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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Hyperform HPR-803

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

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS SUBSTANCE	INTRODUCTION VOLUME	USE
STD/1391	Sylvan Chemical Co. Inc.	Hyperform HPR-803	ND*	≤100 tonnes per annum	Component of plastic articles

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data, the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

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

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

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

Recommendations

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical, as introduced:
  - Automated processes, where possible
  - Local exhaust ventilation and/or appropriate dust extraction systems

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical, as introduced:
  - Use of low-dust handling techniques

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical, as introduced:
  - Respiratory protection during manual handling

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
- additional information has become available to the person regarding the effects of repeated inhalation exposure to the notified chemical.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of plastic articles, or is likely to change significantly;
- the amount of chemical being introduced has increased from 100 tonnes per annum, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

Material Safety Data Sheet
The MSDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Sylvan Chemical Co. Inc. (ABN: 58 142 096 759)
4/345 Plummer Street
Port Melbourne, VIC 3207

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)

Variation to the schedule of data requirements is claimed as follows: flash point, autoignition temperature, explosive properties, acute oral toxicity, acute dermal toxicity and repeat dose toxicity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Hyperform HPR-803

MOLECULAR WEIGHT
<500 Da

ANALYTICAL DATA
Reference IR spectrum was provided.

3. COMPOSITION

DEGREE OF PURITY 99%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: white crystalline powder (fibres/whiskers)

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Decomposes without melting at >275 °C	Measured
Density	2310 kg/m^3 at 23 °C	Measured
Vapour Pressure	<1.7 x 10^{-7} kPa at 25 °C	Measured
Water Solubility	30.2 mg/L at 20 °C and pH 10.2	Estimated. The value was 4 times higher than the top standard solution. In addition, the notified chemical is expected to be soluble through neutralization reaction in water at acidic conditions. See Appendix A for details.
Hydrolysis as a Function of pH	Not determined.	The notified chemical is a salt which may hydrolyse in water to form basic solution. It is also expected to be neutralised under acidic conditions.
Partition Coefficient (n-octanol/water)	Not determined.	Not applicable given the notified chemical is an inorganic compound not readily soluble in water.
Adsorption/Desorption	Not determined.	The notified chemical is a hydrophilic inorganic salt, and is conservatively expected to be mobile in the environment.
Dissociation Constant	Not determined	The notified chemical is a salt and is expected to dissociate when dissolved in water.
Particle Size	i) Inhalable fraction (<100	Measured – full study reports not provided.

	μm): 100% Respirable fraction (<10 μm): 50% ii) Aspect ratio varies from 6-18	
Flammability	Not highly flammable	Measured
Autoignition Temperature	≥400 ºC	Estimated
Explosive Properties	Predicted negative	Contains no functional groups that would imply explosive properties.
Dust Explosivity	Non-explosible	Measured

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use. Decomposition will occur at elevated temperatures and contact with acids should be avoided.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified chemical is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However the data above do not address all Dangerous Goods endpoints. Therefore consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemical.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported at 100% concentration.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	10	25	50	50	100

PORT OF ENTRY
Sydney and Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Sylvan Chemical Co. Inc.

TRANSPORTATION AND PACKAGING
The notified chemical (100%) will be supplied in 10 kg drums or 150-1000 kg flexible bulk containers (super sacks). The chemical will be transported to plastics manufacturers within Australia by road.

USE
The notified chemical will be used as a reinforcing agent for plastic articles at <40% concentration. A variety of plastic articles may be produced for use by workers and the general public, including plastics with food contact uses.

OPERATION DESCRIPTION
The manufacturing processes will vary depending on the plastic article being manufactured and will involve both manual and automated stages and operations at multiple sites within Australia.

It is expected that the notified chemical (100%) will be transferred from the shipping drums into additive hoppers/mixing vessels. The material will then be metered into a closed system such as an extruder, forming machine or mixer with polyolefin resin and other additives to produce finished articles or pellets that will subsequently be converted to finished articles. Following production, the articles (containing <40% notified chemical) will be distributed to end-users.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage	≤5	8-10	50-150
Equipment maintenance	≤5	8-10	50-150
Manufacture and use	≤5	8-10	50-150
Material analysis	≤5	8-10	50-150

EXPOSURE DETAILS

Transport and storage workers may come into contact with the notified chemical (100%) only in the event of accidental rupture of containers.

