File No.: STD/1689
STD/1690

August 2019

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

STD/1689 – RD14156
STD/1690 – RD14153

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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Director
NICNAS

TABLE OF CONTENTS

SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1689	Cintox Australia Pty Ltd	RD14156	No	≤ 15 tonnes per annum	Component of industrial coatings
STD/1690		RD14153		≤ 20 tonnes per annum	

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the available information, the notified chemicals are not classified as hazardous according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

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

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

Environmental Risk Assessment
Based on the low hazard and reported use pattern, the notified chemicals are not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemicals during reformulation and end-use:
  - Local exhaust ventilation with dust extraction systems when handling the notified chemicals in powder form
  - Spray booth for end-use application by spraying

- 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
  - Avoid inhalation of dust

- 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 and end-use:
  - Respiratory protection if inhalation exposure to dusts and aerosols may occur

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

- In the interest of occupational health and safety, the following precautions should be observed for use of the notified chemical as introduced in powder form:
  - The level of atmospheric nuisance dust should be maintained as low as possible. The Safe Work Australia exposure standard for atmospheric dust is 10 mg/m^3.

- 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 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.

Emergency procedures

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

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.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemicals under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemicals, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemicals are listed on the Australian Inventory of Chemical Substances (AICS).

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

(1) Under Section 64(2) of the Act; if
  - the function or use of the chemicals have changed from a component of industrial coatings, or is 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 products containing the notified chemicals provided by the notifier were 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
Cintox Australia Pty Ltd (ABN: 63 122 874 613)
Suite 1, Level 2, 38-40 George Street
PARAMATTA NSW 2150

NOTIFICATION CATEGORY
STD/1689: Standard: Chemical other than polymer (more than 1 tonne per year)
STD/1690: Standard: Chemical other than polymer (more than 1 tonne per year)

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, additives/adjuvants, use details, and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
STD/1689: Schedule data requirements are varied for hydrolysis as a function of pH, dissociation constant, flash point, flammability, autoignition temperature, explosive properties, and oxidising properties.

STD/1690: Schedule data requirements are varied for hydrolysis as a function of pH, dissociation constant, flash point, eye irritation, skin sensitisation, and chromosome damage *in vitro*.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAMES
STD/1689: RD14156
STD/1690: RD14153

MOLECULAR WEIGHT
STD/1689: < 700 g/mol
STD/1690: < 700 g/mol

ANALYTICAL DATA
Reference NMR and IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
STD/1689: > 85%
STD/1690: > 85%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Off-white solids

Property	*Value*	*Data Source/Justification*
Melting Point	STD/1689: 122 °C STD/1690: 122 °C	Measured
Boiling Point	STD/1689: 358.07 °C STD/1690: 346.31 °C	Measured

Property	*Value*	*Data Source/Justification*
Density	STD/1689: 1,040 kg/m^3 STD/1690: 1,030 kg/m^3	Measured
Vapour Pressure	STD/1689: < 0.013 kPa at 25 °C STD/1690: < 0.013 kPa at 25 °C	Measured
Water Solubility	STD/1689: 0.26 g/L at 30 °C STD/1690: 0.32 g/L at 30 °C	Measured Measured
Hydrolysis as a Function of pH	STD/1689: Not determined STD/1690: Not determined	The notified chemicals are expected to be hydrolytically stable in the environmental pH range (4-9) at ambient temperature.
Partition Coefficient (n-octanol/water)	STD/1689: log Pow = 1.2 STD/1690: log Pow = 1.0	Measured Measured
Surface Tension	STD/1689: 64.92 mN/m at 21 °C STD/1690: 64.39 mN/m at 21 °C	Measured Measured
Adsorption/Desorption	STD/1689: Not determined STD/1690: log Koc < 1.25 (28.8%), 5.09 (60.3%) and > 5.63 (6.43%) at 30 °C	Measured
Dissociation Constant	Not determined	The notified chemicals contain no dissociable functionality
Particle Size	STD/1689: Inhalable fraction (< 100 μm): 100% Respirable fraction (< 10 μm): 89% MMAD* = 5.93 μm STD/1690: 98.4% > 250 μm Inhalable fraction (< 100 μm): 0%	Measured (milled powder) Measured (flakes)
Flash Point	Not determined	Not expected to form flammable vapour
Flammability	STD/1689: Not determined STD/1690: Not highly flammable	Not expected to be highly flammable based on measured test for STD/1690 Measured
Autoignition Temperature	STD/1689: Not determined STD/1690: > 140 °C	Not expected to autoignite below melting temperature based on measured test for STD/1690 Measured. Does not autoignite below melting temperature
Explosive Properties	STD/1689: Not determined STD/1690: Predicted negative	Not expected to be explosive based on STD/1690 Based on chemical structure
Oxidising Properties	STD/1689: Not determined STD/1690: Predicted negative	Not expected to be explosive based on STD/1690 Based on chemical structure

*MMAD = Mass Median Aerodynamic Diameter

DISCUSSION OF PROPERTIES

For details of tests on physical and chemical 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 hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemicals will be introduced into Australia neat for reformulation or as a component of finished industrial coatings at ≤ 5% concentration for each chemical.

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

STD/1689

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	≤ 15	≤ 15	≤ 15	≤ 15	≤ 15

STD/1690

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	≤ 20	≤ 20	≤ 20	≤ 20	≤ 20

PORT OF ENTRY
Melbourne and Sydney

IDENTITY OF RECIPIENT
Cintox Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemicals will be imported neat as a powder in 15 kg multi-ply paper bags. The finished industrial coating products containing the notified chemicals at ≤ 5% concentration will be imported in various size containers, including 1, 4 and 10 L cans and 210 kg lined steel drums.

USE
The notified chemicals will be used as a component of industrial coatings at ≤ 5% concentration for each chemical.

OPERATION DESCRIPTION
The notified chemicals will not be manufactured in Australia. The notified chemicals will be introduced into Australia neat as a powder for reformulation into industrial coatings. The notified chemicals will also be introduced as components of finished industrial coatings at ≤ 5% concentration (for each chemical).

Reformulation
The powdered notified chemicals will be manually weighed under a fume-hood into a dispensing container and transferred to a mixing vessel where it will be blended with additional additives to form the finished coatings. Following blending, samples with be taken for quality control testing. The finished coatings containing the notified chemicals at ≤ 5% concentration (for each chemical) will be filled into containers by gravity feed or low-pressure pump and then distributed to end-users.

