File No: STD/1629

March 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Perform LF Soft

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

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1629	Brenntag Australia Pty Ltd Cytec Australia Holdings Pty Ltd	Chemical in Perform LF Soft	Yes	≤ 50 tonnes per annum	A flame retardant treatment for textiles

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Acute toxicity, oral (Category 3)	H 301 - Toxic if swallowed
Skin Corrosion/Irritation (Category 1B)	H 314 - Causes severe skin burns and eye damage
Serious Eye Damage (Category 1)	H 318 - Causes serious eye damage
Sensitisation, Skin (Category 1)	H 317 - May cause an allergic skin reaction
Specific target organ toxicity, repeated exposure (Category 1)	H 372 - Causes damage to organs through prolonged or repeated oral exposure

The notifier has also classified the notified chemical as Reproductive Toxicity (Category 2) : H 361 - Suspected of damaging fertility or the unborn child.

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

Hazard classification	*Hazard statement*
Acute (Category 1)	H 400 - Very toxic to aquatic life
Chronic (Category 2)	H 411- Toxic to aquatic life with long lasting effects

Human health risk assessment
Provided that the recommended controls are being adhered to, 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 reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Acute toxicity, oral (Category 3): H 301 - Toxic if swallowed
  - Skin Corrosion/Irritation (Category 1B): H 314 - Causes severe skin burns and eye damage
  - Serious Eye Damage (Category 1): H 318 - Causes serious eye damage
  - Sensitisation, Skin (Category 1): H 317 - May cause an allergic skin reaction
  - Specific target organ toxicity, repeated exposure (Category 1): H 372 - Causes damage to organs through prolonged or repeated oral exposure

  The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present and the intended use/exposure scenario.

- Due to the corrosive properties of the notified chemical, the notifier should consider their obligations under the Australian Dangerous Goods Code.

Health Surveillance

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

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced and as diluted for use:
  - Enclosed, automated processes, where possible
  - Ventilation system, including local exhaust ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced and as diluted for use :
  - Avoid contact with the skin and eyes
  - Do not inhale mists
  - Avoid contact with contaminated clothing or equipment
  - Clean up spills promptly

- 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 introduced and as diluted for use:
  - Protective clothing, impervious gloves, safety boots
  - Face shield if splashes may occur
  - Goggles
  - Respiratory protection if inhalation exposure may occur

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

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

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

Public Health

- In order to minimise public exposure to formaldehyde from fabrics treated with the notified chemical, the notifier and textile processors should work in accordance with the following Safety Guidance criteria recommended by the Australian Competition & Consumer Commission (ACCC). The safety guidance sets the following indicative concentrations of formaldehyde in clothing and textiles and clothing finishes, as concentrations under which there are not current safety concerns:
  - 30 mg/kg (or 0.003% by weight) for infants' clothing and clothing specifically marked for individuals with sensitive skin.
  - 100 mg/kg (or 0.01% by weight) for garments which contact the skin
  - 300 mg/kg (or 0.03% by weight) for other garments or fabrics.

Disposal

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

Storage

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

Emergency procedures

- Spills or accidental release of the 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
  - Data on the migration potential of the notified chemical from fabrics becomes available;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a flame retardant treatment for textiles, or is likely to change significantly;
  - the amount of chemical being introduced has increased, or is likely to increase, significantly;
  - the chemical has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the chemical on 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 product containing the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Brenntag Australia Pty Ltd (ABN: 84 117 996 595)
262 Highett Road
HIGHETT VIC 3190

Cytec Australia Holdings Pty Ltd (ABN: 45 081 148 629)
Suite 1, Level 1, Norwest Quay, 21 Solent Circuit
Norwest Business Park
BAULKHAM HILLS NSW 2153

NOTIFICATION CATEGORY
Standard (Reduced fee notification): Chemical other than polymer (more than 1 tonne per year) – Similar to a chemical that has been previously assessed by NICNAS as STD/1015 (analogue 1).

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, degree of purity, impurities, additives/adjuvants, use details, import volume and identity of recipients.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: vapour pressure, hydrolysis as a function of pH, partition coefficient, absorption/desorption, dissociation constant, particle size, flammability, autoignition temperature, explosive properties, oxidising properties, acute dermal toxicity, skin irritation, eye irritation, skin sensitisation, repeated dose toxicity, *in vitro* genotoxicity and *in vivo* genotoxicity

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU REACH

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Perform LF Soft (product containing the notified chemical)

MOLECULAR WEIGHT
< 1,000 g/mol

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

3. COMPOSITION

DEGREE OF PURITY
The notified chemical is a UVCB

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: yellow wax solid

Property	Value	Data Source/Justification
Melting Point	No melting point was found from -110 to 100 °C. After evaporation of water, a decomposition of the test substance occurred from	Measured for dried extract of notified chemical

	about 150 to 200 °C and from 225 to 275 °C.	
Boiling Point	64 °C at 101.3 kPa	Measured for the notified chemical in an aqueous solution
Density	1,535 kg/m^3 at 21.6 °C	Measured for dried extract of notified chemical
Vapour Pressure	1.5×10^{-6} kPa at 25 °C	Measured for analogue 1
Water Solubility	≥ 899 g/L at 20 °C	The notified chemical is readily soluble in water.
Hydrolysis as a Function of pH	$t_{1/2}$ = 12.35 h (pH 4) $t_{1/2}$ = 21.06 h (pH 5)	Measured on Analogue 2. Not measureable at pH 7 and 9.
Partition Coefficient (n-octanol/water)	Log Pow -3.0	Estimated, based on individual solubility in water and n-octanol.
Adsorption/Desorption	not determined	The notified chemical is not expected to adsorb to organic carbon in soil due to its water solubility, but may adsorb by ionic interactions.
Dissociation Constant	not determined	The notified chemical has dissociable functionalities, and may dissociate under environmental conditions (pH 4 – 9).
Particle Size	not determined	Imported in an aqueous solution
Flash Point	> 130 °C at 101.325 kPa	Measured for the chemical in an aqueous solution
Autoignition Temperature	282 °C	Measured for analogue 1
Explosive Properties	not determined	Not expected to be explosive
Oxidising Properties	not determined	Not expected to have oxidising properties

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

Reactivity
The notified chemical is expected to react as part of its use.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is 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 chemical will be imported at < 70% concentration in an aqueous solution.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	1-50	1-50	1-50	1-50	1-50

PORT OF ENTRY
Melbourne and other major sea ports

IDENTITY OF RECIPIENTS
Brenntag Australia Pty Ltd
Cytec Australia Holdings Pty Ltd

TRANSPORTATION AND PACKAGING
Perform LF Soft containing the notified chemical at < 70% will be imported in 250 L drums or 1,000 L Intermediate Bulk Containers.

