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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Scotchkote 2000 Series Part B

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:

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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 SUBSTANCE	INTRODUCTION VOLUME	USE
STD/1407	3M AUSTRALIA PTY LTD	Chemical in Scotchkote 2000 Part B	Yes	≤100 tonnes/year	Component of water pipe linings

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]. The classification and labelling details are:

R21/22 Harmful in contact with skin and if swallowed
R35 Causes severe burns
R43 May cause sensitisation by skin contact

and

The classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2009) is presented below. The environmental classification is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	*Hazard statement*
Acute toxicity	Category 3 Category 4	Toxic if swallowed Harmful in contact with skin
Corrosion	Category 1B	Causes severe burns and eye damage
Skin sensitisation	Category 1A	May cause an allergic skin reaction
Environment	Acute Category 1 Chronic Category 1	Very toxic to aquatic life Very toxic to aquatic life with long lasting effects

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, based on leaching tests being carried out at concentrations of actual use.

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

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following health hazard classification for the notified chemical:

- Xn; R21/22 Harmful in contact with skin and if swallowed
- C; R35 Causes severe burns
- Xi; R43 May cause sensitisation by skin contact

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc.≥25%: R21/22, R35, R43
  - 25%>Conc.≥10%: R35, R43
  - 10%>Conc.≥5%: R34, R43
  - 5%>Conc.≥1%: R36/38, R43

- NICNAS will refer the notified chemical to the National Health and Medical Research Council (NHMRC), for their consideration.

Material Safety Data Sheet

- The MSDS provided by the notifier should be amended as follows:
  - To include the full chemical name as per the *NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets 2nd Edition [NOHSC: 2011 (2003)]* for Type I ingredients.

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 for mixing and coating

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  - Avoid contact with eyes and skin

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - Eye protection
  - Appropriately fitted respiratory protection if vapours or aerosols are generated
  - Coveralls
  - Gloves
  - Apron
  - Boots

  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.

- As the notified polymer has skin sensitisation potential, 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.

- 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.

Public Health

- The following measures should be taken to minimise public exposure to the notified chemical:
  - Thorough flushing protocols after coating to ensure removal of residues from treated pipes

Disposal

- The notified chemical should be disposed of according to Federal, State and Local Government requirements.

- There should be no intentional release of uncured notified chemical to water.

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/polymer 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
  - the notifier, importer or manufacturer becomes aware that the notified chemical is found in drinking water at levels of greater than 50 µg/L (50 ppb).

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of an activator for polymeric coatings, 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 product containing 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)
3M Australia Pty Ltd (ABN 90 000 100 096)
Building A, 1 Rivett Road
North Ryde NSW 2113

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, degree of purity, polymer constituents, residual monomers, impurities, additives/adjuvants, use details and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Acute inhalational toxicity, melting point, vapour pressure, hydrolysis as a function of pH, flammability limits, autoignition temperature and explosive properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA, China, Canada, Korea, EU and Japan

2. IDENTITY OF CHEMICAL

ANALYTICAL DATA
Reference FTIR, LCMS, GCMS, GC-FID, 13C-NMR, 1H-NMR and UV-VIS Spectra were provided.

3. COMPOSITION

DEGREE OF PURITY >98%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Clear colourless liquid, amine like odour

Property	Value	Data Source/Justification
Melting Point	-21 to 4°C	Measured, liquid at room temperature
Boiling Point	Decomposed from 200°C	Measured
Density	901.8 kg/m^3 at 20°C 898.3 kg/m^3 at 25°C	Measured
Vapour Pressure	5.89×10^{-7} kPa at 20°C 1.13×10^{-6} kPa at 25°C	Measured
Water Solubility	0.131 g/L at 23°C	Measured
Hydrolysis as a Function of pH	$t_{1/2}$ > 1 year at 25°C (pH 4, 7 and 9)	Measured
Partition Coefficient (n-octanol/water)	log Pow = 1.31at 23°C	Measured. Not expected to partition strongly to octanol from the water column.
Adsorption/Desorption	log K_{OC} > 5.63	Measured. The results indicate the notified chemical is expected to have potential to adsorb strongly to soil or sludge sediment.
Dissociation Constant	Not determined	Expected to be ionized in the environmental pH range of 4-9 due to the presence of potential cationic

		functional groups.
Particle Size	Not determined	Liquid at room temperature
Flash Point	176°C	Measured
Flammability	Not determined	Not expected to be flammable based on the flash point
Autoignition Temperature	310°C	Measured
Explosive Properties	Not determined	Not expected to be explosive based on structure
Oxidising Properties	Not determined	Not expected based on chemical composition

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

Reactivity
The notified chemical is stable under normal conditions of use and hazardous reactions should not occur. However, reactions with oxidising materials are expected and contact with oxidising materials 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 in a formulated activator product at <35% concentration.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	30-100	30-100	30-100	30-100	30-100

PORT OF ENTRY
Sydney

IDENTITY OF RECIPIENTS
3M Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in heat sealed foil bags within 12 L steel drums, or in 208 L steel drums or larger packages as required. The drums or packages will be transported by road from the port to a warehouse. The product will then be transported by road or rail to the end-users.

USE
The notified chemical is present in a formulation (<35%) that will be used as an activator component in a two part coating. The coating will be used to line the inside of water pipes used to carry potable water.

OPERATION DESCRIPTION
No manufacturing or reformulation processes will occur in Australia.

At end user sites, the foil bags containing the activator component (containing the notified chemical at < 35%) will be cut open and the contents will be poured manually into the activator storage tank on the portable lining rig. The activator and base components remain in separate heated tanks and are then passed through individual supply lines contained in umbilical hosing. The two components are then mixed in a static mixer at the end of the umbilical hosing. The mixed material (containing < 20% notified chemical) will then pass through a spinning spray head. The spray head will be fed through the interior of the pipe to be coated, and the coating will be applied as the spray head moves through the pipe. The volume and flow rate, mix ratio, hose line

pressure and lining thickness will be continuously monitored by detection equipment. Upon completion, the spray will be turned off and the spray head then removed from the pipe. The coating will then be allowed to cure for an hour or more followed by a flushing step for up to 30 minutes, which is expected to remove any residual unreacted notified chemical.

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)*
Waterside workers	4 hours/day	70 days/year
Storage and transport workers	6 hours/day	240 days/year
Lining applicators	8 hours/day	240 days/year

EXPOSURE DETAILS

Occupational exposure to dock workers or during storage and transport is unlikely because the notified chemical will be packaged inside steel drums. Exposure will only occur in the unlikely event of an accidental spill during transport or storage.

Dermal and ocular exposure of workers to the notified chemical may occur during pouring of the activator component into the storage tank, connecting and disconnecting of pump pipes and during the cleaning of the rig and its components. Given the high boiling point (355°C) and estimated low vapour pressure (<0.1 kPa at 20°C), inhalation exposure to the notified chemical is not expected unless aerosols are formed. Such exposures should be minimised by the expected use of personal protective equipment (PPE) such as gloves, protective clothing, eye protection and full face respirator.

Exposure is not expected to occur during the application process as these operations occur in an enclosed system.

6.1.2. Public Exposure

The notified chemical will be used in pipes that will carry drinking water for human consumption, therefore the public may be exposed to residues of the notified chemical through consumption of drinking water. The notifier has provided two studies investigating the potential for the notified chemical to leach into drinking water. The notified chemical was not detected in the leaching studies at the limit of detection of 50 ppb (equivalent to 50 µg/L). The concentration of the notified polymer in the cured product tested in the leaching studies was not discussed. In addition, it appears that the notified polymer was only analysed at pH 8.

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 oral toxicity	LD50 = 227 mg/kg bw; toxic
Rat, acute dermal toxicity	2000 > LD50 > 1600 mg/kg bw; harmful
Rabbit, skin irritation	corrosive
Rabbit, eye irritation	corrosive (based on skin corrosion)
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days	NOAEL = 3 mg/kg bw/day
Rat, repeat dose oral toxicity – 28 days (males)	NOAEL = 1 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian cell gene mutation test	non genotoxic
Genotoxicity – in vitro chromosome aberration test	clastogenic
Genotoxicity – in vivo micronucleus test	non-clastogenic

Toxicokinetics, metabolism and distribution.
No toxicokinetic data on the notified chemical were submitted. Absorption across the skin and gastrointestinal (GI) tract is expected based on the low molecular weight (<500 Da), partition coefficient (Log Pow = 1.13) and water solubility (0.131 g/L). This is supported by evidence of systemic toxicity observed in the acute oral and dermal toxicity studies, and the 28-day repeat dose oral toxicity study in rats.

Acute toxicity.
The notified chemical is harmful by the oral (lowest LD50=227 mg/kg bw) and dermal (2000 > LD50 > 1600 mg/kg bw) route in rats. There is no data available on the acute inhalation toxicity of the notified chemical. However, based on the harmful effects (mortalities) observed in the acute oral and dermal toxicity studies, the notified chemical is likely to be harmful by inhalation.

Irritation and Sensitisation.
The notified chemical is corrosive to the skin of rabbit. An eye irritation study was not conducted. However, the notified chemical is likely to be corrosive to the eyes based on the skin corrosivity. The notified chemical is likely to be a skin sensitiser based on a positive result in a LLNA test in mice.

Repeated Dose Toxicity.
In a 28-day repeat dose gavage study, rats were administered the notified chemical at 0, 3, 10 or 30 mg/kg bw/day. The NOAEL was determined to be 3 mg/kg bw/day based on the presence of vacuolative changes in various organs and transitional epithelial hyperplasia in the urinary bladder in males in the higher dose groups tested.

In a combined repeated dose toxicity study and reproductive/developmental screening study, rats were administered the notified chemical at 0, 1, 3, or 10 mg/kg bw/day by gavage. Males were administered the notified chemical for 29 days and females for 42-45 days. Males and females were mated after at least 14 days exposure. Additional groups of treated males were sacrificed following 14 and 28 days recovery. The main toxicological effects were skeletal muscle myofiber degeneration at 10 mg/kg bw/day males and females and urothelial hyperplasia in 3 and 10 mg/kg bw/day males and in 10 mg/kg bw/day females. Less severe effects included alveolar macrophage foci in the lungs at 3 mg/kg bw/day and above males. And in 10 mg/kg bw/day females. The NOAEL was established at 1 mg/kg bw/day for males, based on alveolar macrophage foci and urothelial hyperplasia at 3 mg/kg bw/day and above.

Mutagenicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study or in an *in vitro* mammalian gene mutation assay. There was a clear positive clastogenic response in an *in vitro* chromosome aberration test in Chinese hamster lung cells. However, no chromosomal damage was observed with the notified chemical in an *in vivo* bone marrow micronucleus test in mice. The clinical signs of systemic toxicity in the micronucleus assay indicate that the test material was systemically absorbed, which in turn indicates that bone marrow exposure was likely. The *in vitro* chromosome test suggests the notified chemical has an interaction with nuclear material at the chromosome level, however, the lack of an clastogenic effect in the *in vivo* test suggests that the notified chemical is not clastogenic *in vivo*.