End Use
The finished industrial coatings containing the notified chemicals at ≤ 5% concentration (for each chemical) will only be used by trained industrial users and will be applied by brush, roller or spray at various industrial locations. Spray applications will be conducted in purpose-built spray facilities.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage	1	4
Warehouse	1	4
Process operator	2.5	40

Quality control	0.5	40
Packaging	2	40
End use	1	60

EXPOSURE DETAILS

Transport and storage
Transport, storage and warehouse workers may come into contact with the notified chemicals in neat form or as a component of finished coatings at ≤ 5% concentration, only in the unlikely event of accidental rupture of containers.

Reformulation
Reformulation will be largely enclosed and automated; however dermal and ocular exposure of workers to the notified chemicals at ≤ 100% concentration may occur during weighing and transfer stages, quality control analysis, and cleaning and maintenance of equipment. Given the use of enclosed processes and the low vapour pressure of the notified chemicals (< 0.013 kPa at 25 °C), inhalation exposure is not expected unless dust is generated, particularly during weighing and transfer of the powdered notified chemicals. According to the notifier exposure will be minimised through the use of engineering controls (such as a fume hood and closed weighing/dispensing containers) and personal protective equipment (PPE) by workers (such as protective clothing, eye protection and impervious gloves).

End-use
Finished coatings containing the notified chemicals will be applied by spray, brush or roller. Dermal and ocular exposure to the coatings containing the notified chemicals at ≤ 5% concentration may occur during transfer, application and cleaning of application equipment. Inhalation exposure may also occur during spray application. The potential for exposure will be minimised through the use of PPE (goggles, impervious gloves, protective clothing) by workers, including the use of respiratory protection and spray booths during spray application.

Once the coatings are dried, the notified chemicals will be bound into an inert solid matrix and will not be available for exposure.

6.1.2. Public Exposure
Finished coatings containing the notified chemicals at ≤ 5% concentration will be for industrial use only and will not be made available to the public. The public may come into contact with surfaces that have been coated with products containing the notified chemicals. However, once the coatings are dried, the notified chemicals will be bound into an inert solid matrix and will not be available for exposure.

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

Endpoint	*Result and Assessment Conclusion*
STD/1689	
Acute oral toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Acute dermal toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Skin irritation – rabbit	slightly irritating
Eye irritation – rabbit	slightly irritating
Skin sensitisation – mouse local lymph node assay	no evidence of sensitisation (up to 25% concentration)
Repeat dose oral toxicity study with the reproduction/developmental toxicity screening test – rat	NOAEL (systemic) = 1,000 mg/kg bw/day NOAEL (reprod) = 300 mg/kg bw/day
Genotoxicity – *in vitro* mouse lymphoma assay	non mutagenic
Genotoxicity – *in vitro* chromosome aberration test in human lymphocytes	non clastogenic

STD/1690

Acute oral toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Acute dermal toxicity – rat	LD50 > 2,000 mg/kg bw; low toxicity
Skin irritation – rabbit	slightly irritating
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics
Given the relatively low molecular weight (< 700 g/mol), the notified chemicals may be absorbed across the respiratory or gastrointestinal tract. Although the partition coefficient (low Pow = 1 for STD/1689 and 1.2 for STD/1690) of the notified chemicals favours percutaneous absorption, absorption may be limited by their low water solubility (0.26 g/L for STD/1689 and 0.32 g/L for STD/1690 at 30 °C).

Acute Toxicity
The notified chemicals are of low acute oral and dermal toxicity based on studies conducted in rats.

No acute inhalation toxicity data were provided for the notified chemicals.

Irritation and Sensitisation
The notified chemicals are slightly irritating to skin based on studies conducted in rabbits. For each notified chemical, slight erythema was observed in one animal at the 1 hour observation which was resolved at the 24 hour observation.

The notified chemical (STD/1689) is a slight eye irritant based on a study conducted in rabbits. Slight to moderate conjunctival irritation (redness and discharge) was observed in all 3 animals from the 1 hour observation. All signs of irritation were resolved at the 72 hour observation.

No eye irritation study was submitted for the notified chemical (STD/1690). However, the analogue chemical (STD/1689) is a slight eye irritant therefore the notified chemical (STD/1690) is considered to be a slight eye irritant.

Notified chemical (STD/1689) was determined not to be a skin sensitiser in a mouse local lymph node assay (LLNA) at ≤ 25% concentration.

No skin sensitisation study was submitted for the notified chemical (STD/1690). The analogue chemical (STD/1689), however, is not a skin sensitiser. Therefore the notified chemical (STD/1690) is considered to be a non skin sensitiser.

Repeated Dose Toxicity
In a combined repeated dose oral toxicity study with the reproduction/developmental toxicity screening test in rats with the notified chemical (STD/1689), the No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day for systemic toxicity, based on the absence of treatment related adverse effects up to the highest dose tested. Increased regressing implantation was observed in all females treated at 1,000 mg/kg bw/day therefore the NOAEL for reproductive toxicity was established as 300 mg/kg bw/day.

No long term repeated dose toxicity studies were submitted for the notified chemical (STD/1690). However, in a 14-day repeated dose oral range-finding study no significant adverse effects were observed at doses up to 1,000 mg/kg bw/day (ERL, 2016a).

Mutagenicity/Genotoxicity
The notified chemical (STD/1690) was not mutagenic in a bacterial reverse mutation assay. No bacterial reverse mutation study was submitted for the notified chemical (STD/1689).

The notified chemical (STD/1689) was not mutagenic in an *in vitro* mouse lymphoma assay and not clastogenic in an *in vitro* chromosome aberration test in human lymphocytes.

Health Hazard Classification
Based on the available information, the notified chemicals are not classified as hazardous according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the toxicological information provided, the notified chemicals are slight skin and eye irritants. The notified chemicals are of low water solubility and are likely to be introduced in the powder form with the majority of particles in the respirable range, hence the potential for lung overloading effects cannot be ruled out.

Reformulation
During reformulation, the greatest concern for the health of workers relates potential lung overloading effects from inhalation of dusts during weighing and transfer of the powdered notified chemicals. The risk should be minimised through the use of engineering controls (fume hood and closed weighing/dispensing containers as stated by the notifier). Low-dust handling techniques and respiratory protection where there is inadequate ventilation could also be used to reduce exposure.