At reformulation/manufacturing sites, dermal or ocular exposure to the notified chemical (100%) may occur whilst opening containers, during transfer processes and during equipment maintenance. As the notified chemical is a fibrous powder with particle sizes in the inhalable and respirable size range, inhalation exposure (at 100% notified chemical) is also possible. Exposure should be mitigated by the use of exhaust ventilation and personal protective equipment (PPE), including goggles, gloves, protective clothing and dust mask or respirator, as appropriate.

Once incorporated into the plastic articles, the notified chemical is not expected to be bioavailable and further contact should not lead to exposure.

6.1.2. Public Exposure

The notified chemical is intended for industrial use only. Therefore, the public may be exposed to the notified chemical (100%) only in the event of a transport accident. The public may be exposed to the plastic articles containing the notified chemical (<40%). However, the notified chemical will be bound within a polymer matrix and will be unavailable for exposure.

The plastic articles may have food contact applications. No migration studies for the notified chemical are available. However, the notifier has advised that the notified chemical is not expected to migrate from the articles as it will be bound within a polymer matrix.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute inhalation toxicity	LC50 >5.10 mg/L/4 hours; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	non genotoxic

Toxicokinetics, metabolism and distribution.

Based on the molecular weight (<500 Da) and water solubility of the notified chemical (particularly in acidic conditions), it is expected that some passive diffusion across the gastrointestinal (GI) tract and dermal absorption will occur. The notified chemical is a fibrous powder, with 100% of particles in the inhalable size range and 50% in the respirable range, and an aspect ratio of 6-18. Given the water solubility profile of the notified chemical, its persistence in the lung is not expected.

Acute toxicity.

The notified chemical was found to be of low acute inhalation toxicity in rats (LD50 >2000 mg/kg bw). No acute

oral or dermal toxicity data are provided for the notified chemical. However, particularly in acidic conditions, the notified chemical is expected to afford compounds that are generally of low concern.

Irritation and Sensitisation.
The notified chemical was determined to be non-irritating to the skin of rabbits. In an eye irritation study in rabbits, mild to moderate conjunctival irritation was noted. However, the scores did not warrant classification of the chemical as an eye irritant and thus it is considered to be slightly irritating to the eyes. All treated eyes appeared normal after 72 hours. The notified chemical (tested at up to 10% concentration) was found to be a non-sensitiser in a local lymph node assay in mice.

Repeated Dose Toxicity.
In a published study involving inhalation exposure of rats to the notified chemical, the authors report that there were no significant differences between the biological effects observed in control and treatment groups. In addition, the authors report that the notified chemical was rapidly cleared from the lungs of treated animals.

Mutagenicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study and was not clastogenic in an in vitro mammalian chromosome aberration test.

Health hazard classification
Based on the available data, the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified polymer will be handled by workers at ≤100% concentration as imported and as a component of plastic articles. Based on the information provided, acute toxicity effects from exposure to the notified chemical are not expected. However, given that the chemical is a fibrous powder with particle sizes in the inhalable and respirable size range, hazardous effects from repeated exposure to the chemical cannot be ruled out. Therefore, measures should be taken to avoid exposure to the notified chemical by inhalation.

Provided that control measures are in place to minimise worker exposure, including the use of automated processes and the wearing of PPE (particularly respiratory protection) when handling the notified chemical as imported, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

6.3.2. Public Health
The notified chemical is intended for use in industrial applications by qualified operators. The public may be exposed to the plastic articles containing the notified chemical, in-particular products with food contact applications. A risk assessment for exposure through the use in food contact materials has not been undertaken. However, the notifier has advised that the notified chemical is not expected to migrate significantly from the articles as it will be bound within a polymer matrix. If migration to food occurs, it is expected to be limited to small quantities at the direct contact surface between the food and the article, where the notified chemical may dissolve into the contacted food. The potential for this to occur may be slightly higher in acidic foods. However, any dissolution is expected to result in compounds that are generally of low concern.