Health hazard classification
Based on the acute oral and dermal toxicity studies, the skin irritation study, the local lymph node assay, and the 28-day repeat dose toxicity study, the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:

R21/22	Harmful in contact with skin and if swallowed
R35	Causes severe burns
R43	May cause sensitisation by skin contact

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified chemical is present in foil bags at <35%, therefore the toxicological effects of concern for workers based on the cut-off concentrations set by the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) are as follows: acute dermal toxicity, skin and eye corrosivity and skin sensitisation. Systemic toxicity is also of concern based on the low NOAEL of 1 mg/kg bw/day.

Dermal and ocular exposure of workers to the notified chemical are most likely when workers pour the liquid formulation containing the notified chemical (<35%), when connecting and disconnecting of pump pipes and during the cleaning of the rig and its components. Inhalation of the notified chemical is unlikely because aerosols will not be generated during application. However, inhalation of small amounts of volatilised chemical cannot be ruled out.

The toxicological properties of the notified chemical (i.e., acute dermal toxicity, skin and eye corrosivity, skin sensitisation and systemic toxicity) may result in serious or irreversible damage to the skin, in addition to systemic toxicity from either acute or repeat exposures. Pouring operations represent the highest potential for worker exposure. All workers are expected to be trained in the use of the chemical and are also expected to wear PPE such as coveralls, gloves, goggles, boots, apron and respirator when handling the notified chemical which should minimise exposure.

Overall, provided all workers use the PPE as described above and safe work practices are maintained to reduce exposure, the risk to workers is not considered to be unreasonable.

6.3.2. Public Health

The notifier has stated that the notified chemical will not be available for exposure when cured. The curing period will be a minimum of one hour. The notifier has stated that the notified chemical will not be present in the final cured lining, because an excess reactant will be used to fully consume the notified chemical in the reaction. The pipes will then be flushed with water for a minimum of 30 minutes, which is expected to remove any residual unreacted notified chemical.

The main route of public exposure will be through residual amounts of the notified chemical from drinking water. Based on the detection limit of leaching studies with the cured coating the maximum expected concentration present in drinking water will be 50 µg/L (i.e. 50 ppb). The National Health and Medical Research Council's (NHMRC) *Australian Drinking Water Guidelines 6* (2011) provide information on deriving guideline values for chemicals, using the following formula:

$$Guideline\ \ value = \frac{animal\ dose \times human\ weight \times proportion\ \ of\ \text{intake}\ from\ water}{volume\ of\ \ water\ consumed \times safety\ \ factor}$$

The guideline value is the concentration that based on present knowledge does not result in any significant risk to the health of the consumers over a lifetime of consumption and is consistent with water of good quality.

Using the following parameters/assumptions:

Animal dose:	1 mg/kg bw/day (based on NOAEL derived in 28-day oral study in rats)
Human weight:	70 kg (NHMRC, 2011)
Proportion of intake from water:	1 (100% default, exposure from other sources not expected)
Volume of water consumed:	2 L/day (NHMRC, 2011)
Safety factor:	500-fold (additional 5-fold safety factor to account for subchronic to chronic extrapolation)

$$\text{Guideline value} = \frac{1\ \text{mg/kg bw/day} \times 70\ \text{kg bw} \times 1}{2\ \text{L/day} \times 500}$$
$$= 70\ \mu\text{g/L}$$

As there were no residues of the notified chemical detected in the leaching study (detection limit < 50 ppb or 50 µg/L) from the cured coatings and based on the estimated Guideline Value of 70 µg/L, the notified chemical when incorporated in pipes at concentrations tested in the leaching studies is not expected to cause a concern for public health. The leaching studies were conducted using NSF/ANSI Standard 61.

In addition, the notifier has provided a study showing that cured coatings containing the notified chemical meet the water quality standard for products for use in contact with cold drinking water (AS/NZS 4020 (2005))

Therefore, provided the samples used in the leaching studies reflect the limit of concentration of the notified chemical that will be used to coat water pipes, the risk to the general public is not considered unreasonable.

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 for direct end use in Australia. No further reformulation processes will occur in Australia. The most likely release of the notified chemical may be from a transport accident. No significant release (< 1%) is expected from the process of transportation and storage. Any spills are expected to be contained and collected for disposal according to Federal, State and Local Government requirements.

RELEASE OF CHEMICAL FROM USE

The majority of the notified chemical will be incorporated into an inert coating matrix used to coat water pipes.

It is estimated that less than 1% of the total import volume may be released through splashes and drips during the charging of application rig reservoirs, which is expected to be collected with adsorbent material or rags for disposal according to Federal, State and Local Government requirements. The notified chemical is expected to fully react with other components in the coating formulation upon mixing the activator and base in the application rig. Therefore, release of the notified chemical to the environment is not expected after this point.

Residual notified chemical within the import containers is estimated be about 1% of the total annual volume and it is expected the containers will be crushed for disposal according to Federal, State and Local Government requirements.

Approximately 2% of the total introduction volume is estimated to be lost from the cleaning of equipment, and the organic solvent rinsate is expected to be captured and sent to an authorised waste trader for possible recovery of the solvent and disposal of the collected notified chemical according to Federal, State and Local Government requirements.

RELEASE OF CHEMICAL FROM DISPOSAL

Waste containing the notified chemical resulting from equipment cleaning is expected to be sent to a waste trader, where the notified chemical may to be collected for disposal to according to Federal, State and Local Government requirements after solvent recovery. The empty containers resulting from all the processes are also expected to be disposed according to Federal, State and Local Government requirements. Waste from spill and drips containing polymerised notified chemical is expected be collected with inert adsorbent material for disposal to a sanitary landfill.

7.1.2. Environmental Fate

The provided ready biodegradability study indicates that the notified chemical is not readily biodegradable. The bioconcentration factors (6 and 11) determined via the bioconcentration study suggest that the notified chemical is not expected to be bioaccumulative in aquatic organisms. For the details of the environmental fate studies please refer to Appendix C.

Most of the notified chemical is expected to be incorporated onto an inert coating matrix that is applied to water pipes. In this form, the cured notified chemical is not expected to be mobile or bioavailable. At the end of the water pipes' lives, the notified chemical is expected to be disposed of together with the water pipes to landfill. A minor amount of the notified chemical (<5%) is expected to be disposed of according to Federal, State and Local Government requirements with the empty containers or after collection of spills or equipment washing rinsate. In landfill, the notified chemical is not expected to leach given it is expected to be fully reacted and trapped in the inert matrix upon application. Uncured notified chemical in landfill is not expected to be mobile due to its high soil adsorption coefficient (log K_{OC} > 5.63). It is expected to be slowly degraded via biotic and abiotic pathways to form water, oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The calculation of the PEC is not considered necessary since no significant release of the notified chemical to the aquatic environment is expected.

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	96 h EC50 > 570 mg/L	Not harmful
Daphnia Toxicity	48 h EC50 = 27 mg/L	Harmful
Algal Toxicity	72 h E_rC50 = 0.25 mg/L	Very toxic
Inhibition of Bacterial Respiration	3 h IC50 = 160 mg/L	Not expected to significantly inhibit respiration of sludge microorganisms at concentrations less than 160 mg/L

Three algal ecotoxicity studies conducted on the notified chemical were submitted. Studies 1 and 2 only reported yield endpoints while study 3 reported both yield and growth endpoints. The E_rC50 (growth) endpoint is preferred over the E_yC50 (yield) endpoint for classifying the algal toxicity of a chemical (refer to Paragraph 47, OECD TG 201) and therefore only the endpoint from study 3 was considered in the assessment conclusion for algal toxicity. It is also noted that algal study 2 was modified to investigate the effect of organic carbon on algal toxicity and therefore the endpoints derived from the study are not directly comparable with the endpoints from the other studies.

With respect to the two submitted microbial inhibition studies, study 1 was conducted with the 1984 OECD 209 guidelines while study 2 was conducted with the contemporary 2010 version of the same guidelines. Both studies were deemed valid and reliable, according to their respective guideline. They both demonstrated a slight inhibitory effect on microbial respiration at the nominal concentrations tested. The endpoint from study 2 was considered more representative of the inhibition as the test substance was stirred for an extended time to maximise the concentration exposed to sludge, while this was not carried out in study 1. Moreover, although study 1 was valid under the guidelines which it was conducted, the dissolved oxygen levels in the blank samples were depleted over 1 hour.

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2011) the notified chemical is not harmful to fish. However, it is considered harmful to daphnids and very toxic to fresh water green alga. Based on the effect on alga, it is formally classified as ‘Acute Category 1: Very toxic to aquatic life’. On the basis of its toxicity to algae and since it is not rapidly degradable, the notified chemical is formally classified as ‘Chronic Category 1: Very toxic to aquatic life with long lasting effects’.

7.2.1. Predicted No-Effect Concentration

It is not considered necessary to calculate the PNEC since no significant release of the notified chemical to the aquatic environment is expected from the proposed use pattern.

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has not been calculated since no significant release of the notified chemical to the aquatic environment is expected from the assessed use pattern.

The majority of the imported notified chemical will be fully reacted and trapped in the inert coating matrix after application to water mains pipes and in this form it is not expected to leach or be bioavailable. Therefore, on the basis of limited aquatic exposure and 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 -21 to 4ºC

Method OECD TG 102 Melting Point/Melting Range.
Remarks Melting not observed as a single peak.
Test Facility NOTOX B.V. (2011a)

Boiling Point No boiling point observed

Method OECD TG 103 Boiling Point.
Remarks Reaction and/or decomposition observed at 200°C
Test Facility NOTOX B.V. (2011a)

Density 901.8 kg/m^3 at 20ºC
898.3 kg/m^3 at 25ºC

Method OECD TG 109 Density of Liquids and Solids. Oscillating density meter method.
Remarks Density referenced against the density of water at 4°C.
Test Facility 3M Materials Resource Division (2010)

Vapour Pressure 5.89×10^{-7} kPa at 20°C
1.13×10^{-6} kPa at 25°C

Method OECD TG 104 Vapour Pressure.
Test Facility NOTOX B.V. (2011a)

Water Solubility 0.131 g/L at approximately 23ºC

Method ETS-8-172.3 “Shake Flask Method” (similar to OECD TG 105 Water Solubility)
Remarks Flask Method.