Overall, provided control measures are in place to minimise inhalation exposure to the notified chemicals as introduced in powder form, including local exhaust ventilation and respiratory protection, the risk to the health of workers during reformulation is not considered to be unreasonable.

End-use
Workers may experience dermal and possibly ocular exposure to the notified chemicals at ≤ 5% concentration during transfer, application (through brush or roller) and cleaning processes. The use of PPE by workers will minimise exposure to the notified chemicals. Inhalation exposure is also possible during spray application. The notifier stated that workers will wear air-fed respirators and that spray applications will be conducted under ventilation in purpose built spray facilities.

Once the coatings are dried, the notified chemicals will be bound into an inert solid matrix and will not be available for exposure.

Overall, based on the expected low hazard of the notified chemicals and occupational settings described, the risk to workers during end use is not considered to be unreasonable.

6.3.2. Public Health
Finished coatings containing the notified chemicals at ≤ 5% concentration will be for industrial use only and will not be made available to the public. The public may come into contact with surfaces that have been coated with products containing the notified chemicals. However, once the coatings are dried, the notified chemicals will be bound into an inert solid matrix and will not be available for exposure. Therefore, when used in the proposed manner, the risk to public health is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemicals will be introduced into Australia as components of finished coatings and in their neat form for reformulation into industrial coatings. The notified chemicals will be mixed with solvents and resins and reformulated into coating formulations in a closed system. Solvent used for equipment washing (which contains residues of the notified chemical) is expected to be recycled for reuse on site or disposed of *via* accredited waste disposal contractors. Wastes and spills during reformulation activities (1% of annual import volume) are expected to be contained on site and disposed of in accordance with local regulations. Residues in import containers are expected to be disposed of *via* the trade waste stream in accordance with local regulations. Any spills of the notified chemicals during transportation and storage are expected to be contained with absorbent material and be disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

Coatings containing the notified chemicals may be applied by brush, roller or spray at industrial locations. The notifier has indicated that the coatings containing the notified chemicals will be applied in spray facilities and that the main release of the notified chemicals during industrial spray painting operations will come from overspray, accounting for up to 30% of the annual import volume. Overspray, accidental spills, application equipment washings (up to 5% of the annual import volume) and residues in empty paint containers (up to 2.5% of the annual import volume) are expected to be collected and disposed of to landfill in accordance with local, State and Federal regulations.

RELEASE OF CHEMICAL FROM DISPOSAL

The notified chemicals in coatings are expected to share the fate of articles to which they have been applied. The notified chemicals are likely to be either thermally decomposed during metal reclamation processes or disposed of to landfill at the end of the useful life of the article to which they have been applied.

7.1.2. Environmental Fate

The notified chemicals are not readily biodegradable (23% and 18% biodegradability over 28 days for STD/1689 and STD/1690, respectively) but do show some evidence of biodegradability. For the details of the environmental fate studies refer to Appendix C.

The notified chemicals are expected to be incorporated into an inert matrix of cured coatings as part of their use pattern. The notified chemicals are not expected to be bioavailable in this form. The notified chemicals will eventually degrade in landfill, or by thermal decomposition during metal reclamation processes, to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentrations (PEC) have not been calculated as release of the notified chemicals to the aquatic environment will be limited based on their reported use patterns.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemicals are summarised in the table below. Details of these studies can be found in Appendix C. The endpoints are presented as nominal concentrations (WAFs).

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity		
STD/1689:	96 h LL50 > 100 mg/L	Not harmful to fish up to its water solubility limit
STD/1690:	96 h LL50 > 100 mg/L	Not harmful to fish up to its water solubility limit
Daphnia Toxicity		
STD/1689:	48 h EL50 > 100 mg/L	Not harmful to aquatic invertebrates up to its water solubility limit
STD/1690:	48 h EL50 > 100 mg/L	Not harmful to aquatic invertebrates up to its water solubility limit
Algal Toxicity		
STD/1689:	72 h ErL50 > 100 mg/L	Not harmful to alga up to its water solubility limit
STD/1690:	72 h ErL50 > 100 mg/L	Not harmful to alga up to its water solubility limit

Based on the above ecotoxicological endpoints for the notified chemicals, they are not expected to be harmful to aquatic life up to the limits of their water solubility. Therefore, the notified chemicals are not formally classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) for acute and chronic toxicities (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentrations (PNEC) have not been calculated as the notified chemicals are not expected to be harmful to aquatic organisms up to their water solubility limit.

7.3. Environmental Risk Assessment

Risk quotients (Q = PEC/PNEC) for the notified chemicals have not been calculated as PNEC was not calculated and release to the aquatic environment in ecotoxicologically significant concentrations is not expected based on the reported use patterns as components of industrial coatings. Moreover, after curing, the majority of the imported quantity of the notified chemicals will be irreversibly incorporated into an inert matrix and they are not expected to be mobile or bioavailable. On the basis of the low hazard and assessed use pattern, the notified chemicals are not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

STD/1689

Melting Point 122 °C

Method	OECD TG 102 Melting Point/Melting Range
Remarks	Determined by differential scanning calorimetry (DSC) and the capillary method.
Test Facility	ESI (2016a)

Boiling Point 358.07 °C at 101.3 kPa

Method	Not stated
Remarks	Determined by DSC. No decomposition was observed.
Test Facility	DCL (2018a)

Density 1,040 kg/m^3

Method	OECD TG 109 Density of Liquids and Solids
Remarks	Determined using a pycnometer.
Test Facility	ESI (2016b)

Vapour Pressure < 0.013 kPa at 25 °C

Method	OECD TG 104 Vapour Pressure
Remarks	Modified effusion procedure.
Test Facility	LCSLI (2016a)

Water Solubility 0.26 g/L at 30 °C

Method	OECD TG 105 Water Solubility
Remarks	Flask Method The notified chemical is comprised of at least three main chemical constituents (> 10% w/w) each of which has a different water solubility. The solubilities of each individual component were not determined. Instead, the reported solubility for the notified chemical is an average of the solubility of the three major chemical components. Flask 1 measurements (after 24 h) were omitted because the results were outside the ± 15% range of variation required for the test to be considered valid. This is not considered to have significantly altered the outcome of the test.
Test Facility	ESI (2016c)

Partition Coefficient (n-octanol/water) log Pow = 1.2

Method	OECD TG 107 Partition Coefficient (n-octanol/water).
Remarks	Flask Method The reported log Pow is an average of the log Pows of the three major chemical components present in the notified chemical. The individual log Pows of each component were not determined. Temperatures not reported.
Test Facility	ESI (2016d)