Therefore, when used in the proposed manner, the risk to public health is not considered to be unreasonable. A copy of this report will be forwarded to Food Standards Australia New Zealand (FSANZ) for informational purposes.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia and stored in 10 kg drums and/or 150-1000 kg super sacks on pallets for use as a reinforcing agent for plastic articles. From warehouse locations in Australia, it will be transported to the polyolefin manufacturer for production of the final articles for the plastics industry in Australia. No significant release of the notified chemical is expected to occur in Australia from the processes of transportation.

At the reformulation site, the notified chemical will be transferred from shipping drums to the additive hopper or mixing vessels, and then metered into a closed system such as extruder, forming machine or mixer with the polyolefin resin and other additives to produce pellets, finished articles or coating formulations. The amount of residues in the import containers is estimated to be <1% of the import volume, which is expected to be disposed to landfill together with the containers. The release of the notified chemical at the reformulation site from spills and manufacturing scrap is estimated to be <1% which will most likely be recycled. No use of water will be involved in the reformulation process, and therefore, any release will be in solid form and will likely be disposed of to landfill. No release of the notified chemical to the water environment is expected from the reformulation process.

RELEASE OF CHEMICAL FROM USE

After the notified chemical has been incorporated in the polymer matrix (pellets or finished articles), it will be trapped in the inert bulk polymer matrix. The notified chemical is not expected to be released during the use of the plastic articles containing it.

RELEASE OF CHEMICAL FROM DISPOSAL

The residues in the import containers will be most likely sent to landfill with the containers. Any release of the notified chemical from the reformulation is expected to be recycled due to the high cost of the material. The majority of notified chemical will be incorporated into plastic articles which will end up in landfill at the end of their useful lives.

7.1.2. Environmental Fate

No environmental fate data were submitted given the inorganic nature of the notified chemical. The notified chemical is considered to be hydrophilic despite the low water solubility. This property indicates the low potential for bioaccumulation of the notified chemical to aquatic organisms.

No significant release of the notified chemical to the aquatic environment is expected from the reported use. Most of the notified chemical will be incorporated into a plastic matrix and is not expected to be available for exposure, and will be finally disposed of to landfill together with the final plastic articles at the end of their useful lives. In landfill, the chemical is not expected to leach. It may be degraded into inorganic oxides over time.

7.1.3. Predicted Environmental Concentration (PEC)

The PEC has not been calculated since no significant release of the notified chemical to the water environment is expected based on the reported use pattern.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LC50 >33 mg/L*	Not harmful to fish up to the limit of water solubility
Daphnia Toxicity	EC50 >56 mg/L*	Not harmful to Daphnia up to the limit of water solubility
Algal Toxicity	E_rC50 >14 mg/L*	Not harmful to algae up to the limit of water solubility

* Saturated solution concentrations.

The notified chemical is not harmful to aquatic species on an acute basis up to the limit of its water solubility.

7.2.1. Predicted No-Effect Concentration

Calculation of the PNEC was not considered necessary since no significant release of the notified chemical to the environment is expected from the reported use pattern.

7.3. Environmental Risk Assessment

The Risk Quotient (PEC/PNEC) was not calculated since no significant release of the notified chemical is expected from the reported use. The notified chemical is not expected to have any effects on the aquatic environment based on its reported use pattern.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point Decomposes without melting at >275 ºC

Method OECD TG 102 Melting Point/Melting Range.
Remarks Determined by DSC. The notified chemical decomposed from ~274 ºC, with significant decomposition from 347 ºC.
Test Facility Harlan (2010a)

Density 2310 kg/m^3 at 23 ± 0.5 ºC

Method OECD TG 109 Density of Liquids and Solids.
Remarks Determined using a pycnometer.
Test Facility Harlan (2010a)

Vapour Pressure <1.7 x 10^{-7} kPa at 25 ºC

Method OECD TG 104 Vapour Pressure.
Remarks Determined using a vapour pressure balance. The temperature and pressure readings were taken between 190 ˚C and 200 ˚C with a one hour dwell at 190 ˚C between runs. No statistical analyses were performed since the readings were too low and variable for a line of best fit to have any meaning. Therefore, the maximum value for the vapour pressure at 25 ˚C was estimated by imposing a regression slope on a chosen data point. The data point was chosen from a run from which the sample had been under vacuum for the longest period before the run, and the selected data point gave the highest estimated vapour pressure. The vapour pressure was determined to be < 1.7 × 10^{-7} kPa at 25 ºC.
Test Facility Harlan (2010a)