Three shake flask vessels containing the test substance and pure water (830 mg/L) were prepared in triplicate. Samples were placed in an incubator (30ºC) /shaker (140 RPM) and were removed after 24, 48, and 72 hours. Samples were then placed at room temperature storage for at least 24 hours to equilibrate prior to analysis by LCMS. Each study sample were analysed in triplicate. The overall average solubility was determined to be 0.131 g/L at approximately 23ºC.
Test Facility 3M Environmental Laboratory (2011a)

Hydrolysis as a Function of pH $t_{1/2}$ > 1 year at 25°C (pH 4, 7 and 9)

Method OECD TG 111 Hydrolysis as a Function of pH

pH	*T (°C)*	*$t_{½}$ (years)*
4	25	> 1
7	25	> 1
9	25	> 1

Remarks Test substance was spiked into three buffer solutions (pH 4, 7 and 9) at a target concentration of 1 mg/L using spiking solution in acetonitrile. The solutions were purged with nitrogen gas for 5 minutes. Aliquots of sample solutions were taken from flasks immediately after preparation and after 5 days, and the pH was measured. In each aliquot the concentration of test substance was determined by UHPLC with LC/MS/MS detection. Less than 10% hydrolysis was observed after 5 days at 50°C at pH 4, 7 and 9 and therefore the estimated half-life at 25°C is > 1 year. The test result should be treated with caution as the concentration of the test substance after 5 days was found to be significantly greater than the initial concentration at each pH tested. However, the result is consistent with expectation that the notified chemical is not likely to hydrolyse as there is hydrolysable functionality is present in the chemical.

Test Facility NOTOX B.V. (2011b)

Partition Coefficient (n-octanol/water) log Pow = 1.31 at 23.3ºC

Method OECD TG 107 Partition Coefficient (n-octanol/water): Shake Flask Method
Remarks Flask Method.

Duplicate samples and method blanks were prepared using a predetermined ratio of n-octanol to a pH 6.8 (±0.3) Milli Q water (1:1, 2:1, and 1:2). Each sample and method blank were prepared using n-octanol or water that had been presaturated with the other solvent by shaking in an orbital shaker for 24 hours prior to spiking. All samples were spiked with 126 µL of a concentrated solution (4960 µg/mL) of the test substance, prepared in n-octanol, into a total sample volume of 9 mL resulting in a final sample dose of 70 ppm approximately. Samples were then thoroughly shaken and then centrifuged at 3000 rpm for 20 minutes. The aqueous and n-octanol phases were carefully removed from the centrifuge tube and diluted in 50/50 acetonitrile/water into the appropriate analytical range. The aqueous phase samples were diluted 1:500 with 50/50 acetonitrile/water, similar to the calibration curve samples and the octanol phase samples were diluted 1:1000 with 50/50 acetonitrile/water. Each sample and method blank was analysed in replicates of three using HPLC/MS.

The overall average log Pow of the notified chemical was determined to be 1.31 at 23.3 (±0.4ºC).
Test Facility 3M Environmental Laboratory (2011b)

Adsorption/Desorption (study 1) log K_{OC} = 4.45
– screening test

Method OECD 121 Estimation of the Adsorption Coefficient (K_{OC}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography
Remarks The log K_{OC} of the notified chemical was determined to be 4.45 by comparing its retention times to multiple reference compounds of known log K_{OC} eluted through a C18 reverse phase HPLC column with UV detection. The results should be treated with caution as there was difficulty in detecting the notified chemical. However, the result is consistent with the expected sorption of the notified chemical to soils.
Test Facility Stillmeadow (2005a)

Adsorption/Desorption (study 2) log K_{OC} > 5.63 at pH 7
– screening test

Method OECD 121 Estimation of the Adsorption Coefficient (K_{OC}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography
Remarks The log K_{OC} of the notified chemical was determined to by comparing its retention time to a reference compound (4,4'–DDT) with a known log K_{OC} (5.63) eluted through a cyanopropyl HPLC column with MS detector. It was not possible to analyse the test substance in its non-ionised form as the HPLC column would deteriorate at the high pH required Hence, testing was carried out only at neutral pH. No peaks were observed for the test substance and it was confirmed the test substance was sensitive to MS detection (injection performed omitting the analytical column). It was concluded that the retention time of the test substance was significantly higher than the reference substance and therefore the K_{OC} of the test substance was greater than that of the reference substance.
Test Facility NOTOX B.V. (2011b)

Flash Point 176ºC at 1010.5 hPa

Method EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks Closed cup method.
Test Facility NOTOX B.V. (2011a)

Autoignition Temperature 310ºC at 1007.1-1023.2 hPa

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).
Test Facility	NOTOX B.V. (2011a)

Water quality test

Method	AS/NZS 4020 (2005) Products for Use in Contact with Drinking Water.
Remarks	Water was exposed to the final cured coating and tests were conducted using cold water. **Taste of Water**: Chlorinated and non-chlorinated water were tested. No odour or flavour detected. **Appearance of water**: Colour and turbidity. No significant change in colour or turbidity. **Growth of aquatic microorganisms**: The test material was tested for microorganism growth by determining the mean oxygen dissolved difference. No significant increase in the test sample and the test material (i.e., cured sealant) showed no change in colour or appearance, indicating no microbial growth is present. **Cytotoxic activity of water**: Tested for cytotoxicity in mammalian cells at a concentration of 5×10^5 cells. The test samples were considered non-cytotoxic. **Mutagenic activity of water**: Ames test using *Salmonella typhimurium* strains TA100, TA102 (base-pair substitution mutation) and TA98 (frameshift mutation), with and without metabolic activation. There were no increases in revertant colonies compared to concurrent negative controls. **Extraction of metals**: ICPMS used to characterise antimony, arsenic, barium, cadmium, chromium, copper, lead, mercury, molybdenum, nickel, selenium and silver. All levels of metals were similar to the blank controls and were all below the health limit values outlined in the Australian Drinking Water Guidelines (2004).
Conclusion	The study report stated that "this product has satisfied the criteria set out in AS/NZ 4020: 2005, Section 6 'Test Requirements' and is thus suitable for use with cold water.
Test Facility	WRc-NSF (2011)

Leaching/Migration Study

Method	Materials Extraction NSF/ANSI Standard 61-2010, Section 5 Detailed methods were not provided. From the information provided, it appears that the cured pipe lining containing the notified chemical (concentration not specified) was tested for migration at pH, 8 after 24, 48, 120, 456 and 792 hours exposure.
Results	The method of detection was reported to be according to the EPA 625 method "Methods for organic chemical analysis of municipal and industrial wastewater that specifies GC/MS. The notified chemical was not detected in any of the exposure samples at any pH or time. A detection limit was not reported. The test material was stated to "Pass" the NSF/ANSI Standard.
Test Facility	Water Quality Association (2011)

Leaching/Migration Study

Method	NSF/ANSI Standard 61. Detailed methods were not provided. The activator (containing the notified chemical) and the base were mixed together (1:1) and applied to a substrate (not specified) and cured for one hour at 5°C to a thickness of 484 mm. The cured coating was then exposed to water at 23°C at pH 5, pH 8 or pH 10. The pH 5 and pH 10 samples was stated as being exposed for 16 hours in the field and 16 hours in the laboratory. Additionally, the pH 8 was exposed to 16 hours in the field and 24 hours in the laboratory.

	Analysis of the notified chemical in the pH 8 samples was by LC/MS with a reported detection limit of 50 µg/L (i.e. 50 ppb).
Results	The notified chemical or structurally related chemicals were not detected in any of the exposure samples at any pH or time.
Test Facility	NSF (2011)

Method Validation

Method	An internal standard using a compound similar to the target compound was used for quantification of the notified chemical, by comparing the ratio of mass spectrum response of the target compound with the response of the internal standard. An external standard calibration was conducted using nominal concentrations of between 1 ng/mL to 100 ng/mL. Stability testing using chlorinated water was conducted.
Results	3M Environmental laboratory method ETS-8-246.0 has been validated for the determination of the notified chemical in chlorinated migration water with a linear range from 1 ng/mL (1 ppb) to 100 ng/mL (100 ppb). Stability testing indicates that the notified chemical is not stable in migration water after 24 hours exposure, thus chlorinated leachates must be analysed quickly, preferably within 12 hours.
Test Facility	3M Environmental Laboratory (2012)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

Study 1

TEST SUBSTANCE: Notified chemical

METHOD: 40 CFR 798.1175 Acute Oral Toxicity

Species/Strain: Rat/ Crl:CD®BR

Vehicle: None for the limit and range-finding study, corn oil for the main study.

Remarks - Method: In an acute oral toxicity study, rats (5/sex) were administered a 5000 mg/kg bw limit dose of test material by oral gavage. Following the death of all 5000 mg/kg bw rats, a range-finding study was conducted (1/sex/dose) at 500, 1000, 2000 or 3000 mg/kg bw. At all doses, all animals died within 2 days of treatment. The limit and range-finding study groups were not subject to pathological examination.

For the main study, rats (5/sex/dose) were administered test material by gavage at 250, 500 or 600 mg/kg bw for males, and at 250, 400 and 500 mg/kg bw for females. Clinical observations were made several times on the day of dosing and daily for 14 days. Body weights were measured just prior to dosing on day 0 and on days 7 and 14. All animals in the main study were subject to gross necropsy.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*	*Time of death*
1	5M/5F	5000	10/10	Day of dosing
Preliminary study				
2	1M/1F	500	2/2	Within 2 days of dosing
3	1M/1F	1000	2/2	Within 2 days of dosing
4	1M/1F	2000	2/2	Within 2 days of dosing
5	1M/1F	3000	2/2	Within 2 days of dosing
Main study				
6	5M/5F	250	0/10	n/a
7	5F	400	0/5	n/a
8	5M/5F	500	6/10 (2M/4F)	5-7 days (males) 0-7 days (females)
9	5M	600	5/5	4-12 days

LD50: 460 mg/kg bw (females), 515 mg/kg bw (males), 482 mg/kg bw (combined)

Signs of Toxicity: In the main study, no mortalities were observed at doses of 250 and 400 mg/kg bw. All animals treated at the highest dose of 600 mg/kg bw died and 6 out of 10 (2 males and 4 females) animals dosed at 500 mg/kg bw died.

Clinical signs of toxicity increased with dose in the main study with the 250 mg/kg bw groups mostly unaffected by treatment. The 400 mg/kg bw females exhibited soft stool, yellow/dark stained urogenital area, red stained face, and alopecia. Clinical signs became more common in the 500 and 600 mg/kg bw groups, including red-stained face, staggered gait, hypoactivity, absent righting reflex, absent grasping reflex, dark staining around eyes, hunched posture, few faeces, squinting, miosis, prostration and emaciation.

Effects in Organs: There were no observed effects in the 250 mg/kg bw treated animals at necropsy. The main finding at necropsy of the mortalities was colouration and content changes in the gastrointestinal (GI) tract. The stomach consisted of material of variable colour that was consistent with either the

test material or autolysis. The glandular mucosa from some of these animals was diffusely red or had multiple brown or red foci. Findings in the surviving animals were considered unrelated to treatment. Ocular and nasal discharge was also observed.

Remarks - Results

CONCLUSION The notified chemical is harmful via the oral route.