Surface Tension 64.92 mN/m at 21 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions
Remarks	Concentration: not stated
Test Facility	ESI (2016e)

Particle Size Inhalable fraction (< 100 µm): 100%
Respirable fraction (< 10 µm): 89%

Method OECD TG 110 Particle Size Distribution

Range (µm)	*Mass (%)*
< 100	100
< 10	89
< 5	20

Remarks The test substance was milled to a fine white powder prior to particle size determination using a laser diffraction particle size analyser. The MMAD was 5.93 µm.
Test Facility ESI (2016f)

STD/1690

Melting Point 122 °C

Method OECD TG 102 Melting Point/Melting Range
Remarks Determined by DSC and the capillary method.
Test Facility ESI (2016g)

Boiling Point 346.31 °C at 101.3 kPa

Method Not stated
Remarks Determined by DSC. No decomposition was observed.
Test Facility DCL (2018b)

Density 1,030 kg/m^3

Method OECD TG 109 Density of Liquids and Solids
Remarks Determined using a pycnometer.
Test Facility ESI (2016h)

Vapour Pressure < 0.013 kPa at 25 °C

Method OECD TG 104 Vapour Pressure
Remarks Modified effusion procedure.
Test Facility LCSLI (2016)

Water Solubility 0.32 g/L at 30 °C

Method OECD TG 105 Water Solubility
Remarks Flask Method
The notified chemical is comprised of at least three main chemical constituents (> 10% w/w) each of which has a different water solubility. The solubilities of each individual component were not determined. Instead, the reported solubility for the notified chemical is an average of the solubility of the three major chemical components.
Test Facility ESI (2016i)

Partition Coefficient (n-octanol/water) log Pow = 1.0

Method OECD TG 107 Partition Coefficient (n-octanol/water).
Remarks Flask Method
Each reported log Pow is an average of the log Pows of the three major chemical components present in the notified chemical. The individual log Pows of each component were not determined. Temperatures not reported.
Test Facility ESI (2016j)

Surface Tension 64.39 mN/m at 21 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions
Remarks Concentration: not stated
Test Facility ESI (2016k)

Adsorption/Desorption log Koc = < 1.25 (28.8%), 5.09 (60.3%) and > 5.63 (6.43%) at 30 °C

Method OECD TG 121 Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC)
Remarks The notified chemical eluted as a series of peaks in the chromatogram. The three major peaks, comprising ~ 96% of the total area, were found to have log Koc = < 1.25 (28.8%), 5.09 (60.3%) and > 5.63 (6.43%), respectively.
Test Facility ERL (2016b)

Particle Size 98.4% > 250 µm
Inhalable fraction (< 100 µm): 0%

Method OECD TG 110 Particle Size Distribution

Range (µm)	*Mass (%)*
≤ 4,000	52
≤ 2,000	28.6
≤ 250	1.6
≤ 177	0.5
≤ 74	0.0

Remarks Determined using dry sieve analysis. The test substance was a flaked product. The majority of the flakes (98.4%) are larger than 250 µm.
Test Facility ESI (2016l)

Flammability Not highly flammable

Method EC Council Regulation No 440/2008 A.10 Flammability (Solids)
Remarks The test substance did not burn during the 2 minute Bunsen flame application.
Test Facility ERL (2016c)

Autoignition Temperature > 140 °C

Method EC Council Regulation No 440/2008 A.16 Relative Self-Ignition Temperature for Solids
Remarks On completion of the test, the test item had melted.
Test Facility ERL (2016c)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

STD/1689

B.1. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical (STD/1689)
METHOD	OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure
Species/Strain	Rat/SD
Vehicle	Corn oil
Remarks – Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	1F	2,000	0/1
2	4F	2,000	0/4

LD50	> 2,000 mg/kg bw
Signs of Toxicity	Partially chewed food in pan liner was observed in the Group 1 animal on day 4. Diarrhoea was observed in a Group 2 animal at 1 and 2 hour observations.
Effects in Organs	No abnormalities were observed at necroscopy.
Remarks – Results	One Group 2 animal lost weight between days 7-14. All other animals showed expected body weight gains during the 14 day observation period.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	MBRL (2015a)

B.2. Acute Dermal Toxicity – Rat

TEST SUBSTANCE	Notified chemical (STD/1689)
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test
Species/Strain	Rat/SD
Vehicle	Corn oil
Type of dressing	Semi-occlusive
Remarks – Method	No protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M/5F	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity – Local	At the 24 hour observation, slight erythema (grade 1) was observed in two males, and slight (grade 1) to moderate (grade 2) oedema was observed in four animals (3 males and 1 female). All signs of irritation were resolved at the day 14 observation. No information was provided at any other observation period during the study.
Signs of Toxicity – Systemic	Chromodacryorrhea (red lacrimal secretion) was observed in a male on days 13 and 14. A female showed localised hair loss on days 10 and 11 and another female on day 11. The latter female also appeared emaciated with diminished faecal output at the day 14 observation. Both females showed localised hair loss on shoulder area on days 12-14. Partially chewed food in pan liner was observed in another female from days 11-14.
Effects in Organs	No signs of toxicity were observed at necropsy.
Remarks – Results	A female lost bodyweight between days 7-14. All other animals showed expected body weight gains during the 14 day observation period.

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

TEST FACILITY MBRL (2016a)

B.3. Skin Irritation – Rabbit

TEST SUBSTANCE Notified chemical (STD/1689)

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 1M/2F
- Vehicle: Distilled water
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive
- Remarks – Method: 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	0	0	0	1	< 24 h	0
Oedema	0	0	0	0	-	0

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

Remarks – Results A female showed slight (grade 1) erythema at the 1 hour observation which was resolved at the 24 hour observation.

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY MBRL (2016b)

B.4. Eye Irritation – Rabbit

TEST SUBSTANCE Notified chemical (STD/1689)

METHOD OECD TG 405 Acute Eye Irritation/Corrosion
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 2M/1F
- Observation Period: 72 hours
- Remarks – Method: No 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			
Conjunctiva – Redness	1	0	0	2	< 72 h	0
Conjunctiva – Chemosis	0	0	0	0	-	0
Conjunctiva – Discharge	0.33	0	0	2	< 48 h	0
Corneal Opacity	0	0	0	0	-	0
Iridial Inflammation	0	0	0	0	-	0

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

Remarks – Results Moderate to slight (grade 2 in a male at 1 hour and 24 hour observations and grade 1 at 48 hour observation) and slight (grade 1 in other 2 animals at the 1 hour observation) conjunctival redness was observed. A male showed slight chemosis at the 1 hour observation. Moderate (grade 2 in a male) and slight (grade 1in other 2 animals) discharge was observed at the

1 hour observation. Test article residue was observed in all animals at the 1 hour observation. All animals appeared normal at the 72 hour observation.