Water Solubility 30.2 mg/L at 20 ºC and pH 10.2

Method OECD TG 105 Water Solubility.
EC Directive 440/2008 A.6 Water Solubility.
Remarks The Flask Method was used. Following a preliminary test, triplicate solutions of the notified chemical (about 100 mg/L, pH 10.2) were prepared and analysed for the relevant metal content using Atomic Absorbance Spectroscopy (AAS) in duplicate for each sample solution. Duplicate standard solutions ranging 0.1 to 2.5 mg/L were prepared and analysed, which could not cover the range of the determined solubility of the notified chemical.

The water solubility was determined to be 9.46 mg/L at 20 ºC for the relevant metal in the test solutions, which is equivalent to 30.2 mg/L for the notified chemical (theoretical content of 31.3% based on the molecular formula). The notified chemical is considered to be moderately soluble in water. However, the determined value should be treated with caution based on the following considerations:

1. The tested solubility was nearly 4 times higher than top standard solution concentration.
2. The samples for AAS analysis were filtrates of the dispersions of the notified chemical in water through a filter of 0.2 µm, in which case, dispersed fine particles of the notified chemical may be counted in the tested solubility.

No tests at acidic conditions were conducted. Based on the nature of being an inorganic chemical, the notified chemical is expected to be soluble via a neutralization reaction under acidic conditions.
Test Facility Harlan (2010a)

Flammability Not highly flammable

Method EC Directive 2008/440/EEC A.10 Flammability (Solids).
Remarks An air-rich Bunsen burner flame was applied to one end of a 250 x 20 x 10 mm strip on a

non-porous board for 2 minutes. The notified chemical did not ignite.

Test Facility Harlan (2010a)

Dust Explosivity Non-explosible

Method EN 14034-1 and EN 14034-2 Determination of Explosion Characteristics of Dust Clouds

Remarks The sample was tested under atmospheric conditions over a range of concentrations. It was not possible to ignite the sample by the ignition sources at any of the investigated concentrations, thus the chemical was determined to be non-explosible and cannot give rise to dust explosions.

Test Facility GexCon (2009)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – inhalation

TEST SUBSTANCE: Notified Chemical

METHOD
- Species/Strain: Rat/HsdRccHan™ : WIST
- Vehicle: None
- Method of Exposure: nasal exposure.
- Exposure Period: 4 hours
- Physical Form: solid aerosol (particulate).
- Particle Size: MMAD: 2.91 µm. Inhalable fraction <4 µm = 60.5%
- Remarks - Method: The test substance was ground prior to use to reduce the particle size and facilitate aerosolisation.

RESULTS

Group	*Number and Sex of Animals*	*Concentration <units>*		*Mortality*
		Nominal	*Actual*	
I	5 M/5 F	12.7	5.10	0/10

- LC50: >5.10 mg/L/4 hours
- Signs of Toxicity: Increased respiratory rate and wet fur were noted in all animals during the exposure period and were attributed to the restraint procedure. In addition, upon removal from the chamber and 1-hour post-exposure, hunched posture and pilo-erection were noted in all animals. One day after exposure, the animals appeared normal.
- Effects in Organs: None

CONCLUSION: The notified chemical is of low toxicity via inhalation.

TEST FACILITY: Harlan (2010b)

B.2. Irritation – skin

TEST SUBSTANCE: Notified Chemical

METHOD
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 2
- Vehicle: Distilled water
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviations.

RESULTS
- Remarks - Results: No signs of skin irritation were recorded.

CONCLUSION: The notified chemical is non-irritating to the skin.