TEST FACILITY Hazleton (1993a)

Study 2

TEST SUBSTANCE Notified chemical

METHOD US EPA OPPTS No. 870.1100
Species/Strain Rat/Sprague-Dawley
Vehicle None

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5M	100	0/5
II	5M/5F	250	3/10 (3M)
III	5M/5F	500	9/10 (5M/4F)
IV	5M/5F	5050	10/10 (5M/5F)

LD50 227 mg/kg bw (M), 427 mg/kg bw (F), 306 mg/kg bw/day (combined)
Signs of Toxicity Clinical signs in surviving animals include activity decrease, ataxia, body tremors, crusted/stained fur, diarrhoea, decreased/no defecation, emaciation, hunched posture, loss of limb coordination, piloerection, polyuria and withdrawn testes, that were reversible in all but one male by day 10. Cyanosis, ocular discharge, recumbency, ptosis, salivation, swollen penis and walking on tiptoe were observed in animals that died.
Effects in Organs Observations in the mortalities include withdrawn testes; discoloured lungs, liver, spleen and contents of the gastrointestinal (GI) tract; empty intestines; and gas in the GI tract.

CONCLUSION The notified chemical is harmful via the oral route.

TEST FACILITY Stillmeadow (2005b)

B.2. Acute toxicity – dermal

Study 1

TEST SUBSTANCE Notified chemical

METHOD OECD TG 402 Acute Dermal Toxicity – Limit Test.
US EPA OPPTS No. 870.1200
Species/Strain Rat/Sprague-Dawley
Vehicle None
Type of dressing Semi-occlusive.
Remarks - Method The limit dose is required to be at least 2000 mg/kg bw. In this study the limit dose was only 1000 mg/kg bw. No justification was given as to why the correct limit dose was not used.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5M/5F	1000	0/10

LD50	>1000 mg/kg bw
Signs of Toxicity - Local	Slight to severe irritation was observed that persisted to the end of the study period. Observations included erythema, atonia, coriaceousness, desquamation, eschar and alopecia.
Signs of Toxicity - Systemic	Diarrhea was observed in both sexes on days 12 to 13.
Effects in Organs	No observable findings.
Remarks - Results	Given that the test material was not administered at the correct limit dose, the notified chemical will therefore be classified as a harmful by the dermal route based on an LD50>1000 mg/kg bw.

CONCLUSION: Given that the notified chemical was not administered at the correct limit dose, the toxicity of the notified chemical via the dermal route cannot conclusively be determined.

TEST FACILITY: Stillmeadow (2005c)

Study 2

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 402 Acute Dermal Toxicity – Limit Test.
US EPA OPPTS No. 870.1200

Species/Strain	Rat/Sprague-Dawley
Vehicle	None
Type of dressing	Semi-occlusive.
Remarks - Method	

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5M/5F	1600	0/10
2	5M/5F	2000	8/10 (3M/5F)

LD_{50}	1600-2000 mg/kg bw
Signs of Toxicity - Local	Slight to severe irritation was observed in both dose groups that persisted to the end of the study period.. Effects included edema, atonia, focal bleeding, coriaceousness, desquamation, escher, blanching, alopecia, necrosis, ulceration and bruising. Black skin was observed at test site.
Signs of Toxicity - Systemic	There were no mortalities and no signs of systemic toxicity in the animals dosed at 1600 mg/kg bw. Eight out of 10 animals (3 males/5 females) dosed at 2000 mg/kg bw died. Signs of systemic toxicity observed included decreased activity, hunched postures and prolapsed penis.
Effects in Organs	In the mortalities, observations included discoloured liver and contents of the small intestine, and empty stomach and intestines. No abnormal findings were observed in the surviving animals.
Remarks - Results	

CONCLUSION: The notified chemical is harmful via the dermal route.

TEST FACILITY: Stillmeadow (2005d)

B.3. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD: Not stated

Species/Strain	Rabbit/New Zealand White
Number of Animals	3M/3F
Vehicle	None

Observation Period	96 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	Each animal was treated with 0.5 mL of undiluted test material on three separate sites on shaved areas on the backs of each animal. Each test site was separately covered in gauze patch, secured with paper tape and wrapped in Saran wrap, secured with Elastoplast. Animals were caged but not restrained during the exposure period. Each animal was exposed to the test material for 3 minutes, 1 hour and 4 hours, after which the test site was examined for erythema and oedema formation using the Draize scale. Each test site was cleansed with water following the initial observation. Subsequent observations were made for each test site at 24, 48, 72 and 96 hours.

RESULTS

Exposure time and lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
3-minute exposure				
Erythema/Eschar	2.6	4	96 hrs	4
Oedema	1.6	2	96 hrs	2
1 hour exposure				
Erythema/Eschar	3.8	4	96 hrs	4
Oedema	3.1	4	96 hrs	4
4 hour exposure				
Erythema/Eschar	4.0	4	96 hrs	4
Oedema	3.9	4	96 hrs	4

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL six animals.

Remarks - Results	Necrosis was observed after 3 minutes exposure in two animals but was observed in all animals following 1 and 4 hour exposure.

CONCLUSION The notified chemical is corrosive to the skin.

TEST FACILITY Hazleton (1993b)

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

TEST SUBSTANCE Notified chemical

METHOD US EPA OPPTS 870.2600 Skin Sensitisation

Species/Strain	Mouse/CBA:J
Vehicle	Acetone/olive oil (4:1)
Remarks - Method	A range-finding study was conducted with three mice tested with three consecutive concentrations of the test material at 100, 50 and 25%. Clinical signs of toxicity (decreased activity and swollen face) were observed on day 2 and two animals were found dead on day 3. Based on the range-finding study, concentrations of 2.5, 5 and 10% were selected for the main study. Five female mice were tested for each dose group.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/Mouse)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	1132	n/a
2.5	8479	7.5
5	7134	6.3
10	8128	7.2
Positive Control		
90*	3519	3.1

*alpha-hexylcinnamaldehyde

Remarks - Results	One 2.5% mouse died on day 6 of the study. This death was unlikely to be related to treatment, given that there were no mortalities observed at higher concentrations. All animals treated with 10% lost weight during the study, as well as one 5% animal, two positive control animals and one negative control animal.
CONCLUSION	There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Stillmeadow (2005e)

B.5. Repeat dose toxicity

Study 1
TEST SUBSTANCE

METHOD	OECD TG 407 Repeated Dose 28-Day Oral Toxicity Study in Rodents
Species/Strain	Rat/Crj:CD(SD)IGS
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 14 and 28 days, 14 day recovery Dose regimen: 7 days/week
Vehicle	Olive oil
Remarks - Method	This study was provided from what appears to be a Japanese translation. A document was also provided (see Biotechnics (2011)) that outlined the study results, as well as providing opinion on the pathological findings.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
14-day study			
control	4M/4F	0	0/8
low dose	4M/4F	50	0/8
mid dose	4M/4F	250	8/8*
high dose	4M/4F	1000	8/8
28-day study			
control	6M/6F	0	0/12
low dose	6M/6F	3	0/12
mid dose	6M/6F	10	0/12
high dose	6M/6F	30	0/12
control recovery	6M/6F	0	0/12
mid dose recovery	6M/6F	10	0/12
high dose recovery	6M/6F	30	0/12

*5/8 rats died during the study and the remaining were killed for human reasons but have been considered as mortalities.

Mortality and Time to Death
14-day study: All 1000 mg/kg bw/day animals died by day 4. The mortalities in the 250 mg/kg bw/day occurred on days 5-6.

28-day study: No mortalities were observed in the 28-day study.

Clinical Observations, Body weight and Food Consumption
14-day study: clinical signs of toxicity include salivation, lowered spontaneous motion, decreased breathing, half opened eye or closed eye, staining around mouth and nose, abdominal stain, anal stain, tearing of blood, lowered body temperature, cyanosis, deep breathing, piloerection, paleness, lowered body temperature, decreased excreta, soft and mucoid faeces and mydriasis. Effects were more common at higher doses but the severity was not commented on. Body weight values were not provided for the 14-day study but from the

provided brief qualitative description it appears that there were treatment related effects on body weight at all treatment levels.

28-day study: clinical signs of toxicity were less common than in the 14-day study and included salivation at all doses, and decreased spontaneous locomotion, staining around nose and mouth, incomplete eyelid closure, lacrimation at 30 mg/kg bw/day. At 28 days, clinical signs were similar in the main and recovery animals. The only occurrence of clinical signs in the recovery groups was decreased spontaneous locomotion in a single 30 mg/kg bw/day recovery male, which indicates the potential for recovery from clinical toxicity at the administered doses.

Body weight gains were decreased in 30 mg/kg bw/day males (↓23%) and females (↓25%) after 28 days. The body weight data for the recovery groups from the initial 28-day exposure was not provided but the 30 mg/kg bw/day males and females gained weight at a similar rate to controls during the recovery period, indicating recovery.

Food consumption was lower at some of the measured intervals in 30 mg/kg bw/day males and females but was similar to controls following the recovery period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

14-day study: there were decreases in average erythrocyte volume, the average erythrocyte haemoglobin volume and increased platelet count at 50 mg/kg bw/day. There were also increases in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and γ-GTP (assumed to be γ-glutamyl transpepsidase) in 50 mg/kg bw/day males and females. There were decreased in total protein, albumin, albumin/globulin ratio, creatinine and calcium in 50 mg/kg bw/day males, and alkaline phosphatase, choline esterase, blood glucose, total protein, albumin, albumin/globulin ratio and calcium in 50 mg/kg bw/day females.

28-day study: Haematology findings considered notable by Biotechnics (2011) was a statistically significant increase in ALT in 30 mg/kg bw/day males (↑170%) and females (↑439%) in the main study that persisted in females following the 30 mg/kg bw/day recovery group (↑1160%) but not in males. Higher AST was also observed in 30 mg/kg bw/day males (↑468%) and in the main study that persisted in males (↑285%) and was also observed in females (↑263%) following the recovery period. These findings indicate liver toxicity and may also indicate liver vacuolisation. The reduced alkaline phosphatase observed in 30 mg/kg bw/day males and females and the decreased total protein in 30 mg/kg bw/day males is likely to be associated with the slight decrease in food consumption in these groups. Increased urea was observed in 30 mg/kg bw/day males and females and was attributed by Biotechnics (2011) with the muscle catabolism associated with weight loss. Other clinical pathology findings such as decreased bilirubin in 30 mg/kg bw/day males, decreased cholesterol in recovery females, and some changes in differential leukocyte counts, were considered incidental. Urinalysis did not reveal any notable changes between treatment and control groups.

Effects in Organs

14-day study: there were increases in relative liver weights and adrenal weights in 50 mg/kg bw/day males and females, and in relative kidney and brain weights in 50 mg/kg bw/day males. Macroscopic examinations revealed signs of toxicity at all treatment levels. Microscopic observations were only reported for 50 mg/kg bw/day males and included effects in the stomach and liver.