Slight reduction in terminal body weight was observed in a male and a female. Few faeces were observed in a male at 48 and 72 hour observations.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY MBRL (2016c)

B.5. Skin Sensitisation – LLNA

TEST SUBSTANCE Notified chemical (STD/1689)

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/CBA/J
Vehicle Propylene glycol
Preliminary study Yes
Positive control α-Hexylcinnamaldehyde, technical (85%) in propylene glycol, conducted in parallel with the test substance.
Remarks – Method A preliminary test was conducted using 5%, 10% and 25% of test substance to justify the dose concentrations for the main study.

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	16134	-
5	5F	13336	0.8
10	5F	13434	0.8
25	5F	8606	0.5
Positive Control			
25	5F	113689	7.0

Remarks – Results No unscheduled mortalities or signs of systemic toxicity were observed during the study period.

The stimulation index was < 3 in all test groups, indicating a non-sensitising response.

Slight increase (5.3% increase at days 3 and 6) in mean ear thickness was observed in low dose animals.

Slight reduction in bodyweight gain was observed in a low dose animal.

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY MBRL (2016d)

B.6. Repeat Dose Oral Toxicity Study with Reproduction/Developmental Toxicity Screening – Rat

TEST SUBSTANCE	Notified chemical (STD/1689)
METHOD	OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test
Species/Strain	Wistar Han™/RccHan™/WIST
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: ~6 weeks for males and up to 10 weeks for females (including a 14-day pre-pairing phase, pairing, gestation and early lactation) Dose regimen: 7 days per week
Vehicle	Arachis oil BP
Remarks – Method	In a 14-day dose-range finding study (ERL, 2016d), the test substance in arachis oil was administered by oral gavage to 6 (3M/3F) Wistar Han:RccHan rats at 250, 500 and 1,000 mg/kg bw/day for 14 consecutive days. No unscheduled mortalities occurred during the study. No clinical signs of toxicity were observed. No abnormalities were noted at necropsy. Based on the results, doses of 100, 300 and 1,000 mg/kg bw/day were chosen for the main study. No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
Control	12M/12F	0	0/24
Low Dose	12M/12F	100	0/24
Mid Dose	12M/12F	300	0/24
High Dose	12M/12F	1,000	0/24

Mortality and Time to Death

No unscheduled mortalities were observed during the study.

Clinical Observations

Following statistically significant changes were observed:

- decreased hind limb grip strength values on day 12 *post partum* in low (37.5% less than control groups), mid (49.5% less than control group) and high (30.2% less than control group) dose group females. As there was no dose relationship and these differences were not apparent in the remaining 2/3 tests, this observation was not considered treatment related by the study authors.
- increased pre-coital interval in high dose male group (135% increase than control group). This finding was not considered to be toxicologically significant by the study authors.
- increased mean gestation length for mid (2.2% increase than control group) and high (1.8% increase than control group) dose group females. These increases were reported to be within the historical control range for the rat species.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Following statistically significant effects were observed:

- decreased (1.4% decrease than control group) mean corpuscular haemoglobin concentration in high dose group males but reported as within the historical control range.
- increased (8.6% increase than control group) calcium levels in high dose group males. As this observation was not evident in females and in the absence of any associated microscopic findings in tissues, this change was not considered to be to be toxicologically significant by the study authors.
- increased eosinophil counts in mid (4.2% increase than control group) and high (5.8% increase than control group) dose group males but there were no histopathological effects and the counts were within the historical count range.
- decreased phosphorus levels in low (23.5% decrease than control group), mid (26.5% decrease than control group) and high (16.7% decrease than control group) dose group males. As this observation was not evident in females and in the absence of any associated microscopic findings in tissues, this change was not considered to be to be toxicologically significant by the study authors.

increased (690% increase than control group) bile acid in mid dose group females but not evident in the low and high dose group females. It was considered incidental by the study authors.

Effects in Organs

Several findings were reported as incidental in high dose animals (mainly males) except for a small left testis in a low dose male. The effects observed include:

- fused seminal vesicle and coagulating glands in a high dose male
- slight bilateral tubular atrophy in testes in a low dose and in 2 high dose males
- slight mononuclear cell infiltration (focal) in epididymides and agonal congestion and haemorrhage in lung in a high dose male
- slight inflammation in liver in two high dose males
- cysts in pituitary gland in 3 high dose males
- slight basophile tubular in kidneys, and slight atrophy in pancreas and in spleen in a high dose male
- slight extramedullary haematopoiesis in spleen in 2 high dose males and 4 high dose females
- slight inflammation in focal myocardium in heart and post-mortem haemorrhage in a high dose male
- slight pelvis dilation (unilateral) in kidneys in a high dose female and marked pelvis dilation, slight urothelial diffuse hyperplasia and slight bilateral pyrelitis in kidney in another high dose female
- regressing implantation sites in uterus in all 12 high dose females
- slight foreign body granuloma in lung in a high dose female
  moderate peri-oesophageal inflammation in a high dose female

Remarks – Results

All the 12 high dose females showed regressing implantation sites in uterus and this effect was not observed in other treatment groups.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day for systemic toxicity in this study, based on the absence of treatment related adverse effects.

The NOAEL for reproductive toxicity was established as 300 mg/kg bw/day in this study, based on increased regressing implantation observed in all the exposed females at 1,000 mg/kg bw/day does level.