TEST FACILITY: Harlan (2010c)

B.3. Irritation – eye

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
- Species/Strain: Rabbit/New Zealand White

Number of Animals	2
Observation Period	72 hours
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			
Conjunctiva: redness	1	1	2	<72 hours	0
Conjunctiva: chemosis	0.7	0.7	2	<72 hours	0
Conjunctiva: discharge	0.3	0.3	2	<48 hours	0
Corneal opacity	0	0	0	-	0
Iridial inflammation	0	0	0	-	0

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

Remarks - Results	No corneal or iridial effects were reported. Moderate conjunctival irritation was noted in treated eyes 1- and 24-hours post instillation with minimal irritation noted after 48 hours. The treated eyes were normal after 72 hours.
CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	Harlan (2010d)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain	Mouse/CBA/Ca
Vehicle	Acetone/olive oil (4:1)
Remarks - Method	A preliminary screening test was conducted using one mouse, which was tested at 10% concentration (suspension of notified chemical in the vehicle). Higher doses (25 and 50%) in various vehicles were unsuitable for dosing. Concurrent tests involving a positive control were not run, but had been conducted previously in the test laboratory.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/animal)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	2110.33	-
2.5	2705.46	1.28
5	2443.00	1.16
10	1487.63	0.70

Remarks - Results	There were no mortalities and no signs of systemic toxicity noted for the test and control animals. With regard to the proliferative response, there was no significant difference between the control and test groups.
CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Harlan (2010e)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure/Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	Phenobarbitone/β-naphthoflavone-induced rat liver (S9 homogenate)
Concentration Range in Main Test	a) With metabolic activation: 50, 150, 500, 1500 and 5000 µg/plate b) Without metabolic activation: 50, 150, 500, 1500 and 5000 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	A preliminary toxicity test (0-5000 µg/plate) was performed to determine the toxicity of the test material (TA100 and WP2uvrA). A range-finding study was then conducted using 5 concentrations of the test substance, assayed in triplicate against each tester strain (50-5000 µg/plate), using the plate incorporation procedure. The main study (pre-incubation procedure; Test 2) was conducted on a separate day to the range-finding study (Test 1) using fresh cultures of the bacterial strains and fresh test material formulations. Vehicle and positive controls were used in parallel with the test material (plate incorporation procedure). Positive controls: i) without S9: N-ethyl-N'-nitro-N-nitrosoguanidine (TA100, TA1535, WP2uvrA), 9-aminoacridine (TA1537) and 4-nitroquinoline-1-oxide (TA98); ii) with S9: 2-aminoanthracene (TA100, TA1535, TA1537, WP2uvrA) and benzo(a)pyrene (TA98).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	>5000	>5000	>5000	Negative
Test 2		>5000	>5000	Negative
Present				
Test 1	>5000	>5000	>5000	Negative
Test 2		>5000	>5000	Negative

Remarks - Results	The test substance did not cause a visible reduction in the growth of the bacterial background lawn at any dose level. No toxicologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains up to and including the maximum dose, either with or without metabolic activation. A statistically significant increase was noted in the TA98 strain (Test 2) at 5000 µg/plate, however, as there was no dose-response relationship and the count was within the in-house historical range for the strain, it was considered to be of no biological relevance. The positive controls gave satisfactory responses, confirming the validity of the test system.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Harlan (2010f)

B.6. Genotoxicity – in vitro

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 473 In vitro Mammalian Chromosome Aberration Test.

Species/Strain	Human
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	Phenobarbitone/β-naphthoflavone-induced rat liver (S9 homogenate)
Vehicle	Minimal Essential Medium (MEM); suspension
Remarks - Method	The water content (~12%) was adjusted for when preparing test substance formulations. A preliminary toxicity study (18.20 to 4660 µg/mL) was performed to define the dose levels for the main test. Vehicle and positive controls (cyclophosphamide and mitomycin C) were used in parallel with the test material.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 300, 600*, 1200*, 1600*, 2400*, 3200	4	24
Test 2	0*, 300, 600*, 1200*, 1600*, 2400*, 3200	24	24
Present			
Test 1	0*, 300*, 600*, 1200*, 1600*, 2400, 3200	4	24
Test 2	0*, 300, 600*, 1200*, 1600*, 2400*, 3200	4	24

*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	≥2330	≥2400	≥2400	Negative
Test 2	≥2330	≥2400	≥1600	Negative
Present				
Test 1	≥4660	≥1600	≥1200	Negative
Test 2		>2400	≥600	Negative

Remarks - Results: For the main experiments, precipitates were observed at the end of the observation period in all exposure groups (at ≥300 µg/mL in Test 1 and at ≥300 and ≥1600 µg/mL in Test 2, with and without metabolic activation, respectively). In addition, haemolysis was seen in both tests (at ≥1600 and ≥1200µg/mL in Test 1, with and without metabolic activation, respectively, and at ≥1600 µg/mL in Test 2, with metabolic activation).