28-day study: The only change in absolute organ weights was increased adrenal weights in 30 mg/kg bw/day males and females that were statistically significant in recovery males and in the main study females. There were a number of relative organ weight increases including liver, kidney and adrenals in 30 mg/kg bw/day males and females, and the testes and brain weights in 30 mg/kg bw/day males. The increased relative liver weights persisted in the recovery 30 mg/kg bw/day females, as did the increased adrenal weights in 30 mg/kg bw/day males and females.

As indicated by Biotechnics (2011), the translation was poor quality as there were a number of unclear or mis-spelled reported microscopic effects and as such, some the effects are based on assumption. The main toxicological histopathological effect was foam cells (engorged macrophages) in a number of organs. Biotechnics (2011) considered these changes were likely due to phospholipidosis, a condition associated with excess accumulation of intracellular phospholipids (Halliwell 1997). However, Biotechnics (2011) pointed out that these effects require further clarification to definitively classify the effects as phospholipidosis.

Foam cells were observed in 10 and 30 mg/kg bw/day in the liver, lung, kidneys and urinary bladder (see following Table). Fine vacuolisation and hypertrophy were also observed in the adrenals at 30 mg/kg bw/day, but was attributed to animals stress. Foamy cells were observed in the jejunum and a number of lymph tissues at 30 mg/kg bw/day.

	Males (mg/kg bw/day)				*Females (mg/kg bw/day)*			
	10	*10(R)*	*30*	*30(R)*	*10*	*10(R)*	*30*	*30(R)*
Lung								
Foamy cells	1(1.0)	0	6(1.5)	4(1.3)	0	0	6(1.2)	3(1.0)
Foamy change of bronchial epithelium	0	0	6(1.2)	2(1.0)	0	0	6(1.2)	1(1.0)
Liver								
Fine vacuolisation of hepatocytes	0	0	6(2.0)	0	2(1.0)	0	6(1.0)	0
Foamy cells in sinusoid	0	0	0	0	0	0	2(1.0	0
Foamy changes in bile duct epithelium	1(1.0)	0	6(2.0)	6(1.0)	0	0	6(2.0)	6(1.7)
Microgranuloma	0	0	0	0	1(1.0)	0	3(1.7)	4(2.0)
Kidney								
Fine vacuolisation of transitional epithelium	0	0	6(0.8)	1(0.5)	0	0	5(0.8)	0
Urinary bladder								
Diffuse hyperplasia of transitional epithelium	2(1.0)	1(1.0)	5(1.4)	3(1.0)	0	0	4(1.0)	1(1.0)
Fine vacuolisation of transitional epithelium	4(0.8)	0	6(1.0)	1(0.5)	0	0	5(0.8)	0

R, Recovery group.
( ), Average severity of affected animals: 0.5=very slight, 1=slight, 2=moderate.
Note: Control and 3 mg/kg bw/day groups not included because incidence was zero in all cases.

In general, the observation of foamy cells/changes decreased with incidence and severity following the recovery period, indicating some recovery, but some effects were still prominent in the 30 mg/kg bw/day recovery groups, especially in the lungs and liver.

Remarks – Results
The translation set a NOEL for the study at 3 mg/kg bw/day based on the presence of vacuolative changes and foamy cells at 10 mg/kg bw/day. However, Biotechnics (2011) agree on the NOEL of 3 mg/kg bw/day, but commented that effects are not likely to be adverse. The marked clinical laboratory findings at 30 mg/kg bw/day were considered to be supportive of the organ weight changes and histopathological findings at this dose and indicate the threshold for systemic toxicity (possibly phospholipidosis), thus Biotechnics (2011) considers the NOAEL to be 10 mg/kg bw/day. However, in the absence of further repeat-dose studies with the notified chemical (i.e., subchronic and chronic) to further characterise these effects, the vacuolative changes are considered to be treatment related toxicologically relevant effects and will be used to set the NOAEL.

CONCLUSION
The NOAEL was established at 3 mg/kg bw/day in this study, based on the presence of vacuolative changes in various organs and transitional epithelial hyperplasia in the urinary bladder in males in the higher dose groups tested.

TEST FACILITY Kagaku Busshitsu Hyoka Kenyuusho (2002a)
Biotechnics (2011)

Study 2
TEST SUBSTANCE Notified chemical

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents
OECD TG 421 Reproduction/Developmental Toxicity Screening Test
OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test

Species/Strain Rat/Crl:WI(Han)

Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 29 (Males), 42-45 (Females) Dose regimen: 7 days per week Post-exposure observation period: 14 or 28 days (Males only)
Vehicle	Propylene glycol
Remarks - Method	Dosing was based on the results of screening study at doses from 10-100 mg/kg bw/day (results not reported). P generation males and females (10/sex/dose) were administered the test material by gavage at 0, 1, 3 or 10 mg/kg bw/day. Males were treated for 29 days, and females for 42-45 days until at least day 4 of lactation. Following a minimum 14 days exposure, one male and one female were mated. Day 0 of gestation was assigned when there was evidence of mating. The offspring (F1 generation) were examined for mortality/viability, clinical and body weight changes during lactation. The reproductive indices of P generation females were calculated. One low dose female, two middle dose females, and one high dose female were not dosed during littering. An additional group of males (5/dose/recovery period) were administered 0 or 10 mg/kg bw/day for either 14 or 28 days, after administration for one month. These animals were not mated. Urinalysis was not conducted in this study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10 M + 10 F	0	1/20
low dose	10 M + 10 F	1	0/20
mid dose	10 M + 10 F	3	0/20
high dose	10 M + 10 F	10	0/20
control 14-day recovery	5 M	0	0/5
high dose 14-day recovery	5 M	0	0/5
control 28-day recovery	5 M	10	0/5
high dose 28-day recovery	5 M	10	0/5

Mortality and Time to Death (P generation and recovery groups)

One control female was killed *in extremis* due to a probable forelimb fracture. No mortality was observed in treatment groups.

Clinical and Functional Observations (P generation and recovery groups)

There were no treatment related clinical signs during the observation period. Sporadic findings (scabs, alopecia and scales) that were considered incidental. There were statistically significant decreases in body weight gains in 10 mg/kg bw/day males during the dosing period, which persisted until the 14-day recovery but body weights were similar at the end of the 28-day period. In females, the 10 mg/kg bw/day did not gain weight between days 1 and 8 but body weight gains were only slightly decreased during gestation. Food consumption was slightly decreased at most observation points in 10 mg/kg bw/day females but food consumption relative to body weight was similar. There were no changes in functional observations that were considered related to treatment but there was some variation in motor activity in 3 mg/kg bw/day females that was not considered treatment related due to lack of a dose response.

Laboratory Findings – Clinical Chemistry and Haematology (P generation)

Clinical chemistry changes mostly occurred in 10 mg/kg bw/day groups. There were statistically significant increases in ALT in males (↑76%) but was similar to controls in recovery groups. There were statistically significant increases in AST in 10 mg/kg bw/day males (↑533%) and females (↑123%), with the male recovery groups only slightly increased (~↑20% for both recovery groups). Cholesterol was statistically decreased in 10 mg/kg bw/day males (↓17%) and females (↓36%), but was similar to controls in the recovery groups. There were slight but statistically significant decreases in total protein, cholesterol, potassium at high doses, but these changes were considered incidental and within expected biological variability. The ALT and AST are suggestive of hepatotoxicity.

Statistically significant haematological changes occurred mostly in 10 mg/kg bw/day males, including neutrophils (↑35%), lymphocytes (↓8%), monocytes (↑52%), mean cell volume (↓3%) and platelets (↑30%). These changes were not observed in recovery groups. The only changes observed in recover groups were increased reticulocytes (↑31%) at 14 days and eosinophils (↑108%). There were no statistically significant changes in haematology parameters in females and treated groups were similar to controls.

Effects in Organs

There were no treatment related macroscopic findings. In 10 mg/kg bw/day males, there were statistically significant increases in relative kidney (↑16%) and adrenal weights (↑27%), but recovery was observed after 28 days. Slight but statistically significant increases in relative epididymal weights were also observed in 10 mg/kg bw/day males at the end of dosing (↑8%) and after 28 days recovery (↑8%), but are unlikely to be of toxicological concern due to the low magnitude of the change. Relative testes weights were also statistically increased at the end of the 28-day recovery period (↑10%). In females, the only organ weight change attributed to treatment was a statistically significant increase in relative kidney weights at 10 mg/kg bw/day (↑9%).

The histopathological findings are summarised in the following two tables for males and females, respectively. There was an increased incidence and severity of alveolar macrophage foci in the lungs that appear to be treatment related in 3 and 10 mg/kg bw/day males and in 10 mg/kg bw/day females, although there were three animals affected in the 28-day recovery control group with minimal to slight severity, demonstrating a high background incidence and that this effect is only indicative of minimal toxicity.

Urothelial hyperplasia was observed in 3 and 10 mg/kg bw/day males and in 10 mg/kg bw/day females. The effect was still present in recovery groups, although the incidence and severity decreased from day 14 to 28, demonstrating recovery.

Diffuse cortical hypertrophy in the adrenal glands was observed in one 3 mg/kg bw/day male with minimal severity. This effect was also observed at higher incidence and severity in 10 mg/kg bw/day males, with some indication of recovery at 14 days (28 day recovery group not analysed). Four 10 mg/kg bw/day females were affected. These effects are likely to be associated with the increased adrenal weights observed in 10 mg/kg bw/day males.

Increased apoptosis/single cell necrosis in the prostate was observed in 3 and 10 mg/kg bw/day males, although was not considered toxicologically significant at 3 mg/kg bw/day as it was only observed in one animal with minimal severity. Some recovery was observed at 14 days (28 day not analysed).

Myofiber degeneration in skeletal muscle was observed in 3 and 10 mg/kg bw/day males and females (occurrence in 1 mg/kg bw/day was low and not considered toxicologically significant). In males, the effects in treated groups were accompanied by occurrences in control groups. This effect was most severe in 10 mg/kg bw/day males and females, but recovery was observed at 14 and 28 days male recovery groups.

Hepatocellular midzonal/centrilobbular hypertrophy was observed at low severity in both control and high dose males and females, thus is not considered treatment related. Hyaline casts and tubular basophilia were observed in both sexes. These effects are not considered treatment related due to occurrence in controls, the low severity in treated groups and the lack of a clear dose response. Macrophage foci of the mesenteric lymph node were observed in all treated and control groups, with some increases in treated groups. The relevance of this effect is unclear.