TEST FACILITY ERL (2017)

B.7. Genotoxicity – *In Vitro* Mouse Lymphoma Assay

TEST SUBSTANCE Notified chemical (STD/1689)

METHOD OECD TG 490 *In vitro* Mammalian Cell Gene Mutation Test Using the Thymidine Kinase Gene

Species/Strain	Mouse
Cell Type/Cell Line	L5178Y Mouse lymphoma cells ($TK^{+/-}$-3.7.2C)
Metabolic Activation System	S9 mix from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	Acetone
Remarks – Method	The positive controls used were: • ethyl methane sulphonate (EMS) without S9-mix and • cyclophosphamide (CP) with S9-mix. A preliminary test was conducted at a concentration range of 2.44 to 625 µg/mL.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	0, 1.25, 2.5, 5, 10, 20 and 30	4 h	2 days	10-12 days
Test 2	0, 1.25, 2.5, 5, 10, 20 and 30	24 h	2 days	10-12 days
Present				
Test 1	0, 1.25, 2.5, 5, 10, 20 and 30	4 h	2 days	10-12 days

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	312.5	> 30	≥ 20	Negative
Test 2	156.25	> 30	≥ 20	Negative
Present				
Test 1	312.5	> 30	≥ 20	Negative

Remarks – Results

In the preliminary cytotoxicity test there was evidence of toxicity at dose levels beyond the onset of precipitation (at and above 19.53 µg/mL).

In the main test there was no evidence of any marked dose-related toxicity. The test substance did not induce any toxicologically significant increases in the mutation frequency at any of the test concentrations up to 30 µg/mL, either with or without S9-mix.

The positive controls induced marked increases in the mutant frequency validating the sensitivity of the assay and the efficacy of the S9-mix.

CONCLUSION

The notified chemical was not mutagenic to mouse lymphoma cells treated *in vitro* under the conditions of the test.

TEST FACILITY

ERL (2016e)

B.8. Genotoxicity – *In Vitro* Chromosome Aberration Test in Human Lymphocytes

TEST SUBSTANCE

Notified chemical (STD/1689)

METHOD

OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test

Species/Strain: Human
Cell Type/Cell Line: Lymphocytes
Metabolic Activation System: S9 mix from phenobarbital/β-naphthoflavone induced rat liver
Vehicle: Acetone
Remarks – Method: The positive controls used were:

- mitomycin (MMC) without S9-mix and
- cyclophosphamide (CP) with S9-mix.

A preliminary test was conducted at a concentration range of 2.44 to 625 µg/mL.

No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 0.625*, 1.25*, 2.5*, 5*, 10, 20, 30	4 h	24 h
Test 2	0*, 0.625, 1.25, 2.5*, 5*, 10*, 20*, 30	24 h	24 h
Present			
Test 1	0*, 2.5*, 5*, 10*, 20*, 30, 40, 50	4 h	24 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 9.77*	5	≥ 10	Negative
Test 2	> 4.88	> 20	≥ 20	Negative
Present				
Test 1	> 39.06*	20	≥ 20	Negative

*Maximum dose with mitotic index data

Remarks – Results

In the preliminary toxicity test up to 625 µg/mL, the test substance induced some evidence of toxicity.

No statistically significant increase in the number of cells with aberrations was observed at any concentration, with and without S9-mix. There was also no statistically significant increase in the numbers of polyploidy cells.

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

CONCLUSION

The notified chemical was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY

ERL (2016f)

STD/1690

B.9. Acute Oral Toxicity – Rat

TEST SUBSTANCE	Notified chemical (STD/1690)
METHOD	OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure
Species/Strain	Rat/SD
Vehicle	Corn oil
Remarks – Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	1F	2,000	0/1
2	4F	2,000	0/4

LD50	> 2,000 mg/kg bw
Signs of Toxicity	No signs of toxicity were observed.
Effects in Organs	No abnormalities observed at necroscopy.
Remarks – Results	All animals showed expected bodyweight gain during the study.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	MBRL (2015b)

B.10. Acute Dermal Toxicity – Rat

TEST SUBSTANCE	Notified chemical (STD/1690)
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test
Species/Strain	Rat/SD
Vehicle	Corn oil
Type of dressing	Semi-occlusive
Remarks – Method	No protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M/5F	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity – Local	At the 24 hour observation, slight erythema (grade 1) was observed in one male and two females, and slight (grade 1) oedema was observed in three males. All signs of irritation were resolved at the day 14 observation. No information was provided at any other observation period during the study.
Signs of Toxicity – Systemic	No signs of systemic toxicity was observed.
Effects in Organs	No signs of toxicity at necropsy.
Remarks – Results	All exposed animals gained expected body weight during the study.
CONCLUSION	The notified chemical is of low acute toxicity via the dermal route.
TEST FACILITY	MBRL (2016e)

B.11. Skin Irritation – Rabbit

TEST SUBSTANCE	Notified chemical (STD/1690)
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White

Number of Animals	2M/1F
Vehicle	Distilled water
Observation Period	72 hours
Type of Dressing	Semi-occlusive
Remarks – Method	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	0	0	0	1	< 24 h	0
Oedema	0	0	0	0	-	0

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

Remarks – Results	A male showed slight (grade 1) erythema at the 1 hour observation which was resolved at the 24 hour observation.

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY MBRL (2016f)

B.12. Genotoxicity – Bacteria

TEST SUBSTANCE Notified chemical (STD/1690)

METHOD OECD TG 471 Bacterial Reverse Mutation Test
Plate incorporation (Test 1) and pre incubation procedures (Test 2)

Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98 and TA100 *Escherichia coli*: WP2uvrA
Metabolic Activation System	S9 mix from phenobarbitone/ß-naphthoflavone induced rat liver
Concentration Range in Main Test	<u>Test 1</u> a) With metabolic activation: 1.5, 5, 15, 50, 150, 500, 1,500 and 5,000 µg/plate b) Without metabolic activation: 1.5, 5, 15, 50, 150, 1,500 and 5,000 µg/plate <u>Test 2</u> a) With metabolic activation: 15, 50, 150, 500, 1,500 and 5,000 µg/plate b) Without metabolic activation: 15, 50, 150, 1,500 and 5,000 µg/plate
Vehicle	Dimethyl formamide (DMF)
Remarks – Method	Solvent control: DMF Positive control: with S9-mix: 2-aminoanthracene (TA100, TA1535, TA1537 and WP2uvrA) and benzo(a)pyrene (TA98) without S9-mix: *N*-ethyl-*N*'-nitro-*N*-nitrosoguanidine (TA100, TA1535 and WP2uvrA), 9-aminoacridine (TA1537) and 4-nitroquinoline-1-oxide (TA98) Preliminary toxicity test was not conducted.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	Not conducted	≥ 5,000	≥ 500	Negative
Test 2	Not conducted	> 5,000	≥ 500	Negative
Present				

Test 1	Not conducted	> 5,000	≥ 500	Negative
Test 2	Not conducted	> 5,000	≥ 500	Negative

Remarks – Results

No relevant increase in the number of revertant colonies of any of the tested strains were observed following treatment with the test substance at any dose level, with or without metabolic activation, in either mutation test.