USE

The notified chemical will be used in a flame retardant treatment for textiles.

OPERATION DESCRIPTION
There will be no manufacture or reformulation in Australia.

At the textile treatment site, the imported product containing the notified chemical will be pumped from the import containers directly to an enclosed pad bath as a 1:1 dilution with water. Fabric will be treated with the chemical as it progresses between rollers and any excess liquid is squeezed out between subsequent rollers. The excess liquid will be returned to the bath. When the bath is exhausted, the chemical will be replenished from the drums. Any unused chemical will be collected and used in a subsequent treatment.

The fabric will progress to further processing stages which are predominantly automated but involve some manual steps. The processes involve heating in an enclosed oven to initiate polymerisation, followed by curing/crosslinking with a gas, oxidisation with an oxidising agent and finally neutralisation/washing. The washing process will start after the treated fabric leaves the cure unit, at which stage polymerisation and crosslinking of the notified chemical to the fabric is complete. The washing steps will involve oxidative wash off using an oxidising agent to give maximum wash fastness, and further chemical washing steps. The fabric will be then washed thoroughly to remove any traces of water-soluble, unreacted residues of the notified chemical. The fabric will be then dried.

Specialist textile finishers will used the treated textiles to produce articles such as protective workwear, bedding, soft furnishings or curtains prior to further packaging for distribution to specialised trade and retail outlets.

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	1-2	20
End use-process workers	8	260

EXPOSURE DETAILS
Transport and Storage
Transport and storage workers may come into contact with the notified chemical at < 70% concentration only in the event of accidental rupture of containers.

Process workers
At the textile treatment plant, process workers will open the import containers and will connect hose and pumping equipment between the container and the treatment bath and disconnect the hose when the drum is empty. There is potential for dermal and ocular exposure of workers to the notified chemical at a concentration of < 70% from leaks and spills or splashes during this transfer process. Workers will wear personal protective equipment (PPE) consisting of protective clothing, PVC apron, impervious gloves, safety boots and face shield to minimise the exposure. The transfer process will occur in a bunded area to capture any spills. The area is also supplied with both local and general ventilation to capture any vapours and aerosols. The notifier stated that local exhaust ventilation would be present in a minimum of two locations within the process: at both the stenter (where hot air is used to dry the textile) and the curing unit. The subsequent process will take place within an enclosed and automated process and the potential for exposure is minimal. The fabric will leave the processing line after it has been thoroughly washed. Once the fabric has been impregnated with the notified chemical and dried in a continuous oven it is rolled up. Process workers may be required to transfer these rolls of treated fabric to another part of the same plant, where the fabric will be unrolled and passed through a cure unit. There will be minimal potential for exposure to trained professionals, wearing PPE. Thus, minimal exposure to the notified monomer is expected to occur from handling of processed fabric.

The notifier stated that manual handling of rolls of fabric would generally not occur because the process is automated. However, if the rolls of treated fabric do not enter the oven unit and beyond at the end of the shift, a worker may be requested to wrap the roll in polythene. This task is performed while wearing appropriate PPE.

To mitigate any exposure to the treated fabric, there will be an initial leader fabric and one leader fabric at the end of the roll which does not make contact with the notified chemical; this ensures that the worker has no exposure via the external surface area of the roll during the wrapping process.

By the later stages of the process the notified chemical is expected to have polymerised and thus not available for exposure. The washing steps would remove any residual unreacted chemical from the textiles. After these stages there is not expected to be worker exposure to the notified chemical. The treated fabric that leaves the textile processing plant is not expected to contain residues of the notified chemical.

Users of treated textiles
Workers may wear protective clothing, made of textiles that are treated with the notified chemical. No data on migration of the notified chemical from textiles is available. However the chemical is expected to be reacted and not available for exposure. The notifier stated that no measurable levels of the notified chemical would be expected to be present in extracts of treated fabrics, and it is also expected to be resistant to leaching during laundering. Therefore workers wearing protective clothing are not expected to be exposed to the notified chemical.

6.1.2. Public Exposure

The notified chemical will not be sold to the public. The only likely exposure of the public would occur in the event of an accident during transportation of the imported product containing the notified chemical. The notified chemical will be polymerised and incorporated into the fabric fibres where it is expected to be bound. Any residual of the notified chemical is washed out of the fabric, prior to finalisation of the fabric treatment process.

No data on migration of the notified chemical from textiles is available. It is expected that once reacted onto the textiles, the notified chemical will not be available for exposure, and will be also resistant to leaching during washing. Therefore, exposure to the notified chemical is not expected to occur from contact with treated textiles such as clothing, bedding or curtains.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical and two analogues are summarised in the following table. For full details of the studies not previously assessed in STD/1015, refer to Appendix B.

Endpoint	*Test substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity*	Notified chemical	LD50 = 50-300 mg/kg bw; toxic
Rat, acute oral toxicity	Analogue 2	LD50 > 50 mg/kg bw; toxic
Rat, acute dermal toxicity	Analogue 2	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	Analogue 2	corrosive
Rabbit, eye irritation	Analogue 2	severely irritating
Guinea pig, skin sensitisation – adjuvant test	Analogue 2	evidence of sensitisation
Rat, repeat dose oral toxicity – 90* days	Analogue 1	No Observed Adverse Effect Level (NOAEL) = 2.5 mg/kg bw/day
Rat, repeat dose oral toxicity – 28 days	Analogue 2	NOAEL = 5 mg/kg bw/day
Mutagenicity – bacterial reverse* mutation	Notified chemical	non mutagenic
Mutagenicity – bacterial reverse mutation	Analogue 2	mutagenic
Genotoxicity – *in vitro* mammalian cell gene mutation test	Analogue 2	genotoxic
Genotoxicity – *in vivo* unscheduled DNA synthesis test with mammalian liver cells*	Analogue 1	non genotoxic
Genotoxicity – *in vivo* mammalian erythrocyte micronucleus test	Analogue 2	non genotoxic
Rabbit, prenatal developmental toxicity	Analogue 1	no clear maternal NOAEL could be found

foetal NOEL = 40 mg/kg bw/day

* Not previously evaluated in STD/1015

Consideration on analogues
As the analogues differ from the notified chemical only in containing different anions, with analogue 2 also having a slightly different carbon chain length, these analogues were considered adequate for hazard assessment of the notified chemical for human health endpoints. As UVCB's, some variation of the level of different species may also occur.