No statistically significant increase in the number of cells with aberrations was noted at any test level, with and without metabolic activation.

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: Harlan (2010g)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Bioaccumulation

TEST SUBSTANCE	Notified chemical
CONCLUSION	The study for bioaccumulation was not conducted. The notified chemical has a low molecular weight. However, a low potential for bioaccumulation is expected based on its nature of being a hydrophilic inorganic compound.

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test –semi-static conditions.
Species	Rainbow trout *(Oncorhynchus mykiss)*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	140 mg $CaCO_3$/L
Analytical Monitoring	The test concentrations were measured by Atomic Absorbance Spectroscopy (AAS) using a magnesium external standard at 0, 24, 48, 72 and 96 hours of the test. The limit of quantitation was assessed as 5.4 mg/L for the notified chemical.
Remarks – Method	Following a range-finding test, a limit test was conducted at saturated concentration of 18 mg/L (nominal) in duplicate at 14 ˚C with a photoperiod of 16 hours light and 8 hours darkness with 20 minutes dawn and dusk transition periods. A blank control was performed in one replicate. 7 fish were used in each replicate for both the control and treatment groups. The saturated solutions were prepared by stirring excess amounts of the notified chemical in dechlorinated water for a period of 24 hours prior to removing any undissolved test item present by filtration (0.2 µm Sartorius Sartopore). The test vessels were aerated and the preparations were renewed on a daily base. The test solutions were clear and colourless throughout the test period.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	0	14	0	0	0	0	0
18	33	14	0	0	0	0	0

LC50	>33mg/L at 96 hours (measured).
NOEC	33 mg/L at 96 hours (measured).
Remarks – Results	The measured concentrations at 24, 48, 72 and 96 hours (old media) ranged from 28.9 to 36.3 mg/L with a mean value of 33 mg/L. The significant difference between the actual and measured concentrations is probably due to the measurements that were done on samples of different trials. Any difference in stirring speed and water quality could have an impact on the outcome of the measured sample concentrations (noting the samples were filtrates through a 0.2 µm filter). No decline of the

measured concentrations was observed over the dosing period. The determined saturated concentration should be taken with caution since it was higher than the top standard solution concentration (8 mg/L).

Throughout the test period of 96 hours, the oxygen concentration maintained >84% of the saturation value for both the control and treatment replicates, the pH value ranged 8.8 – 9.6 for the treatment replicates and 8.0 – 8.3 for the control.

Neither mortalities nor sub-lethal effects in either the control or the treatment groups were observed over the 96 hours.

Since no mortalities or sub-lethal effects were observed in the saturated solution, the test substance is considered not harmful to rainbow trout up to the limit of its water solubility.

CONCLUSION The notified chemical is not harmful to fish up to the limit of its water solubility.

TEST FACILITY Harlan (2010h)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test – static conditions.

Species *Daphnia magna*

Exposure Period 48 hours

Auxiliary Solvent None

Water Hardness 140 mg $CaCO_3$/L

Analytical Monitoring

The test concentrations were measured by AAS using a magnesium external standard at 0 and 48 hours of the test. The limit of quantitation was assessed as 5.4 mg/L for the notified chemical.

Remarks - Method

Following a range-finding test, a limit test was conducted at saturated concentration of 18 mg/L (nominal) at 21 to 22 ˚C with a photoperiod of 16 hours light and 8 hours darkness with 20 minutes dawn and dusk transition periods. A blank control was performed in one replicate. Both the control and treatment groups were established in 4 replicates with 5 animals in each replicate. The determined saturated concentration should be taken with caution since it was higher than the top standard solution concentration (8 mg/L).

A reference control was conducted using potassium dichromate at 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L.

The saturated solutions were prepared by stirring excess amount of the notified chemical in dechlorinated water for a period of 24 hours prior to removing any undissolved test item present by filtration (0.2 µm Gelman Acrocap). The test vessels were not aerated and the preparations were not renewed during the test.

The test solutions were clear and colourless throughout the test period.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	0	20	0	0
18	56	20	0	0

EC50 >56 mg/L at 48 hours

NOEC 56 mg/L at 48 hours

Remarks - Results	The measured concentrations were 51.5 and 55.7 mg/L at 0 h, 60.6 and 56.9 mg/L at 48 hours. The mean concentration for the whole test period was calculated as 56 mg/L. The significant difference between the actual and measured concentrations is probably due to the measurements that were done on samples of different trials. Any difference in stirring speed and water quality could have an impact on the outcome of the measured sample concentrations (noting the samples were filtrates through a 0.2 µm filter). No decline of the measured concentrations was observed over the dosing period. The determined saturated concentration should be taken with caution since it was higher than the top standard solution concentration (8 mg/L). Throughout the test period of 48 hours, the oxygen concentration maintained >97% of the saturation value for both the control and treatment replicates, the pH value ranged from 8.8 – 9.0 for the treatment replicates and 7.6 – 8.2 for the blank control. The 48 h EC50 for the reference control was determined to be 1.2 (95% CL 1.1 – 1.3) mg/L. The 48 h NOEC was determined to be 0.32 mg/L. No mortalities in either the blank control or the treatment groups were observed over the 48 hours. Since no mortalities were observed in the saturated solution, the test substance is considered not harmful to *Daphnia magna* up to the limit of its water solubility.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates up to the limit of its water solubility.
TEST FACILITY	Harlan (2010i)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 6.25, 12.5, 25, 50 and 100% v/v saturated solution. Actual: 1.1, 2.4, 4.0, 6.8 and 14 mg/L at 0 hour.
Auxiliary Solvent	None
Water Hardness	Not provided
Analytical Monitoring	The cell concentrations were determined using a Coulter® Multisizer Particle Counter. The test concentrations were measured by AAS using a magnesium external standard at 0 and 72 hours of the test. The limit of quantitation was assessed as 0.73 mg/L for the notified chemical.
Remarks - Method	Following a range-finding test, *Desmodesmus subspicatus* was exposed to solutions of the notified chemical at 5 concentrations for 72 hours, under constant illumination and shaking at the temperature of 24±1 ˚C with a initial cell density of 4×10^3 cells/mL. Three and six replicates were established for each of the treatment groups and control group, respectively. The saturated solutions were prepared at 21 ˚C by stirring an excess amount of the notified chemical in the culture medium for a period of 48 hours prior to removing any undissolved test item present by filtration (0.2 µm Gelman Acrocap). A reference control was conducted using potassium dichromate at 0.0625, 0.125, 0.25, 0.5 and 1.0 mg/L.

Statistical analysis of the test data was carried out in the study using Dunnett's multiple comparison procedure for comparing several treatments with a control (Dunnett, 1995).

RESULTS

Biomass(Based on 0-hour measured concentrations)		*Growth (Based on 0-hour measured concentrations)*	
E_bC50	*NOEC*	*E_rC50*	*NOEC*
mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
10	4.0	>14	6.8

Remarks - Results

A slight decline in each of the test concentration groups was observed, and this is considered due to the adsorption of the notified chemical to the algal cells present. In addition, the determined saturated concentration should be taken with caution since it was higher than the top standard solution concentration (6.4 mg/L).

The pH values ranged 7.3 – 7.9 for the control. The start pH values for the treatment groups showed a concentration dependent increase with increasing concentration in the range of 7.3 – 9.9.

The 72 h E_rC50 for the reference control was determined to be 0.49 mg/L, the 72 h E_bC50 was determined to be 0.18 (95% CL 0.16 – 0.21) mg/L.

The study author determined to NOEC for yield as 6.8 mg/L. Considering 21% of inhibition (yield) was observed at this level, the NOEC for yield is determined to be 4.0 mg/L.

Based on the E_rC50 value, the notified chemical is considered not harmful to *Desmodesmus subspicatus* up to the limit of its water solubility.

CONCLUSION

The notified chemical is considered not harmful to alga up to the limit of its water solubility.

TEST FACILITY

Harlan (2010j)

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