The positive controls induced a distinct increase of revertant colonies during the study indicating the validity of the test system.

CONCLUSION

The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY

ERL (2016g)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

STD/1689

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE: Notified chemical (STD/1689)

METHOD: OECD TG 301 F: Ready Biodegradability: Manometric Respirometry Test

Inoculum	Effluent from a sewage treatment plant which treats primarily domestic sewage.
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	BOD, TOC
Remarks – Method	Test media were prepared by dispersing a nominal amount of the solid test substance in mineral medium (nominal concentration of 100 mg/L) and adding inoculum.

RESULTS

Test Substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
2	0	2	17
7	12	7	62
14	17	14	67
21	20	21	72
28	23	28	75

Remarks – Results: All validity criteria were satisfied. The toxicity control attained 44% biodegradation after 14 days and 53% biodegradation after 28 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. Aniline (procedure control) attained 67% biodegradation after 14 days and 75% biodegradation after 28 days.

The test substance is a mixture comprised of several components and the biodegradation of the individual components was not delineated. Therefore, no definitive statement can be made about the biodegradability of the test substance as a whole, only that at least one component of the mixture is biodegradable.

CONCLUSION: The test substance shows evidence of biodegradability.

TEST FACILITY: ERL (2016h)

C.2. Ecotoxicological Investigations

C.2.1. Acute Toxicity to Fish

TEST SUBSTANCE: Notified chemical (STD/1689)

METHOD: OECD TG 203: Fish, Acute Toxicity Test – Semi-static

Species	*Oncorhynchus mykiss* (Rainbow trout)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	140 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS

Remarks – Method	A limit test was performed using a Water Accommodated Fraction (WAF) of the test substance based on the results of a range finding test. The WAF (loading rate of 100 mg/L) was used directly, without dilution, as the test medium. WAFs were prepared by stirring solid test item in water for 23 hours followed by a one hour settling period and then siphoning the middle fraction of the medium through a sintered glass-wool plug. Analysis showed that the test substance was consumed during the course of the experiment so semi-static conditions were utilised. Test media were replaced daily. Temperature was maintained at 14 °C. Nominal concentrations (at 0 hours) are reported (instead of a measured concentrations), consistent with international guidelines for WAFs (OECD, 2019).

RESULTS

Loading Rate (mg/L WAF)	*Number of Fish*	*Mortality*				
		1 h	*24 h*	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0	0
100	7	0	0	0	0	0

LL50	> 100 mg/L at 96 hours
NOEL	100 mg/L at 96 hours
Remarks – Results	All validity criteria were satisfied. The dissolved oxygen concentration in the test solution during the test was ≥ 9.2 mg/L at 14 °C (≥ 86 % air saturation, USGS, 2011). No abnormalities or mortalities were observed in any of the fish up to 96 hours.

CONCLUSION The test substance is not harmful to fish up to its water solubility limit.

TEST FACILITY ERL (2016i)

C.2.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE Notified chemical (STD/1689)

METHOD OEC TG 202: Daphnia sp. Acute Immobilisation Test – Semi-static

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS
Remarks – Method	Based on the results of a range finding test, the test substance was prepared as a Water Accommodated Fraction (WAF) at concentrations of 10–100 mg/L. WAFs were prepared and used directly, without dilution, as the test media by stirring solid test item in water for 23 hours followed by a one hour settling period and then siphoning the middle fraction of the medium through a sintered glass-wool plug. Nominal concentrations (at 0 hours) are reported (instead of measured concentrations), consistent with international guidelines for WAFs (OECD, 2019). Temperature was maintained at 22 ± 1 °C. Test media were replaced daily. A positive control test was run separately using potassium dichromate.

RESULTS

Loading Rate (mg/L WAF)	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
Control	15	0	0
10	20	0	0
18	20	0	0
32	20	0	0

56	20	0	0
100	20	0	0

EL50	> 100 mg/L at 48 hours
NOEL	100 mg/L at 48 hours
Remarks – Results	All validity criteria were satisfied. Dissolved oxygen concentrations were ≥ 8.1 mg/L at 22 °C (≥ 92 % air saturation, USGS, 2011). One of the control replicates (containing five daphnids) was discarded because four of the daphnids were immobilised at 24 hours. The three remaining control samples showed no adverse effects throughout the test so this amendment is not considered to have significantly affected the results of the study. The temperature reached 23 °C in some of the test samples but this is not considered to have significantly affected the results of the study given that no immobilisation was observed in any of the samples. The 48 h EC50 of the positive control experiment was 0.64 mg/L which is within the acceptable range according to the test guidelines (0.6 – 2.1 mg/L).
CONCLUSION	The test substance is not harmful to aquatic invertebrates up to its water solubility limit.
TEST FACILITY	ERL (2016j)

C.2.3. Algal Growth Inhibition Test

TEST SUBSTANCE	Notified chemical (STD/1689)
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 1.0 – 100.0 mg/L
Auxiliary Solvent	None
Water Hardness	Not determined
Analytical Monitoring	HPLC-MS, Multisizer Particle Counter
Remarks – Method	The test substance was prepared as a Water Accommodated Fraction (WAF) at various nominal concentrations based on the results of a range finding test. WAFs were prepared and used directly, without dilution, as the test media by stirring solid test item in water for 23 hours followed by a one hour settling period and then siphoning the middle fraction of the medium through a sintered glass-wool plug. The measured concentration of the test chemical declined significantly over 72 hours (to below the LOQ in some cases) indicating that the test item was unstable over the test duration. Nominal concentrations (at 0 hours) are reported (instead of a measured concentrations), consistent with international guidelines for WAFs (OECD, 2019). Temperature was maintained at 24 ± 1 °C. A positive control test was run separately using potassium dichromate.

RESULTS

Biomass		*Growth*	
EyL50 (mg/L at 72 h)	*NOELR (mg/L)*	*ErL50 (mg/L at 72 h)*	*NOELR (mg/L)*
35	10	> 100	10

Remarks – Results	All validity criteria were satisfied. The cell concentration of the control cultures increased by a factor of 245 after 72 hours. The 72 h ErC50 for the positive control was 1.5 mg/L which is within the normal range for this reference item.
CONCLUSION	Based on the results of the growth-inhibition test, the test substance is not

harmful to algae up to its water solubility limit.