Toxicokinetics, metabolism and distribution
Given the relative low molecular weight of the notified chemical (< 1,000 Da), there is potential for absorption across biological membranes. However, dermal absorption may be limited by the hydrophilic nature of the notified chemical, as demonstrated by its high water solubility and low partition coefficient (log Pow < -3).

Acute toxicity
The notified chemical was toxic *via* the oral route in rats. Analogue 2 was toxic *via* the oral route (LD50 > 50 mg/kg bw: no mortality was observed at this dose). Analogue 2 was found to be of low toxicity *via* the dermal route (LD50 > 2,000 mg/kg bw) in rats. No acute inhalation toxicity study was available.

Irritation
Based on the results of studies on rabbits using analogue 2, the notified chemical was considered to be corrosive to the skin and severely irritating to eyes.

Sensitisation
Based on the results of a guinea pig study on analogue 2, the notified chemical was considered to be a skin sensitiser.

Repeated dose toxicity
A NOAEL was established by the study authors for analogue 1 as 2.5 mg/kg bw/day in a 90-day oral repeat dose study in rats, based on no laboratory or histopathology changes observed at this dose level.

In this study, adverse microscopic findings were noted in the liver of male and female animals at 15 mg/kg bw/day. These included minimal to moderate vacuolar degeneration seen in the hepatocytes of periportal areas in males and females, linked with minimal to slight hepatocellular hypertrophy and minimal single cell necrosis/apoptosis in these areas, some focal necrosis associated with inflammation in the periportal areas in two males, and minimal to slight brown pigment in Kupffer cells in 2 females. Some effects were linked with higher ALAT activity in males. These changes had partially reversed at the end of the recovery period. Non adverse hypertrophy of cortical cells was shown in the adrenal glands of a few females, linked with minimally increased adrenal weights. These changes disappeared at the end of the recovery period, suggesting total reversibility.

In the same study, adverse microscopic findings were noted in the liver of males at 5 mg/kg bw/day. The effects were minimal to moderate vacuolar degeneration seen in the hepatocytes of periportal areas, linked with minimal to slight hepatocellular hypertrophy and minimal single cell necrosis/apoptosis in these areas. These findings were considered by the study authors to be linked with minimally higher ALAT activity.

In a 28-day oral repeat dose study in rats, analogue 2 exhibited toxic effects on the liver (increased liver weights in females at 40 mg/kg bw/day, speckled livers in two males and accentuated lobular pattern/paleness in two females at 40 mg/kg bw/day). In the microscopic findings, moderate to minimal periportal hepatocellular vacuolar degeneration in all animals at 40 mg/kg bw/day and minimal periportal hepatocellular vacuolar degeneration in two males at 15 mg/kg bw/day were seen. A NOAEL was established as 5 mg/kg bw/day based on organ weight changes and pathological effects at 15 and 40 mg/kg bw/day dose levels.

Adverse systemic effects were seen in rats at 10, 40 and 120 mg/kg bw/day in a developmental study. It was not clear whether the only effect at 10 mg/kg bw/day (pale livers) was test substance related. Effects on the liver at 40 mg/kg bw/day were pale livers and minimal periportal hepatocyte vacuolisation. At the 120 mg/kg bw/day dosage, effects included pale liver, increased liver weight, periportal hepatocyte vacuolation, with centrilobular vacuolation and hepatocyte necrosis and periportal hepatocyte hypertrophy also observed in premature decedents.

Mutagenicity/Genotoxicity
Analogue 2 was mutagenic in bacteria in strain TA1537 without metabolic activation and in mouse lymphoma cells *in vitro.* The notified chemical was not mutagenic in a bacterial reverse mutation assay. However, in this study it was noted that strain TA1537 showed equivocal results without metabolic activation.

Analogue 1 was not mutagenic in an *in vivo* unscheduled DNA synthesis (UDS) test with mammalian liver cells. However, it is considered that negative results in the UDS test alone are insufficient to eliminate a positive gene mutation (EFSA 2017).

Analogue 2 was non-genotoxic in a mouse *in vivo* erythrocyte micronucleus test. There were adverse clinical signs in the mice, an indication of systemic exposure to the chemical.

Prenatal developmental toxicity
In a prenatal development toxicity study (only a summary was provided), New Zealand White rabbits were treated with analogue 1 at dose levels of 0, 10, 40 and 120 mg/kg bw/day. No clear maternal NOAEL could be established. The foetal NOEL was established as 40 mg/kg bw/day by the study authors, based on foetal findings at 120 mg/kg bw/day. It is not clear whether or not the adverse foetal effects were based on maternal toxicity.

Impurity
The notified chemical contains formaldehyde as an impurity at < 0.1%.

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

Hazard classification	***Hazard statement***
Acute toxicity, oral (Category 3)	H 301 - Toxic if swallowed
Skin Corrosion/Irritation (Category 1B)	H 314 - Causes severe skin burns and eye damage
Serious Eye Damage (Category 1)	H 318 - Causes serious eye damage
Sensitisation, Skin (Category 1)	H 317 - May cause an allergic skin reaction
Specific target organ toxicity, repeated exposure (Category 1)	H 372 - Causes damage to organs through prolonged or repeated oral exposure

The notifier has also classified the notified chemical as Reproductive Toxicity (Category 2) : H 361 - Suspected of damaging fertility or the unborn child. The study provided to NICNAS indicated maternal toxicity from 10 mg/kg bw/day and developmental effects at 120 mg/kg bw/day. It was not clear whether the developmental effects were due to maternal toxicity.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Dermal and ocular exposure to the notified chemical at a concentration of < 70% may occur during the transfer of the notified chemical from import containers or manual handling of fabrics treated with the notified chemical. Once the notified chemical is reacted onto the textiles, it will not be available for exposure, and will be also resistant to leaching during washing.