	Males (mg/kg bw/day)							
	0	*1*	*3*	*10*	*0 (14R)*	*0 (28R)*	*10 (14R)*	*10 (28R)*
Lung								
Alveolar macrophage foci	2(0.5)	2(0.5)	4(1.3)	4(1.3)	1(0.5)	3(0.7)	4(0.6)	2(2.0)
Urinary bladder								
Urothelial hyperplasia	0	0	3(0.7)	5(1.2)	0	0	3(1.5)	2(0.8)
Adrenal glands								
Diffuse cortical hypertrophy	0	0	1(0.5)	3(0.7)	0	-	2(0.5)	-
Prostate								
Increased apoptosis/single cell necrosis	0	0	1(0.5)	5(1.0)	0	-	3(0.5)	-
Skeletal muscle								

Myofiber degeneration	3(0.5)	2(0.5)	5(0.6)	5(1.3)	2(0.5)	3(0.5)	1(0.5)	1(0.5)

14R, 14-day recovery group. 28R, 28-day recovery group.
( ), Average severity of affected animals: 0.5=minimal, 1=slight, 2=moderate.

	Females (mg/kg bw/day)			
	0	*1*	*3*	*10*
Lung				
Alveolar macrophage foci	5(0.5)	4(0.8)	4(0.6)	5(1.8)
Urinary bladder				
Urothelial hyperplasia	0	0	0	5(0.6)
Adrenal glands				
Diffuse cortical hypertrophy	0	0	0	4(0.6)
Skeletal muscle				
Myofiber degeneration	0	1(0.5)	2(0.5)	2(1.3)

( ), Average severity of affected animals: 0.5=minimal, 1=slight, 2=moderate.

Reproductive and Developmental Assessment

Mating, fertility and conception indices, precoital time, and the number of corpora lutea and implantation sites were no affected by treatment. The gestation index was similar to controls. There were no mortalities or clinical signs that were attributed to treatment. There was a slight decrease in pup body weight in the 10 mg/kg bw/day groups on days 1 and 4, however, this was attributed to the decreased parental body weight and not considered to be of toxicological significance due to the low severity. There were no treatment related findings at necropsy.

Remarks – Results

The study pathologist noted that the histopathological effects in the study were mostly of minimal severity and that they are indicators of borderline toxicity, however, the muscle degeneration was considered toxicologically significant at 10 mg/kg bw/day males and females, in addition to the urothelial hyperplasia at 3 mg/kg bw/day males and in 10 mg/kg bw/day males and females.

CONCLUSION

The NOAEL was established at 1 mg/kg bw/day for males and 3 mg/kg bw/day for females, based on alveolar macrophage foci and urothelial hyperplasia at higher doses. Under the conditions of the study, the NOAEL for reproductive and developmental toxicity was established at 10 mg/kg bw/day, based on the lack of observed effects.

TEST FACILITY NOTOX (2012)

B.6. Genotoxicity – bacteria

Study 1

TEST SUBSTANCE	Notified chemical
METHOD	HWA Protocol 401, Edition 17 Plate incubation procedure
Species/Strain	*S. typhimurium*: TA1538, TA1535, TA1537, TA98, TA100
Metabolic Activation System	S9 mix from Aroclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 100, 333, 667, 1000, 3330 and 5000 µg/plate b) Without metabolic activation: 100, 333, 667, 1000, 3330 and 5000 µg/plate
Vehicle	Ethanol
Remarks - Method	The selected strains may not detect certain oxidizing mutagens, cross-linking agents and hydrazines. A preliminary cytotoxicity assay was conducted in strain TA100. All concentrations were conducted in triplicate but the assay was not repeated.

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	Not observed	Negative
Test 2	-	-	-	-
Present				
Test 1	>5000	>5000	Not observed	Negative
Test 2	-	-	-	-

CONCLUSION The notified chemical was not mutagenic to the test strains of bacteria under the conditions of the test. This assay is unlikely to have detected mutagenic from certain oxidizing mutagens, cross-linking agents and hydrazines.

TEST FACILITY Hazleton (1993c)

Study 2

TEST SUBSTANCE Notified chemical

METHOD Not stated, but compliant with OECD 471 Bacterial Reverse Mutation Test
Pre-incubation procedure

Species/Strain	*S. typhimurium*: TA100, TA 1535, WP2uvrA, TA98, TA 1537
Metabolic Activation System	S9 mix from phenobarbitone and 5,6-benzoflavone induced liver
Concentration Range in Main Test	a) With metabolic activation: 156, 313, 625, 1250, 2500 and 5000 µg/plate b) Without metabolic activation: 156, 313, 625, 1250, 2500 and 5000 µg/plate
Vehicle	Distilled water

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	Not observed	Negative
Test 2	-	-	-	-
Present				
Test 1	>5000	>5000	Not observed	Negative
Test 2	-	-	-	-

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

TEST FACILITY Kagaku Busshitsu Hyoka Kenyuusho (2002b)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 476 In vitro Mammalian Cell Gene Mutation Test.
EC Directive 2000/32/EC B.17 Mutagenicity - In vitro Mammalian Cell Gene Mutation Test.

Cell Type/Cell Line	L5178Y mouse lymphoma cells
Metabolic Activation System	S9 mix from phenobarbitone and β-naphthoflavone induced liver
Vehicle	Ethanol
Remarks - Method	The humidity was accidentally lowered to 58% for one hour during test 2.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*
Absent			
Test 1	0*, 10*, 30*, 50*, 70*, 90, 100*, 110*, 120*, 130, 140*, 150, 160, 180, 200, 225, 250, MMS*	3 hours	48 hours
Test 2	0, 0.3, 1*, 3*, 10*, 20*, 30*, 40*, 45*, 50*, 55, 60, 65, 70, 80, 90, 100, MMS*	24 hours	48 hours
Present			
Test 1 (8%)	0*, 33*, 100*, 150, 200, 250*, 300*, 310, 320*, 330, 340*, 350, 360*, 380*, 400, CP*	3 hours	48 hours
Test 2 (12%)	0*, 10, 50*, 100, 200*, 250*, 300*, 325*, 350*, 365, 380*, 400*, CP*	3 hours	48 hours

*Cultures selected for mutation frequency measurement.
MMS, methyl methane sulfonate. CP, cyclophosphamide.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*		*Mutation frequency per 10^6 survivors*		
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Control*	*Treated**	*HC*
Absent					
Test 1	>100	≥140	75	167	51-169
Test 2	≥100	≥50	75	135	50-154
Present					
Test 1 (8%)	≥333	≥360	157	205	50-170
Test 2 (12%)	-	≥400	101	122	

Cytotoxicity considered being 10-20% relative survival.
*Highest total mutation frequency (sum of small and large mutations), does not include the mutation frequency from cytotoxic concentrations.
HC, Historical control data presented as the range of all negative controls (plate, ethanol and DMSO).

Remarks - Results	There were increases in some test concentrations compared to concurrent controls. However, there was no dose-response and the maximum values (indicated in the Table above) were either within or only slightly outside historical control data and therefore these results are not considered to be positive.
CONCLUSION	The notified chemical is not mutagenic to mouse lymphoma cells treated in vitro under the conditions of the test.
TEST FACILITY	NOTOX (2011a)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical
METHOD	Guideline not stated but the results suggest it was conducted using OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Cell Type/Cell Line	Chinese Hamster Lung Cells
Metabolic Activation System	S9 mix from phenobarbitone and 5,6-benzoflavone induced rat liver
Vehicle	Acetone
Remarks - Method	Detailed methodology was not provided.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 16.2*, 51.2*, 162*, 512*, 1620, 0.1 MMC*	6 hours	18 hours
Test 2	0*, 12.5*, 15*, 17.5*, 20.0*, 0.05 MMC*	24 hours	None
Present			

Test 1	0*, 51.2*, 162*, 512*, 1620*, 6 CPA*	6 hours	18 hours

*Cultures selected for metaphase analysis.
MMC, mitomycin-C. CPA, cyclophosphamide.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥50.5	≥51.2	-	Negative
Test 2	≥20.0	≥15.0	-	Positive
Present				
Test 1	≥404	≥1620	-	Negative

Remarks - Results: Under continuous treatment in the absence metabolic activation, there was a clear concentration dependent increase in structural and numerical chromosomal aberrations in treated plates.

CONCLUSION: The notified chemical was clastogenic to Chinese hamster lung cells treated in vitro under the conditions of the test.

TEST FACILITY: Kagaku Busshitsu Hyoka Kenyuusho (2002c)

B.9. Genotoxicity – in vivo

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
Species/Strain: Mice/NMRI BR (SPF)
Route of Administration: Intraperitoneal (IP) injection
Vehicle: Corn oil
Remarks - Method: In a dose range finding study, animals were dosed with 100 or 200 mg/kg bw by IP. The two animals dosed at 200 mg/kg bw died and toxicity was observed at 100 mg/kg bw and thus was chosen as the high dose for the study.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5M/5F	0	24 hours
II (low dose)	5M/5F	25	24 hours
III (mid dose)	5M/5F	50	24 hours
IV (high dose)	5M/5F	100	24 hours
V (high dose)	5M/5F	100	48 hours
VI (positive control, CP)	5M/5F	40	24 hours

CP=cyclophosphamide.

RESULTS
Doses Producing Toxicity: Lethargy and ataxia observed in 100 mg/kg bw/day. Animals appeared normal after 19 hours.
Genotoxic Effects: The number of micronucleated polychromatic erythrocytes and the ratio of polychromatic/monochromatic erythrocytes were similar in treated groups and controls.

CONCLUSION: The notified chemical was not clastogenic under the conditions of this in vivo micronucleus assay.

TEST FACILITY: NOTOX (2011b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE: Notified chemical (> 99%)

METHOD
- Inoculum: Sewage and sludge sediments
- Exposure Period: 28 days
- Auxiliary Solvent: None
- Analytical Monitoring: The biochemical oxygen demand (BOD), dissolved organic carbon (DOC), and the concentrations (using LC-MS) of the notified chemical were analysed for determination of biodegradation percentage of the notified chemical.
- Remarks - Method: The notified chemical was exposed to activated sludge (30 mg/L) at a concentration of 100 mg/L in triplicate for 28 days at 25±1˚C. A reference control test with aniline, a blank control (sludge only) and a sterile control (water plus the notified chemical) were also established.

RESULTS

Test substance				*Aniline*	
Day	*% Degradation*			*Day*	*% Degradation*
	BOD	*DOC*	*LC-MS*		
28	2	0	0	7	56
				14	65

- Remarks - Results: No significant deviations in protocol. The biodegradability of aniline in 7 days and 14 days was determined from the BOD and found to be 56% and 65%, respectively, thereby confirming the validity of the test.
  The notified chemical in both the sterile control and the test solutions was not dissolved at start. At the end of the cultivation, no insoluble matter was found in the sterile control, but a white insoluble matter was observed in the test solution. This matter was considered according to the notifier to be due to the inorganic ions contained in the basic culture medium and did not influence the solubility of the notified chemical in the test solution.
  The notified chemical is considered not to be readily biodegradable based on the test results.

CONCLUSION: The notified chemical is not readily biodegradable.