TEST FACILITY ERL (2016k)

STD/1690

C.3. Environmental Fate

C.3.1. Ready Biodegradability

TEST SUBSTANCE Notified chemical (STD/1690)

METHOD OECD TG 301 F: Ready Biodegradability: Manometric Respirometry Test
- Inoculum: Effluent from a sewage treatment plant which treats primarily domestic sewage.
- Exposure Period: 28 days
- Auxiliary Solvent: None
- Analytical Monitoring: BOD, TOC
- Remarks – Method: Test media were prepared by dispersing a nominal amount of the solid test substance in mineral medium (nominal concentration of 100 mg/L) and adding inoculum.

RESULTS

Test Substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
2	0	2	17
7	5	7	62
14	10	14	67
21	13	21	72
28	18	28	75

Remarks – Results: All validity criteria were satisfied. The toxicity control attained 45% biodegradation after 14 days and 52% biodegradation after 28 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. Aniline (procedure control) attained 67% biodegradation after 14 days and 75% biodegradation after 28 days.

The test substance is a mixture comprised of several components and the biodegradation of the individual components was not delineated. Therefore, no definitive statement can be made about the biodegradability of the test substance as a whole, only that at least one component of the mixture is biodegradable.

CONCLUSION The test substance shows evidence of biodegradability.

TEST FACILITY ERL (2016l)

C.4. Ecotoxicological Investigations

C.4.1. Acute Toxicity to Fish

TEST SUBSTANCE Notified chemical (STD/1690)

METHOD OECD TG 203: Fish, Acute Toxicity Test – Semi-static
- Species: *Oncorhynchus mykiss* (Rainbow trout)
- Exposure Period: 96 hours
- Auxiliary Solvent: None
- Water Hardness: 140 mg $CaCO_3$/L
- Analytical Monitoring: HPLC-MS

Remarks – Method	A limit test was performed using a Water Accommodated Fraction (WAF) of the test substance based on the results of a range finding test. The WAF (loading rate of 100 mg/L) was used directly, without dilution, as the test medium. WAFs were prepared by stirring solid test item in water for 23 hours followed by a one hour settling period and then siphoning the middle fraction of the medium through a sintered glass-wool plug. Analysis showed that the test substance was consumed during the course of the experiment so semi-static conditions were utilised. Test media were replaced daily. Temperature was maintained at 14 °C. Nominal concentrations (at 0 hours) are reported (instead of a measured concentrations), consistent with international guidelines for WAFs (OECD, 2019).

RESULTS

Loading Rate (mg/L WAF)	*Number of Fish*	*Mortality*				
		1 h	*24 h*	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0	0
100	7	0	0	0	0	0

LL50	> 100 mg/L at 96 hours
NOEL	100 mg/L at 96 hours
Remarks – Results	All validity criteria were satisfied. The dissolved oxygen concentration in the test solution during the test was ≥ 9.1 mg/L at 14 °C (≥ 88 % air saturation, USGS, 2011). Sub-lethal effects were observed in the test solution at 6 and 24 hours where up to six fish were sitting at the bottom of the test vessel. Beyond 24 hours, no sub-lethal effects were observed. These observations are not considered to have impacted the validity of the test.

CONCLUSION The test substance is not harmful to fish up to its water solubility limit.

TEST FACILITY ERL (2016m)

C.4.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE Notified chemical (STD/1690)

METHOD OECD TG 202: Daphnia sp. Acute Immobilisation Test – Semi-static

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS
Remarks – Method	A limit test was performed using a Water Accommodated Fraction (WAF) of the test substance based on the results of a range finding test. The WAF (loading rate of 100 mg/L) was used directly, without dilution, as the test medium. WAFs were prepared by stirring solid test item in water for 23 hours followed by a one hour settling period and then siphoning the middle fraction of the medium through a sintered glass-wool plug. Nominal concentrations (at 0 hours) are reported (instead of measured concentrations), consistent with international guidelines for WAFs (OECD, 2019). Temperature was maintained at 22 ± 1 °C. Test media were replaced daily. A positive control test was run separately using potassium dichromate.

RESULTS

Loading Rate (mg/L WAF)	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
Control	20	1	1
100	20	0	0

EL50	> 100 mg/L at 48 hours
NOEL	100 mg/L at 48 hours
Remarks – Results	All validity criteria were satisfied. Dissolved oxygen concentrations were ≥ 8.7 mg/L at 22 °C (≥ 99 % air saturation, USGS, 2011). The 48 h EC50 of the positive control experiment was 0.64 mg/L which is within the acceptable range according to the test guidelines (0.6 – 2.1 mg/L).
CONCLUSION	The test substance is not harmful to aquatic invertebrates up to its water solubility limit.
TEST FACILITY	ERL (2016n)

C.4.3. Algal Growth Inhibition Test

TEST SUBSTANCE	Notified chemical (STD/1690)
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 1.0 – 100.0 mg/L
Auxiliary Solvent	None
Water Hardness	Not determined
Analytical Monitoring	HPLC-MS, Multisizer Particle Counter
Remarks – Method	The test substance was prepared as a Water Accommodated Fraction (WAF) at various nominal concentrations based on the results of a range finding test. WAFs were prepared and used directly, without dilution, as the test media by stirring solid test item in water for 23 hours followed by a one hour settling period and then siphoning the middle fraction of the medium through a sintered glass-wool plug. The measured concentration of the test chemical declined significantly over 72 hours (to below the LOQ in some cases) indicating that the test item was unstable over the test duration. Nominal concentrations (at 0 hours) are reported (instead of a measured concentrations), consistent with international guidelines for WAFs (OECD, 2019). Temperature was maintained at 24 ± 1 °C. A positive control test was run separately using potassium dichromate.

RESULTS

Biomass		*Growth*	
EyL50 (mg/L at 72 h)	*NOELR (mg/L)*	*ErL50 (mg/L at 72 h)*	*NOELR (mg/L)*
6.8	3.2	> 100	3.2

Remarks – Results	All validity criteria were satisfied. The control was the same as that used in STD/1689. The 72 h ErC50 for the positive control was 1.5 mg/L which is within the normal range for this reference item.
CONCLUSION	Based on the results of the growth-inhibition test, the test substance is not harmful to algae up to its water solubility limit.
TEST FACILITY	ERL (2016o)

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