Toxicological studies on the notified chemical indicate that it is toxic if swallowed, causes severe skin burns and eye damage, may cause an allergic skin reaction and causes damage to organs through prolonged or repeated oral exposure. It may be suspected of damaging fertility or the unborn child. Therefore, use of the notified chemical is only considered to be reasonable when sufficient engineering controls, safe work practices and personal protective equipment (PPE) are used to reduce the potential for exposure. Dermal and ocular exposure is expected to be limited with the use of PPE (protective clothing, impervious gloves, safety boots, face shield, goggles (and respiratory protection if inhalation may occur).

Therefore, provided that the recommended controls are being adhered to, under the occupational settings described, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

Possible release of formaldehyde from treated fabrics is considered in section 6.3.2.

6.3.2. Public Health

Members of the public may experience repeated exposure to fabrics treated with the notified chemical. However, it is expected that once the notified chemical is reacted onto the textiles, it will not be available for exposure, and will be also be resistant to leaching during washing.

The fabrics treated with the notified chemical may release low levels of formaldehyde during use, particularly from new, unwashed fabrics. The levels of release are not directly related to the concentrations of formaldehyde as an impurity in the notified chemical. The most likely health effects arising from release of formaldehyde from fabrics are irritation of the eyes and nose, and allergic reactions on skin in contact with the clothes (NICNAS, 2013).

Safety Guidance from the Australian Competition and Consumer Commission (ACCC) lists indicative concentrations of formaldehyde, "under which there are not current safety concerns", for various types of textiles (ACCC, 2014). The risk of adverse effects from formaldehyde in textiles treated with the notified chemical would be minimised if these concentration recommendations are met:
- 0.003% for infants' clothing and clothing specifically marked for individuals with sensitive skin,
- 0.01% for garments which contact the skin; and
- 0.03% for other garments or fabrics.

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

Potential release of the notified chemical from textile treatment sites will be spillage during transfer from the import container to the textile treatment bath, estimated by the notifier as ~1%. However, it is expected that this spillage will be absorbed onto inert materials and collected for disposal to landfill. Waste generated from equipment cleaning will be recycled back into the treatment bath. Residues in empty containers will be rinsed out with water and recycled into the treatment bath. Washings from the treatment process are likely to be reused or recycled. Any wastes that are not able to be reused or recycled are expected to be disposed of by a licensed waste contractor. There is not expected to be any releases to the sewer at fabric treatment sites.

RELEASE OF CHEMICAL FROM USE

The notified chemical is a monomer/precursor that will be consumed and transformed within the textile treatment process. Finished garments having traces of unreacted residues will be washed post-treatment, but limited release is expected to occur from routine treated textile cleaning. No further release of the notified chemical from garments is expected once polymerisation has occurred.

RELEASE OF CHEMICAL FROM DISPOSAL

The notified chemical will be completely transformed and consumed within the fabric treatment process. The precursor monomer will be in a polymeric state and strongly bound to the fabric. Therefore, its fate is tied to the treated fabric, which will eventually disposed of to landfill where it is expected to slowly degrade.

7.1.2. Environmental Fate

Environmental fate test studies were performed on either the notified chemical or analogues of the notified chemical. The major differences of the analogues from the notified chemical are the use of different counter ions and potential variation of the relative percentages of the UVCB constituents. Therefore, the analogues were considered acceptable for the purposes of the fate assessment.

Analogue 1 can be classified as very slightly volatile, and hence the notified monomer is not likely to be present in air at significant levels. The water solubility of the notified chemical is readily soluble, and has a low affinity to octanol (solubility in octanol < 902 mg/L and estimated log Pow < -3). The monomer is not expected to be mobile in soil, based on its ionic interactions with soil. Given the hydrophilic nature of the monomer it is not

expected to bioaccumulate. The monomer is not readily biodegradable in the environment, and hence is expected to be persistent.

No significant release of the notified chemical to the environment is expected given that the majority of the monomer will be transformed and consumed, during manufacture of the textiles. Any monomer released from spills is expected to slowly degrade in landfill via biotic and abiotic processes, eventually forming water and oxides of carbon, nitrogen, phosphorous and sulphur.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) for the notified chemical has not been calculated since no significant release to the environment is expected based on its 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, not previously evaluated in STD/1015, can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (acute)	Analogue 2: 96 h LC50 = 3.8 mg/L*	The analogue is toxic to fish
Fish Toxicity (chronic)	Analogue 2: 28 d NOEC = 2.5 mg/L*	The analogue is toxic to fish with long lasting effects
Daphnia Toxicity (acute)	Notified chemical: 48 h EC50 = 1.1 mg/L Analogue 2: 48 h EC50 = 6.5 mg/L*	The notified chemical and the accepted analogue are toxic to invertebrates.
Daphnia Toxicity (chronic)	Analogue 2: 21 d NOEC = 0.64 mg/L*	The analogue is toxic to aquatic invertebrates with long lasting effects
Algal Toxicity	Notified chemical: 72 h ErC50 = 1.2 mg/L Analogue 2◊: 72 h ErC50 = 0.15, 1.7 & 1.2 mg/L* Analogue 2#: 72 h ErC50 = 18, 8.8 & 32 mg/L*	The notified chemical and accepted analogue (non-oxidised form) are toxic to algae. The analogue in the oxidised form is very toxic to algae.
Inhibition of Bacterial Respiration	Analogue 2: 3 h IC50 = 10 - 100 mg/L*	The analogue is moderately toxic to sewage micro-organisms.

◊ Values from Tests 1, 5 & 6, respectively; test substance in non-oxidised form
Values from Tests 2, 3 & 4, respectively; test substance in oxidised form
* Studies have been evaluated in STD/1015

The aquatic toxicity tests indicate that the notified chemical and analogue 2 are acutely toxic to aquatic organisms, with the lowest acute toxicity value for the notified chemical of 0.84 mg/L (72-hour ErC50). Under the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS*) (United Nations, 2009), the notified chemical (non-oxidised form) is formally classified as "Acute Category 1: Very toxic to aquatic life". Based its expected persistence (not rapidly biodegradable), and the chronic fish toxicity data for analogue 2, the notified chemical is considered toxic to aquatic life with long lasting effects under the GHS chronic classification for substances hazardous to the aquatic environment. Oxidisation of the notified chemical, which is expected to occur during the textile treatment process, may reduce the toxicity of this monomer.