TEST FACILITY: Chemical Evaluation and Research Institute (2001)

C.1.2. Bioaccumulation

TEST SUBSTANCE: Notified chemical

METHOD
- Species: Carp (*Cyprinus carpio*)
- Exposure Period: Exposure: 28 days Depuration: not conducted
- Auxiliary Solvent: HCO-40 (dispersant)
- Concentration Range: Nominal: 1) 0.1 mg/L, 2) 0.01 mg/L
  Actual: 1) 0.0961 ± 0.00339 mg/L, 2) 0.00948 ± 0.000193 mg/L
- Analytical Monitoring: HPLC-MS
- Remarks - Method: After rearing and acclimatization, fish (aged < 1 year) was exposure to the notified chemical at two concentrations for 28 days at about 25˚C and pH 8.0. Dispersant HCO-40 was used for preparation of the stock solutions (10 times in volume to the notified chemical). A control test

with the dispersant was performed. Sample fish was analysed 5 times for the treatment test and 2 times (at start and the end of exposure) for the control test. Each analysis used 4 fish that was divided into two groups.

RESULTS

Bioconcentration Factor	6.1 for the 0.1 mg/L concentration and 11 for the 0.01 mg/L concentration.
CT50	N/A
Remarks - Results	The test substance concentrations in test water remained over 93% of the nominal levels. The average lipid content in the sample fish was 3.34% at start and 3.80% at the end of the exposure. The bioconcentration factor in stationary state was determined to be 6.1 for the 0.1 mg/L concentration test and 11 for the 0.01 mg/L concentration test. The notified chemical is considered to be slightly concentrating.

CONCLUSION The notified chemical is slightly concentrating.

TEST FACILITY Chemical Evaluation and Research Institute (2002)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE Notified chemical (> 90%)

METHOD Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss)* Under Static Conditions TSCA Guideline 797.1400

Species	Rainbow Trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	160 mg $CaCO_3$/L
Analytical Monitoring	The actual test concentrations were not determined.
Remarks – Method	The dilution water was from a 100-meter deep bedrock well. The test solutions were not aerated. In a range finding study conducted using nominal concentrations of 1.0, 2.5, 5.0, 10 and 20 mg/L no mortality or sublethal effects were observed. Following this, an additional preliminary test was performed to evaluate the toxicity of the notified chemical at the highest level of solubility (determined in this study by solubility trials to be 570 mg/L adjusted to pH 7) for an exposure period of 24 hours. No mortality was observed in this trial. Stock solution of the test substance was clear and colourless containing no visible undissolved test substance after pH adjustment to about 7 using HCl. Based on the results from the range finding tests, a limit definitive test at 570 mg/L, including a blank control, was conducted in triplicate at 12 – 13˚C, pH 6.9-7.3, and > 60% saturation for the dissolved oxygen throughout the exposure. Ten animals were used in each replicate.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality (%)*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	-	30	0	0	0	0	0
570	-	30	0	17	27	30	30

LC50	> 570 mg/L at 96 hours
NOEC	< 570 mg/L at 96 hours.
Remarks – Results	No significant deviation in protocol. The validity criteria were met. At the termination of the definitive test (96 hours) mortality of 30% was

observed in the 570 mg/L treatment group. One of the surviving organisms at this dose level was lethargic. The test notified chemical had a purity of > 90% and is considered to be acceptable for the study.
The notified chemical is not considered to be harmful to fish based on the test results.

CONCLUSION The notified chemical is not harmful to fish.

TEST FACILITY Springborn Laboratories (1995a)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical (> 90%)

METHOD Acute Toxicity to Water Fleas (*Daphnia magna*) Under Static Conditions TSCA Guideline 797.1300

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	160 mg $CaCO_3$/L
Analytical Monitoring	The actual test concentrations were not determined.
Remarks - Method	Following a range finding test, the definitive study was conducted by exposing daphnids in four replicate to the notified chemical at nominal concentrations of 5.0, 10, 20, 40, 80 and 160 mg/L, 19 – 21˚C, pH 7.0 – 7.9 and > 91% saturation for dissolved oxygen. Stock solution of the test substance (160 mg/L) was clear and colourless containing no visible undissolved test substance after pH adjustment to 7 using HCl. A blank control test was also performed in four replicate under identical conditions except containing no notified chemical.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	-	20	0	0
5.0	-	20	0	0
10	-	20	1	1
20	-	20	0	1
40	-	20	3	18
80	-	20	14	20
160	-	20	20	20

EC50	27 mg/L at 48 hours
NOEC	5.0 mg/L at 48 hours
Remarks - Results	No significant deviation in protocol. The validity criteria were met. The study author has calculated the LC50 by moving average angle analysis to be 27 mg/L with a 95% confidence interval calculated by binomial probability of 21 to 35 mg/L. DSEWPaC has not checked the calculation and accept the endpoints considering only 5% of immobility was reported at 20 mg/L. The test notified chemical had a purity of > 90% and is considered to be acceptable for the study. The notified chemical is considered to be harmful to daphnids.

CONCLUSION The notified chemical is harmful to daphnids.

TEST FACILITY Springborn Laboratories (1995b)

C.2.3. Algal growth inhibition test (study 1)

TEST SUBSTANCE Notified chemical (> 90%)

METHOD	96-Hour Toxicity Test with Freshwater Green Alga *Selenastrum capricornutum* following TSCA Guideline 797.1050.
Species	*Selenastrum capricornutum*
Exposure Period	96 hours
Concentration Range	Nominal: 0.26, 0.89, 3.0, 9.9, 33, 110 µg/L
Auxiliary Solvent	None
Water Hardness	Algal growth medium used (AAP medium)
Analytical Monitoring	The actual test concentrations were not determined. The algal cell counts were conducted using a hemacytometer (Neubauer Improved) and an Olympus compound microscope.
Remarks - Method	Following a range finding study, a definitive study was conducted in a blank control and at 6 levels of the notified chemical up to 110 µg/L and an initial cell concentration of 1.0 x 10^4 cells/mL. The test for all the treatment groups and the control were conducted in triplicate and at 24 ± 1˚C, with a continuous light intensity of 300 to 500 footcandles. The pH ranged 7.1 to 7.4 at test initiation and 7.6 to 9.3 at termination.

RESULTS

Yield	
E_yC50	*NOEC*
µg/L at 72 h	*µg/L at 72 h*
39	0.26

Remarks - Results	No significant deviations in protocol. The validity criteria were met. At termination of the definitive study, bloated cells and cell fragments were observed in the top three test concentrations (9.9 to 110 µg/L). The cells at the three lower test concentrations appeared normal. At study termination, the control culture averaged 239 x 10^4 cells/mL. The cell densities in treatment groups ranged from the lowest to highest treatment group from 220 x 10^4 cells/mL to 38 x 10^4 cells/mL. Statistical analysis using the Williams' Test demonstrated a significant reduction in cell density in the 3.0, 9.9, 33, and 110 µg/L treatment groups compared to the control at 96 hours. To investigate the algicidal/algistatic effects of the notified chemical, aliquots of the treatment culture from the highest treatment group were diluted in fresh AAP medium to give a treatment concentration of 0.26 µg/L. The estimated cell density in the new culture was 0.091 x 10^4 cells/mL. After eight days, substantial increase in cell density (55 x 10^4 cells/mL) was observed, and thus the study author indicated based on this that the notified chemical is algistatic rather than algicidal. DSEWPaC classifies the effects of the notified chemical to algae by using the 72 h E_rC50. However the E_yC50 can be used when the endpoint based on growth rate (E_rC50) is not available. The 72 h E_yC50 was reported by the study author to be 39 µg/L (95% confidence limits of 1.5 – 75 µg/L). The NOEC for yield has been visually determined by DSEWPaC to be 0.26 µg/L since biologically significant effect (19%) was reported at the concentration of 0.89 µg/L. The notified chemical is considered to be very toxic to algae.
CONCLUSION	The notified chemical is very toxic to *Selenastrum capricornutum*.
TEST FACILITY	Springborn Laboratories (1995c)

C.2.4. Algal growth inhibition test (study 2)

TEST SUBSTANCE	Notified chemical (> 90%)

METHOD	96-Hour Toxicity Test with Freshwater Green Alga *Selenastrum capricornutum* following TSCA Guideline 797.1050 Modified for Addition of Humic Acid.
Species	*Selenastrum capricornutum*
Exposure Period	96 hours
Concentration Range	Nominal: 2.4, 8.0, 27, 90, 300, 1000 µg/L
Auxiliary Solvent	None
Water Hardness	Algal growth medium used (AAP medium with 10 mg/L or 20 mg/L humic acid)
Analytical Monitoring	The actual test concentrations were not determined. The algal cell counts were conducted using a hemacytometer (Neubauer Improved) and an Olympus compound microscope.
Remarks - Method	Following a range finding study, a definitive study was conducted in a blank control, a humic acid control, and at 6 levels of the notified chemical up to 1000 µg/L and an initial cell concentration of 1.0 x 10^4 cells/mL. The test for all the treatment groups and the control were conducted in triplicate and at 24 ± 1˚C, with a continuous light intensity of 300 to 500 footcandles. The pH ranged 7.3 to 7.6 at test initiation and 7.7 to 10.2 at termination.

RESULTS

Humic acid level (mg/L)	*Yield E_yC50^* (µg/L)*			*NOEC (µg/L at 72 h)*
	48 h	*72 h*	*96 h*	
10	56	640	60	90
20	16	170	53	2.4

* Endpoints provided by the study author, unclear if this was compared to the blank control or the humic acid control.

Remarks - Results

No significant deviations in protocol. The validity criteria were met.

10 mg/L humic Acid

At termination of the definitive study, bloated cells were observed in the top three test concentrations (90 to 1000 µg/L). Cell fragments were also observed in 300 µg/L test concentration. The cells at the three lower test concentrations appeared normal. At study termination, control and the humic control cultures, averaged 178 and 179 x 10^4 cells/mL, respectively. The cell densities in treatment groups ranged from the lowest to highest treatment group from 153 x 10^4 cells/mL to 13 x 10^4 cells/mL.

Statistical analysis using the Williams' Test demonstrated a significant reduction at 96 h in cell density in all treatment groups compared to control. The humic acid control showed some inhibition effects compared to the blank control. Biologically significant effects comparing to the humic acid control were observed at 72 h at levels ≥ 90 µg/L (13% at 90 µg/L). The study author estimated a 72 h E_yC50 of 640 µg/L with a confidence limit of 89 – 1300 µg/L.

20 mg/L humic Acid

At termination of the definitive study all treatment and control cells appeared normal. At study termination, control and the humic control cultures averaged 181 and 168x 10^4 cells/mL, respectively. The cell densities in treatment groups ranged from the lowest to highest treatment group from 153 x 10^4 cells/mL to 13 x 10^4 cells/mL.

Statistical analysis using the Williams' Test demonstrated a significant reduction at 96 h in cell density in all treatment groups compared to control. The humic acid control showed some inhibition effects compared to the blank control. Biologically significant effects comparing to the humic acid control were observed at 72 h at levels > 8.0 µg/L (9.6% at 2.4 µg/L). The study author estimated a 72 h E_yC50 of 170 µg/L with a confidence limit of 17 – 1800 µg/L.

It is noted that there is an inconsistency of the trend for the determined E_yC50 with exposure time. Therefore, the test results should be treated with caution.

The study author indicated that the notified chemical is algistatic rather than algicidal to the test alga based on the results of a six day recovery study. DSEWPaC classifies the effects of the notified chemical to algae by using the 72 h E_rC50, however, the E_yC50 can be used when the E_rC50 is not available.

The notified chemical is considered to be very toxic to algae. This conclusion is the same as the previous study without use of humic acid in the medium, although the endpoints obtained from this study showed lower toxicity to the test alga.

CONCLUSION The notified chemical is very toxic to *Selenastrum capricornutum*.

TEST FACILITY Springborn Laboratories (1996)

C.2.5. Algal growth inhibition test (study 3)

TEST SUBSTANCE Notified chemical (purity > 98%)

METHOD OECD TG 201 Alga, Growth Inhibition Test

Species	*Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum*)
Exposure Period	96 hours
Concentration Range	Nominal: Control, 0.010, 0.032, 0.10, 0.32, 1.0, 3.2 and 10 mg/L Actual: < 0.0011, 0.0079, 0.025, 0.082, 0.23, 0.84, 2.6 and 10 mg/L (initial exposure concentrations)
Auxiliary Solvent	None reported
Water Hardness	0.24 mmol/L Ca^{2+} and Mg^{2+}
Analytical Monitoring	UHPLC with LC/MS/MS detector
Remarks - Method	Following a range finding test, a definitive test was conducted according the guidelines above and in compliance with GLP principles. No significant deviations to protocol were reported. A stock solution (nominally 10 mg/L test substance) was prepared with 15 min of magnetic stirring to accelerate dissolution of the test substance. The other test concentrations were prepared by dilution of the 10 mg/L solution. Three replicates per concentration of test substance and six replicates of the control were run. A positive control was run with potassium dichromate. Test conditions: temperature 22.0 – 22.7°C, pH 7.9 – 8.7. The NOEC was the determined by statistical analysis of growth rate and inhibition by the Bonferroni t and Tukey tests, $\alpha = 0.05$. The EC50 values were calculated by log-linear regression analysis of the percentages of growth rate reduction and percentage of yield inhibition versus logarithms of the corresponding initial exposure concentrations of the test substance. At the end of the exposure period two samples were cultured in M2 medium without test substance to determined if inhibition effects were algicidal or algistatic. The concentrations showing maximum inhibition were intended to be used but the wrong samples (0.23 and 0.84 mg/L) were inadvertently used.

RESULTS

Biomass		*Growth*	
E_yC50 mg/L at 72 h	*NOEC mg/L at 72 h*	*E_rC50 mg/L at 72 h*	*NOEC mg/L at 72 h*
0.046 (95% CI 0.024 – 0.088)	Not reported	0.25 (95% CI 0.095 – 0.64)	Not reported

E_yC50 mg/L at 96 h	NOEC mg/L at 96 h	E_rC50 mg/L at 96 h	NOEC mg/L at 96 h
0.038 (95% CI 0.018 – 0.080)	0.0079	0.24 (95% CI 0.085 – 0.70)	0.0079

Remarks - Results

All validity criteria were satisfied. The 72 h E_rC50 for the positive control was 1.4 mg/L (95% CI 1.1 – 1.9 mg/L) which was in the historical range for the algal culture tested. The initial measured test substance concentrations (71 –101% of nominal) were slightly lower than the mean measured concentrations, and were therefore used for calculation of endpoints. DSEWPaC classifies the effects of the notified chemical to algae by using the 72 h E_rC50 which was 0.25 mg/L (95% CI 0.095 – 0.64 mg/L).

At the end of the exposure period the cells exposed to 0.082 mg/L and lower test substance appeared normal and healthy compared to the control. The cells exposed to 0.23 and 0.84 mg/L test substance appeared to be smaller and clustered together and to the wall after 72 h. After 96 h most of these cells were observed to be shrivelled and malformed or swollen. Cells exposed to the two highest concentrations (2.6 and 10 mg/L) were observed to be shrivelled and malformed from 72 h onwards. The subsamples placed in M2 medium after 72 h had increased by a factor > 16 and appeared normal and healthy. Therefore the effects of the test substance appeared to be algistatic rather than algicidal, up to and including a concentration of 0.84 mg/L.

CONCLUSION

The notified chemical is very toxic to algae.

TEST FACILITY

NOTOX B.V. (2011c)

C.2.6. Inhibition of microbial activity (study 1)

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 209 Activated Sludge, Respiration Inhibition Test.

Inoculum

Synthetic sewage and activated sewage sludge

Exposure Period

3 hour

Concentration Range

Nominal: 0, 125, 250, 500, 1000, 2000mg/L

Remarks – Method

The study was conducted by exposing activate sludge to five concentrations of the notified chemical. Two blank controls and a reference control using 3,5-dichlorophenol (at 5, 10, 20, and 40 mg/L) were established. All the tests were conducted in duplicate.
Dissolved oxygen content was measured with an electronic dissolved oxygen meter.

RESULTS

IC50

683.77 mg/L

NOEC

<125 mg/L

Remarks – Results

No significant deviation in protocol. The validity criteria were met.
The oxygen consumption rates in the blanks were within 15% of each other and their mean. The EC50 of positive control was determined to be 24.04 mg/L, which is within the acceptable range of 5 – 30 mg/L.
An EC50 of 683.77 mg/L with 95% confidence limits of 663.73 – 703.80 mg/L was reported by the study author. The NOEC was not established since an average inhibition of 12.11% was observed at the lowest test level (125 mg/L).

Although the study was valid under the guidelines which it was conducted, the dissolved oxygen levels in the blank samples were

depleted over 1 hour. Therefore the study results should be treated with caution and have not been used in the environmental risk assessment.

CONCLUSION	The notified substance is not expected to inhibit respiration of sludge micro-organisms.
TEST FACILITY	Stillmeadow Inc (2005g)

C.2.7. Inhibition of microbial activity (study 2)

TEST SUBSTANCE	Notified chemical (purity > 98%)
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test (Carbon and Ammonium Oxidation)
Inoculum	Activated sewage sludge
Exposure Period	3 hours
Concentration Range	Nominal: 46, 100, 220, 460 and 1000 mg/L Actual: Not reported
Remarks – Method	Following a combined range-finding/limit test, a definitive test was conducted with five replicates per concentration and seven replicates in the untreated control group in accordance with the guidelines above. Reference controls (3,5-dichlorophenol) were not replicated. Test solutions were not adjusted for pH and were stirred for 25 - 26 h due to the low water solubility of the test substance. No significant deviations to protocol were reported. Blank and reference controls were run in parallel. In the range-finding/limit test only slight effect on nitrification was observed, hence a nitrification control was not run in the definitive test. Test conditions were: 19.8 – 21.5°C, pH 7.8 – 9.2. The statistical significance of inhibitory effect of the test substance was determined by the Bonferroni t-Test, $\alpha = 0.05$. The IC50 and IC10 were calculated by linear regression analysis.
RESULTS	
IC50	160 mg/L (95% CI 97 – 250 mg/L)
IC10	42 mg/L (95% CI 25 – 70 mg/L)
NOEC	< 46 mg/L
Remarks – Results	All validity criteria were satisfied. Since a statistical significant inhibition of the respiration rate was observed in all loading rates tested, the NOEC was below the lowest concentration tested and the EC10 was reported instead.
CONCLUSION	The notified substance is not expected to significantly inhibit respiration of sludge micro-organisms at concentrations less than 160 mg/L
TEST FACILITY	NOTOX B.V. (2011d)

BIBLIOGRAPHY

3M Environmental Laboratory (2011a) Solubility of [notified chemical] in water (Project ID: GLP10-0008, 2011). 3M Center, St. Paul, MN 55144-1000, USA, 3M Environmental Laboratory. (Unpublished report submitted by 3M Australia Pty Ltd).

3M Environmental Laboratory (2011b) Partition Coefficient (n-octanol/water) of [notified chemical] (Project ID: GLP11-0001, 2011). St. Paul, MN 55144-1000, USA, 3M Environmental Laboratory. (Unpublished report submitted by 3M Australia Pty Ltd).

3M Environmental Laboratory (2012) Revised Final Analytical Report. Method Validation – Quantitation of the [Notified Chemical] in Chlorinated Drinking Water Using Liquid Chromatography and Tandem Mass Spectrometry (3M Environmental Lab Method ETS-8-246.0). Laboratory Project E11-0724 (Unpublished report submitted by 3M Australia Pty Ltd).

3M Materials Resource Division (2010) Density of Clearlink 1000. Analytical Request GID:158756. 3M Materials Resource Division Analytical Laborator (address not provided).

Biotechnics (2011) Review Summary. MTDID 25575: 28-Day Oral Gavage Study in Rats.

Chemical Evaluation and Research Institute (2001) Biodegradability Test of [notified chemical] in Microorganisms (Test No.: 13759, 2001), Japan, Kurume Laboratory Chemical Evaluation and Research Institute. (Unpublished report submitted by 3M Australia Pty Ltd).

Chemical Evaluation and Research Institute (2002) Bioconcentration Test of notified chemical in Carp (Test No.: 43795, 2002). Japan, Kurume Laboratory Chemical Evaluation and Research Institute. (Unpublished report submitted by 3M Australia Pty Ltd).

EPHC (2009) Environmental Risk Assessment Guidance Manual for Industrial Chemicals. Environment Protection and Heritage Council, Australia, 109 pp, <http://www.ephc.gov.au/taxonomy/term/75>. Accessed 2012, Mar 28.

Halliwell (1997) Cationic Amphiphilic Drug-Induced Phospholipidosis. Toxicological Pathology. Volume 25(1): 53-60.

Hazleton (1993a) Acute Oral Toxicity Study of [Notified Chemical] in Rats. Lab Project ID: WHI 30402757. Hazleton, WI, USA.

Hazleton (1993b) Skin Corrosivity Study of [Notified Chemical] in Rabbits. Lab Project ID: WHI 30402758. Hazleton, WI, USA.

Hazleton (1993c) Mutagenicity Test on [Notified Chemical] in the Salmonella/Mammalian-Microsome Reverse Mutation Assay (Ames Test). Lab Project ID: WHI 15728-0-401. Hazleton, WI, USA.

Kagaku Busshitsu Hyoka Kenyuusho (2002a) K01-2659.

Kagaku Busshitsu Hyoka Kenyuusho (2002b) Report on the Results of Toxicity Test by Repeated Adminstration for 28 Days Using the Mammals. B11-0679.

Kagaku Busshitsu Hyoka Kenyuusho (2002c) Report of Test Results of Chromosomal Aberrations Using Incubated Mammals Cells. K06-0911.

NHMRC (2011) