concentration was tested but not evaluated.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Absent			
Experiment A	≥ 312.5	> 625	Negative
Experiment B	≥ 312.5	> 625	Negative
Present			
Experiment A	≥ 312.5	> 625	Negative
Experiment B	≥ 625	> 625	Negative

Remarks – Results

In Experiment A, there were no biologically significant increases in the number of cells showing structural chromosome aberrations in both the absence and presence of S9 mix.

In Experiment B, there were no biologically significant increases in the frequency of cells showing structural chromosome aberrations in both the absence and presence of S9 mix up to the cytotoxic concentration (625 µg/mL). No dose-response relationships were reported. No increase in the rate of polyploid and endoreduplicated metaphases.

The positive and negative controls performed as expected confirming the validity of the assay.

CONCLUSION

The assessed chemical was not clastogenic to Chinese Hamster V79 cells treated *in vitro* under the conditions of the test.

TEST FACILITY

TOXI-COOP ZRT (2011o)

B.10. Genotoxicity – *In Vitro* Mammalian Cell Gene Mutation Test: HPRT Assay

TEST SUBSTANCE

Assessed Chemical

METHOD

OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test
EC Directive 2000/32/EC B.17 Mutagenicity – *In vitro* Mammalian Cell Gene Mutation Test
Cell Type/Cell Line: CHO-K1
Metabolic Activation System: S9 fraction from phenobarbital/β-naphthoflavone induced rat liver
Vehicle: Dimethyl sulfoxide (DMSO)
Remarks – Method: GLP Compliant
No significant protocol deviations

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	150, 200, 250, 300, 350, 400, 450*	5 hrs	1-6 days	3-7 days

Test 2	150, 200, 250, 300, 350, 400, 450*	20 hrs	1-6 days	3-7 days
Present				
Test 1	50, 100, 150, 20, 250, 300, 350, 400, 450	5 hrs	1-6 days	3-7 days
Test 2	50, 100, 150, 20, 250, 300, 350, 400, 450	20 hrs	1-6 days	3-7 days

* Not evaluated due to high cytotoxicity at this concentration

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 300	> 450	Negative
Test 2	≥ 300	> 450	Negative
Present			
Test 1	≥ 250	> 450	Negative
Test 2	≥ 250	> 450	Negative

Remarks – Results: The test substance did not cause any relevant increase in the mutant frequencies either with or without metabolic activation.

The positive and negative controls gave a satisfactory response confirming the validity of the test system.

CONCLUSION: The notified chemical was not mutagenic to CHO cells treated *in vitro* under the conditions of the test.

TEST FACILITY: TOXI-COOP ZRT (2011p)

B.11. Reproductive/Developmental Toxicity – Rat One Generation Study

TEST SUBSTANCE: Assessed Chemical

METHOD

Species/Strain: Rat/ Hsd.Brl.Han

Route of Administration: Oral – gavage

Exposure Information: Exposure period – female: 14 days pre-mating, up to 14 days mating, through gestation (22-23 days) and up to lactation days 3, 4 or 5. Non-pregnant and non-mated female animals were treated up to and including the day before necropsy (day 40).
Exposure period – male: 41 days (14 days pre-mating, 14 days mating and 13 days post-mating)

Vehicle: Sunflower oil

Remarks – Method: OECD TG 421, Reproduction/Developmental Toxicity Screening Test
GLP Compliant

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	12/sex	0	0/24
Low dose	12/sex	50	0/24
Mid dose	12/sex	250	0/24
High dose	12/sex	750	0/24

Mortality and Time to Death

The study reported no test item related mortality. Two dams (1 in control group and 1 in 250 mg/kg bw/day group) were euthanised in moribund condition due to an elaborated delivery on lactation day 0.

Effects on Parental animals:

In the high dose male group, salivation (12/12), decreased activity (12/12), prone position (12/12), nuzzling of bedding (12/12) and narrowed eye orifices (5/12) were reported. In the high dose female group, salivation

(12/12), decreased activity (12/12), prone position (7/12), nuzzling of bedding (12/12) and narrowed eye orifices (1/12) were reported during the pre-mating period. During gestation, the incidence of decreased activity (5/12), prone position (3/12) and narrowed eye orifices (0/12) decreased. During the lactation period, only salivation (12/12) and nuzzling up of bedding (12/12) were reported. In the mid dose male group, salivation was reported for all animals over the course of the treatment period. In the mid dose female group, salivation was observed during pre-mating (12/12), gestation (11/12) and lactation periods (4/12). Alopecia and fur-discolouration (reddish-brown) were reported in one animal each.

Food consumption was decreased during weeks 1-2 in all high dose animals. Treatment resulted in a reduction in body weight of male rats throughout the study. Body weight reductions in female rats occurred only during week 1 of the pre-mating period.

In the low dose male and female groups no treatment related clinical signs were reported. Alopecia was reported in 2 female animals.

Reproduction
There were no test substance-related effects for male and female reproduction performance (including gonad function, mating behaviour, conception, pregnancy, parturition, fertility indices) and delivery data (including post-implantation loss, total intrauterine mortality, corpora lutea, number/percent of stillborn).

Effects on 1st Filial Generation (F1)
There were no test substance-related effects for litter data (including pup number and status at delivery, pup viability index/mortality and sex ratio), pup clinical observations, pup body weight data, and pup necropsy observations.

Remarks – Results
In the high dose group clinical signs (salivation, decreased activity, prone position, nuzzling up of bedding and narrow eye orifices), reduction in body weight gain and reduced food consumption were reported in male and female rats. There were no test substance-related adverse findings in male and female low and mid dose groups and all pups. The test item did not impact reproductive performance.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established by the study authors as 250 mg/kg bw/day following adverse findings for females and male rats in the high dose group mainly due to clinical signs, reduced body weight and food consumption.

The NOAEL for reproductive/developmental toxicity was established by the study authors as 750 mg/kg bw/day based on no test substance-related reproductive/developmental effects observed up to the highest dose tested.

TEST FACILITY TOXI-COOP ZRT (2011q)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks – Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Test Substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	11.3	7	64.6
14	5.4	14	69.7
21	8.0	21	73.2
28	5.9	28	73.8

Remarks – Results	All validity criteria for the test were satisfied. The oxygen depletion in the inoculum control was maintained at 1.38 mg O_2/L after 28 days. The residual oxygen concentration in the test flasks did not drop below 0.5 mg O_2/L at any time. The percentage degradation of the toxicity control reached the threshold level of 28.3% by 14 days (33.8% in 28 days), showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The results of the percentage biodegradation are not monotonic, but no explanation was provided. The mean biodegradation of assessed chemical was 5.9% during the 28 days period.
CONCLUSION	The assessed chemical is not readily biodegradable.
TEST FACILITY	TOXI-COOP ZRT (2011d)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Static
Species	*Danio rerio*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	239 mg $CaCO_3$/L
Analytical Monitoring	High Performance Liquid Chromatography (HPLC)
Remarks – Method	No significant deviations from the test guidelines were reported. Since mortality was observed during the limit test a subsequent full test was performed. The test solutions were freshly prepared just before the start of the treatments.

RESULTS

Concentration mg/L *Nominal*	*Number of Fish*	*Mortality*			
		24 h	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0
6.25	7	0	0	0	0
12.5	7	0	1	1	1
25	7	1	1	1	1
50	7	2	5	6	7
100	7	7	-	-	-

LC50 27.79 (95% CI of 18.73 - 41.23) mg/L at 96 hours (calculated using Probit Analysis).

Remarks – Results The assessed chemical was not hydrolytically stable and was not detected in test media. However, major degradation products were detected.

All validity criteria for the test were satisfied. Oxygen saturation concentration was 68.6-96% during the test. The temperature was maintained at 23-25.5°C.

The measured concentrations of the degradation products of the test substance varied in the range from 93% to 105% of the nominal value at the start of the study and from 101% to 106% at the end of the study. The deviation of the measured concentrations from the nominal values was lower than 20%, therefore, the results are based on the nominal concentration.

CONCLUSION The assessed chemical and its degradants are harmful to fish.

TEST FACILITY TOXI-COOP ZRT (2011e)

C.2.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE Assessed chemical

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

Species *Daphnia magna*
Exposure Period 48 hours
Auxiliary Solvent None
Water Hardness 219.5 mg $CaCO_3$/L
Analytical Monitoring High Performance Liquid Chromatography (HPLC)
Remarks – Method No significant deviations from the test guidelines were reported. A stock solution of the test substance was prepared (100 mg/L) by dissolution in the test medium. The mixture was sonicated for 30 minutes followed by centrifuged for 10 minutes and filtered. The stock solution was further diluted for the test concentrations. A reference test was also run.

RESULTS

Concentration (mg/L) *Nominal*	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
Control	20	0	0
6.25	20	0	0
12.5	20	0	0
25	20	0	0
50	20	3	5
100	20	4	16

EC50 68.79 mg/L at 48 hours (calculated using Probit Analysis).

Remarks – Results	The assessed chemical was not hydrolytically stable and was not detected in test media. However, major degradation products were detected. All validity criteria for the test were satisfied. Oxygen concentration was maintained at ≥ 3 mg/L in all test vessels. The reference test showed an EC50 value for potassium dichromate of 2.05 mg/L which is within the expected range. The measured concentrations of the degradation products of the test substance varied in the range from 86% to 103% of the nominal value at the start of the study and from 87% to 116% at the end of the study. The deviation of the measured concentrations from the nominal values was lower than 20%, therefore, the results are based on the nominal concentration.
CONCLUSION	The assessed chemical and its degradants are harmful to aqueous invertebrates
TEST FACILITY	TOXI-COOP ZRT (2011f)

C.2.3. Algal Growth Inhibition Test

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test EC Council Regulation No 440/2008 C.3 Algal Inhibition Test
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 1.875, 3.75, 7.5, 15, and 30 mg/L Geometrical mean measured: 1.64, 3.22, 6.13, 12.22 and 24.81 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	High Performance Liquid Chromatography (HPLC)
Remarks – Method	No significant deviations from the test guidelines were reported. A stock solution of the test substance (30 mg/L) was prepared by dissolution in the test medium. The mixture was sonicated for 30 minutes followed by centrifuged for 10 minutes and filtered. The stock solution was further diluted for the test concentrations. A reference test was also run.

RESULTS

Biomass		*Growth*	
EyC50 (mg/L at 72 h)	*NOEC (mg/L)*	*ErC50 (mg/L at 72 h)*	*NOEC (mg/L)*
8.66 (95% CI of 7.8-9.61)	1.64	14.8 (95% CI of 13.11-16.71)	6.13

Remarks – Results	The assessed chemical was not hydrolytically stable and was not detected in test media. However, major degradation products were detected. All validity criteria for the test were satisfied. The cell concentration in the control cultures increased by a factor of more than 16 within 72 hours. The mean coefficient of variation for section-by-section specific growth rates in the control cultures did not exceed 35%. The mean coefficient of variation for section-by-section specific growth rates was 7.54%. The reference test showed an ErC50 value for potassium dichromate of 0.82 mg/L which is within the expected range. The measured concentrations of the degradation products of the test substance varied in the range from 80 - 104% to of the nominal value at the start of the study and from 74 - 86% at the end of the study. The

	deviation of the measured concentrations from the nominal values was higher than 20%, therefore, the results are based on geometrical mean measured concentrations.
CONCLUSION	The assessed chemical and its degradants are harmful to algae.
TEST FACILITY	TOXI-COOP ZRT (2011g)

C.2.4. Inhibition of Microbial Activity

TEST SUBSTANCE	Assessed chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated sludge
Exposure Period	3 hours
Concentration Range	Nominal: 62.5, 125, 250, 500 and 1000 mg/L
Remarks – Method	No significant deviations from the test guidelines were reported.
RESULTS	
IC50	375.38 (95% CI of 115.97 – 7592.08) mg/L at 3 hours
NOEC	< 62.5 mg/L [Statistically determined using Bonferroni t-Test ($\alpha = 0.05$)]
Remarks – Results	The specific respiration rate of the blank controls was 35.07 mg oxygen per one gram of activated sludge in an hour with a coefficient of variation of 3.36%. The reference test showed an EC50 value for 3,5 dichlorophenol of 6.03 mg/L which is within the expected range.
CONCLUSION	The assessed chemical and its degradants are not inhibitory to microbial respiration.
TEST FACILITY	TOXI-COOP ZRT (2011h)

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