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) was calculated for the notified chemical using the 72-h ErC50 of 0.84 mg/L and, as three acute and chronic studies were available, an assessment factor of 10. The PNEC for the notified chemical is 84 µg/L.

7.3. Environmental Risk Assessment

The risk quotient (Q = PEC/PNEC) for the notified chemical has not been calculated as based on its reported use pattern, significant quantities are not expected to be released to the aquatic environment.. Therefore, the release of the notified chemical to the aquatic environment is not expected to reach eco-toxicologically significant quantities. Accordingly, on the basis of the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point No melting point was found from -110 to 100 °C. After evaporation of water, a decomposition of the test substance occurred from about 150 to 200 °C and from 225 to 275 °C.

Method EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature
Remarks Differential scanning calorimetry method was used for the dried extract of notified chemical.
Test Facility Defitraces (2016a)

Boiling Point 64.0 ± 0.5 °C at 101.3 kPa (aqueous solution of notified chemical)

Method EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks Differential scanning calorimetry method was used for the aqueous solution.
Test Facility Defitraces (2016b)

Density 1,535 ± 5 kg/m^3 at 21.6 °C (dried extract of notified chemical)

Method EC Council Regulation No 440/2008 A.3 Relative Density
Remarks Gas comparison pycnometer method was used.
Test Facility Defitraces (2016a)

Vapour Pressure 1.5 × 10^{-6} kPa at 25 °C (analogue 1 as a dried extract of gel)

Method OECD TG 104 Vapour Pressure
EC Council Regulation No 440/2008 A.4 Vapour Pressure
Remarks The vapour pressure balance method was used, at temperatures between 70 and 80 °C. This was extrapolated to 25 °C. One of the five measurements was considered an outlier and not included in the analysis.
Test Facility Harlan Laboratories Limited (2011)

Water Solubility ≥ 899 g/L at 20 °C (dried extract of notified chemical)

Method OECD TG 105 Water Solubility
EC Council Regulation No 440/2008 A.6 Water Solubility
Remarks Flask Method. Active ingredients were quantified by titration.
Test Facility Defitraces (2016c)

Surface Tension 56.4 mN/m at 22 ± 0.5 °C (analogue 1 as a dried extract of gel)

Method ISO 304, which differs slightly from OECD TG 115 Surface Tension of Aqueous Solutions
EC Council Regulation No 440/2008 A.5 Surface Tension
Remarks The surface tension result was not corrected using the Harkins-Jordan correction table (as the correction is not applicable to the apparatus used). The test substance is considered to be a surface active (< 60 mN/m), which is consistent with notified chemical's structure.
Test Facility Harlan Laboratories Limited (2011)

Flash Point > 130 °C at 101.325 kPa (aqueous solution of notified chemical)

Method EC Council Regulation No 440/2008 A.9 Flash Point
Remarks Closed cup was used.
Test Facility Defitraces (2016b)

Autoignition Temperature 282 ± 5 °C (analogue 1)

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Remarks Testing used the commercial product grade of the test substance, a pale straw coloured clear liquid.
Test Facility Harlan Laboratories Limited (2011)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method (2001) EC Council Regulation No 440/2008 B.1 tris Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain	Rat/Crl:WI
Vehicle	Water
Remarks - Method	Dosage was adjusted to account for the purity of 67.7%.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	3 F	300	2/3
2	3 F	50	0/3
3	3 F	50	0/3

LD50	50-300 mg/kg bw
Signs of Toxicity	The animals in the 300 mg/kg bw group showed slightly to severely decreased activity, prone position, hunched back and piloerection during day 0-1. After 2 of 3 animals died on day 1, there were no effects on the single surviving animal from day 2. At 50 mg/kg bw animals showed no effects.
Effects in Organs	No external or internal macroscopic changes were noted in the surviving animals at the scheduled necropsy on day 14. At the necropsy of animals found dead in the 300 mg/kg bw group, there was reddish or yellowish liquid material on the fur of the perinasal area. Thickening and/or dark red, diffuse discoloration in the glandular mucosa of the stomach, yellowish mucoid material in the stomach or duodenum/jejunum were considered to be test substance related. Dark red diffuse discolouration in the non-collapsed lungs and/or reddish, foamy material in the trachea were also noted.
Remarks - Results	The body weight and body weight gain were normal.
CONCLUSION	The notified chemical is toxic via the oral route.
TEST FACILITY	CiToxLAB Hungary Ltd (2016a)

B.2. Repeat dose toxicity

TEST SUBSTANCE	Analogue 1
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents (1998)
Species/Strain	Rats/Wistar Han
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 91 or 92 days Dose regimen: 7 days per week Post-exposure observation period: 4 weeks
Vehicle	Drinking water containing 0.003% (w/v) citric acid, treated by reverse osmosis using ELIX 5 (Millipore SA).
Remarks - Method	The dose-levels were selected based on the results of a previous study

performed on the same species, in which the test substance was administered daily by gavage at dose levels of 5, 10, 20 or 50 mg/kg bw/day for 4 weeks.

Minor protocol deviations were considered not to have compromised the validity or integrity of the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
control	10 per sex	0	0/20
low dose	10 per sex	2.5	1/20
mid dose	10 per sex	5	0/20
high dose	10 per sex	15	0/20
control recovery	10 per sex	0	0/20
high dose recovery	10 per sex	15	0/20

Mortality and Time to Death

One female in the 2.5 mg/kg bw/day group was sacrificed on day 76 for humane reasons due to signs of poor clinical condition (thin appearance, hunched posture, piloerection, hypoactivity and abdominal breathing) from day 75, but with a minimal body weight loss between days 64 and 71. The moribundity of this animal was considered by study authors not to be related to the test substance administration as it occurred only in the low dose group. The cause of moribundity could not be established.

Clinical Observations

No test substance related clinical signs or behavioural or neurological abnormalities were noted during the treatment or recovery period. Motor activity (60-minute recording period), the mean body weight changes, food consumption, ophthalmology findings and the oestrous cycle were reported as not affected by the treatment.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No effects on the haematology parameters were observed at the end of the treatment period. There were some dose-related reduction in sperm motility (from 2.5 mg/kg bw/day group) and numbers of spermatozoa in epididymides and testes (statistically significant not reported). These were not accompanied by histopathological changes and therefore not considered as treatment related by the study authors.

For blood chemistry, at the end of the treatment period, mean alanine aminotransferase (ALAT) activity was statistically significantly higher in males at 5 or 15 mg/kg bw/day compared to controls (1.4 to 2-fold respectively). These changes, were linked with high aspartate aminotransferase (ASAT) activity in some animals. Females were not affected.

There were microscopic findings observed in the liver from 5 mg/kg bw/day onwards, such as periportal vacuolar degeneration, hepatocellular hypertrophy and single cell necrosis/apoptosis.

At the end of the recovery period, higher mean ALAT and ASAT activity persisted (statistically significant) in males, however the differences from controls were minimal, suggesting partial reversibility. This correlated with the minimal changes (vacuolar periportal degeneration) observed in the liver of these animals.

Effects in Organs

At the end of the treatment period, increased absolute and relative-to-body adrenal gland weights (not statistically significant) were noted in females treated at 15 mg/kg bw/day. The microscopic changes (hypertrophy of cortical cells) shown in a few females treated at 15 mg/kg bw/day, were considered to be related to possible stress and the test substance treatment.

The other organ weight changes, including statistically significantly increased liver weights, were considered by the study authors not to be related to the test substance as they were of low frequency, were not dose-related and/or had no gross or microscopic findings. However, there were microscopic lesions in the liver.

There were no organ weight changes related to test substance administration at the end of the recovery period.

Macroscopic post-mortem examination showed no test substance related effects in animals at unscheduled

death, terminal sacrifice at the end of treatment period or recovery period.

At the end of the treatment period, test substance-related microscopic findings were seen in the liver of males treated at 5 mg/kg bw/day and males and females treated at 15 mg/kg bw/day, and in the adrenal glands of females treated at 15 mg/kg bw/day.

Minimal to moderate vacuolar degeneration was seen in the hepatocytes of periportal areas in males treated at 5 mg/kg bw/day and in males and females treated at 15 mg/kg bw/day. This was linked with minimal to slight hepatocellular hypertrophy and minimal single cell necrosis/apoptosis in these areas. In two males at 15 mg/kg bw/day, focal necrosis associated with inflammation was seen in the periportal areas. Although not related toincreased liver weights, these lesions were considered to be related to the test substance administration. Minimal to slight brown pigment in Kupffer cells was seen in 2/10 females at 15 mg/kg bw/day. Based on the linked degenerative/necrotic changes and the clinical pathology correlates, such as increased ALAT activity in males at 5 or 15 mg/kg bw/day, these findings were considered to be adverse at 5 and 15 mg/kg bw/day.

At the end of the recovery period, minimal vacuolar periportal degeneration was seen in the livers of 10/10 males and 1/10 females previously treated at 15 mg/kg bw/day. No hepatocellular hypertrophy or single necrosis/apoptosis was shown in these animals, suggesting partial reversibility of the findings noted at the end of the treatment period, and correlating with the minimal increased ALAT and ASAT activity in the males previously treated at 15 mg/kg bw/day when compared to controls sacrificed at the end of the recovery period. For females previously treated at 15 mg/kg bw/day, no hypertrophy of adrenal gland cortical cells was observed, suggesting complete reversibility.

Remarks – Results

At 15 mg/kg bw/day, adverse microscopic findings were noted in the liver of animals, linking notably with higher ALAT activity in males. These changes had partially reversed at the end of the recovery period. Non adverse hypertrophy of cortical cells was shown in the adrenal glands of a few females, linked with minimally increased adrenal weights. These changes were not seen at the end of the recovery period, suggesting total reversibility.

At 5 mg/kg bw/day, adverse microscopic findings were noted in the liver of males and study authors considered these findings were linked with minimally higher ALAT activity.

At 2.5 mg/kg bw/day, no laboratory or histopathological changes were observed.

CONCLUSION

The No Observed Effect Level (NOEL) was established by the study authors for the test substance as 2.5 mg/kg bw/day, based on no laboratory or histopathology changes at this dose level.

TEST FACILITY	CiToxLAB France (2014)

B.3. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test (1997) EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria Plate incorporation procedure (an initial mutation test-test 1)/Pre incubation procedure (a confirmatory mutation test: test 2 and a complementary mutation test: test 3)
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100, *Escherichia coli*: WP2uvrA
Metabolic Activation System	A post mitochondrial supernatant (S9 fraction) prepared from the livers of phenobarbital/β-naphthoflavone-induced rats
Concentration Range in Main Test	a) Test 1 with and without metabolic activation: 0, 1.581, 5, 15.81, 50, 158.1, 500, 1,581 µg/plate b) Test 2 with and without metabolic activation: 0, 0.5, 1.581, 5, 15.81, 50, 158.1, 500, 1,581 µg/plate c) Test 3 without metabolic activation: 0, 0.05, 0.1581, 0.5, 1.581, 5,

	15.81, 50, 158.1 µg/plate for *Escherichia coli*: WP2uvrA only
Vehicle	Dimethylsulfoxide (DMSO)
Remarks - Method	Dosages for the main studies were determined on the basis of range-finding tests. Doses were adjusted to account for the purity of 67.7%. Because of excessive cytotoxicity with WP2uvrA without metabolic activation in Test 2, this study was repeated as Test 3, using a different range of concentrations. A minor deviation to the study protocol did not affect the validity of the study.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	≥ 1,000			
Test 1		≥ 500	> 1,581	negative
Test 2		≥ 158.1	> 1,581	negative
Test 3		≥ 50	> 158.1	negative
Present	≥ 1,000			
Test 1		≥ 500	> 1,581	negative
Test 2		≥ 158.1	> 1,581	negative

Remarks - Results	No biologically relevant or dose-related increases in revertants were noted with any of tester strains in either the presence or absence of S9 activation. Equivocal results with TA1537 without metabolic activation were noted. No precipitate was observed, however, various levels (absent/reduced/slightly reduced) in background lawn development were noted in all three tests. The concurrent positive and negative controls produced satisfactory responses, thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	CiToxLAB Hungary Ltd (2016b)

B.4. Genotoxicity – *in vivo* Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells

TEST SUBSTANCE	Analogue 1
METHOD	OECD TG 486 Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *in vivo* (1997) EC Directive 2000/32/EC B.39 Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *in vivo*
Species/Strain	Rats/Wistar Hanlbm: WIST (SPF)
Route of Administration	Oral – gavage
Vehicle	Deionised water
Remarks - Method	Doses were adjusted to take account of the 65.8% dry content concentration of the test substance. Animals were sourced from two different suppliers. Minor deviations did not affect the validity of the study. The high dose of test substance applied in the main experiment was estimated in pre-experiments to be close to the maximum tolerated dose. The main experiment was performed using male rats only, since the males could tolerate slightly higher dosages than females without inducing mortality.

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Sacrifice Time (hours)*
I (vehicle control)	4 M	0	2 h
	4 M	0	16 h
II (low dose)	4 M	175	2 h
	4 M	175	16 h
IV (high dose)	4 M	350	2 h
	4 M	350	16 h
V (positive control, DMH)	4 M	40	2 h
2-AAF	4 M	100	16 h

DMH=N,N'-dimethylhydrazinedihydrochloride 2-AAF=2-acetylaminofluorene

RESULTS

Doses Producing Toxicity	In the main study, low and high dose animals showed ruffled fur and reduction of spontaneous activity.
Genotoxic Effects	The viability of the hepatocytes was not substantially affected due to the *in vivo* treatment at any of the treatment period or dose groups. The inter-individual variations for the numbers and viabilities of the isolated hepatocytes were in the range of the historical laboratory control.
Remarks - Results	No dose level revealed UDS induction in the hepatocytes of the treated animals when compared to the concurrent vehicle controls. Both the nuclear grains and the resulting net nuclear gains were not significantly enhanced due to the *in vivo* treatment for 2 h or 16 h. Therefore, the net nuclear gain values obtained after treatment were considered negative. No substantial shift to higher values was observed in the percentage of cells in repair. *In vivo* treatment with positive controls showed significant increases in the number of nuclear and net nuclear gain counts. The change in the urine colour of the treated animals, which was reported to occur in the main study, could be attributed to the systemic distribution of the test substance, showing its bioavailability.
CONCLUSION	The test substance was reported to be not clastogenic under the conditions of this in vivo unscheduled DNA synthesis (UDS) test in mammalian liver cells.
TEST FACILITY	RCC (2005)

B.5. Prenatal developmental toxicity (only summary was provided)

TEST SUBSTANCE	Analogue 1
METHOD	OECD TG 414 Prenatal Developmental Toxicity Study (2001)
Species/Strain	Rabbit/New Zealand White (Hsdlf)
Route of Administration	Oral – gavage
Exposure Information	Exposure days: up to 22 days (days 6 to 28 gestation, inclusive, besides two high dose animas for which the exposure was stopped early on gestation day 16 or 17, due to severity of clinical signs) Post-exposure observation period: none
Vehicle	Water
Remarks - Method	Dose selection was determined in range-finding study. Active ingredient accounted for 62.3%.

RESULTS

Group	*Number of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
1	24 F	0	0
2	24 F	10	0
3	24 F	40	0
4	24 F	120	6/24 were killed prematurely

Mortality and Time to Death

Six animals in the high dose group were killed prematurely on gestation days 15, 18, 20, 21 (2), 22 due to severe clinical signs and anorexia.

Effects on Dams

Significant maternal toxicity was seen at the high dose of 120 mg/kg bw/day, including premature mortality of 6/24 animals, and marked reduction in body weight gain and food consumption. One animal gave birth prematurely at Day 29. Necropsy results in the surviving animals mostly involved liver effects, which were increased in weight. Pale colour and prominent lobulation of the liver were seen at necropsy. Mild or moderate periportal hepatocyte vacuolation and moderate or marked centrilobular hepatocyte vacuolisation were seen, the latter in premature decedents. Mild to marked coagulative necrosis and mild to moderate periportal hepatocyte hypertrophy occurred in premature decedents. Blood chemistry changes such as significant rises in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDIL) and reductions in haemoglobin and red blood cell counts were all considered to be consistent with the liver findings at this level.

At 40 mg/kg bw/day, pale livers and minimal periportal hepatocyte vacuolisation were observed in some animals, however liver weight was not increased. There was an increase in the changes to faecal output compared to the controls. At the low dose of 10 mg/kg bw/day there were no dose related histopathological findings or increased liver weight, however two animals had pale livers.

Effects on Foetus

At the high dose of 120 mg/kg bw/day there was an increase in dead implants compared to the controls, both early embryonic deaths and late deaths. At this dose there was an increase in foetuses with a major foetal abnormality, the majority of which were in the eyes and/or the hindlimbs/digits. An increase in minor visceral defects, small foetuses and those with incisors not erupted was seen. Skeletal defects included a reduced state of ossification (which may be attributed to the small size of the foetuses), and increased incidence of bilateral caudal displacement of the pelvic girdle.

At the lower doses of 10 and 40 mg/kg bw/day, pregnancy performance and foetal weights were comparable to controls. The type and distribution of major foetal abnormalities, visceral or skeletal abnormalities were not considered to be treatment related.

CONCLUSION

No clear maternal No Observed Adverse Effect Level (NOAEL) could be established.

The foetal No Observed Adverse Effect Level (NOEL) was established as 40 mg/kg bw/day in this study, based on foetal findings at 120 mg/kg bw/day.

TEST FACILITY Charles River Tranent (2010)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test and Reproduction Test – Static system
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	254 mg $CaCO_3$/L
Analytical Monitoring	High performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS).
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance comprises 67.7% active content and had 35.2% primary constituent. Potassium dichromate was used as the reference toxicant. HPLC-MS/MS analysis of the test media was carried out on the primary constituent of the notified chemical, and its degradation product.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal (test item)	*Actual (geometric mean of measured primary constituent)*		*24 h*	*48 h*
Control	0	20	0	0
4.27	0.23	20	0	5
9.39	1.24	20	3	12
20.7	4.12	20	2	10
45.5	13.3	20	1	20
100	21.8	20	20	20

EC50	1.1 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. No immobilisation was observed in the control. Dissolved oxygen concentrations in the control and test vessels at the end of the test were ≥ 8.7 mg/L. The concentrations range of the analysed substance was 14.7 and 88.1%, but was reported to be stable over the test period. The effect concentrations were determined using the measured primary constituent concentrations as these were < 80% of the nominal. There was no reported precipitant, films, or cloudy appearance of the test media once the test substance was added. A clear dose response relationship was observed for the *Daphnia* with immobilisation occurring at higher test concentrations. The effect concentrations were determined by Probit analysis with linear maximum likelihood regression. The 95% confidence intervals were not determined. The reference test with potassium dichromate performed in a separate study resulted in a 24-h EC50 of 1.68 mg/L, and is within an acceptable range.
CONCLUSION	The notified chemical is toxic to aquatic invertebrates.
TEST FACILITY	Solvay (2017)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Raphidocelis subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 0 – 4.0 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	HPLC-MS/MS
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance comprises 67.7% active content and had 35.2% primary constituent. Potassium dichromate was used as the reference item. HPLC-MS/MS analysis of the test media was carried out on the primary constituent of the notified chemical, and its degradation product.

RESULTS

Yield *EyC50* *mg/L at 72 h*	*Growth* *ErC50* *mg/L at 72h*
0.72 (95% confidence interval (CI): 0.63 – 0.99)	1.2 (95% CI: 1.1 – 1.4)

Remarks - Results

All validity criteria for the test were satisfied. The mean biomass increase in the controls within the 72-h exposure period was a factor of 344. The mean coefficient of variation for section-by-section specific growth rates in the controls was 19.5%. The coefficient of variation of average specific growth rates during the exposure period was 1%.

The measured concentrations of the primary constituent of the notified chemical, and its degradation product were < limit of quantification or low. Therefore, measured concentration was not within 20% of nominal concentrations. There were no issues with the analysis, however the analysed compound was tested for stability and was found not to be stable in the algal test media. As a result EC values are based on nominal loading rates of the test substance and nominal (%) active ingredient (determined by iodine titration). The EC values were determined by Probit analysis using linear maximum likelihood regression.

There was not apparent interaction between the test medium and the test substance, and no reported films, visible particles or cloudy appearance of the test media.

The ErC50 of *Raphidocelis subcapitata* was determined to be 1.245 mg/L based on nominal concentration. The ErC50 for the active ingredient was calculated by multiplying the ErC50 for test substance by 0.677, resulting in 0.843 mg/L.

The reference test with potassium dichromate performed in a separate study resulted in an ErC50 of 0.91 (95% CI: 0.89 – 0.94 mg/L), and is outside the recommended range of the TG.

CONCLUSION	The notified chemical is toxic to algae.
TEST FACILITY	Solvay (2018)

BIBLIOGRAPHY

ACCC (2014) Safety guidance on concentrations of particular chemicals in certain consumer goods, https://www.productsafety.gov.au/system/files/Safety%20guidance%20on%20concentrations%20of%20particular%20chemicals%20in%20certain%20consumer%20goods_0.pdf Australian Competition and Consumer Commission, published on 21 October 2014 and accessed on 14 February 2018.

Charles River Tranent (2010) Analogue 1: Development Toxicity Study in Rabbits (Report No. 30263, August 2010). Charles River Tranent, Edinburgh, EH33 2NE, UK (Unpublished report submitted by the notifier).

CiToxLAB France (2014) Analogue 1: 13-Week Toxicity Study by the Oral Route (Gavage) in Rats Followed by a 4-week Treatment-free Period (Laboratory Study Number: 39993 TCR, April 2014). CiToxLAB France, BP 563-27005 Evreux - France (Unpublished report submitted by the notifier).

CiToxLAB Hungary Ltd (2016a) Notified Chemical: Acute Oral Toxicity Study in Rats (Study Code: 16/156-001P, August 2016). CiToxLAB Hungary Ltd, H-8200 Veszprem, Szabadsagpuszta, Hungary (Unpublished report submitted by the notifier).

CiToxLAB Hungary Ltd (2016b) Notified Chemical: The Testing with Bacterial Reverse Mutation Assay (Study Code: 16/156-007M, September 2016). CiToxLAB Hungary Ltd, H-8200 Veszprem, Szabadsagpuszta, Hungary (Unpublished report submitted by the notifier).

Defitraces (2016a) Notified Chemical: Physico-chemical Tests (Dried Extract) (Study Plan No. 16-918028-001, August 2016). Defitraces, 69126 Brindas, France (Unpublished report submitted by the notifier).

Defitraces (2016b) Notified Chemical: Physico-chemical Tests (Aqueous Solution) (Study Plan No. 16-918028-004, August 2016). Defitraces, 69126 Brindas, France (Unpublished report submitted by the notifier).

Defitraces (2016c) Solubility in Water and Solubility in *n*-Octanol of Notified Chemical (Dried Extract) (Study No. 16-918028-002, November, 2016). Brindas, France (Unpublished report submitted by the notifier).

EFSA (2017) Clarification of some aspects related to genotoxicity assessment Scientific Opinion, EFSA Journal 16 November 2017, European Commission.

Harlan Laboratories Limited (2011) Analogue 1: Determination of Physico-chemical Properties (Project No. 41101318, June 2011). Harlan Laboratories Ltd, Shardlow Business Park, Shardlow, Derbyshire DE72 2GD, UK (Unpublished report submitted by the notifier).

NICNAS (2013) Formaldehyde in clothing and textiles, https://www.nicnas.gov.au/chemical-information/factsheets/chemical-name/formaldehyde-in-clothing-and-textiles, updated on 1 May 2013 and accessed on 15 February 2018.

NTC (2017) Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), Edition 7.5, National Transport Commission, Commonwealth of Australia

RCC (2005) Analogue 1: in vivo Unscheduled DNA Synthesis in Rat Hepatocytes (Reference number: 855844, April 2005). RCC, Cytotest Cell Research GmbH (RCC-CCR), R-64380, Rossdorf, Germany (Unpublished report submitted by the notifier).

Solvay (2017) Notified Chemical: A Study on the Acute Toxicity to *Daphnia Magna* (Study No. 16EI2DA, November, 2017). Oldbury, United Kingdom, Solvay Solutions UK LTD (Unpublished report submitted by the notifier).

Solvay (2018) Notified Chemical: A Study on the Toxicity to Freshwater Green Algae (*Raphidocelis subcapitata*) (Study No. 16EI2AO, January, 2018). Oldbury, United Kingdom, Solvay Solutions UK LTD (Unpublished report submitted by the notifier).

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, https://www.safeworkaustralia.gov.au/doc/model-code-practice-managing-risks-hazardous-chemicals-workplace

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >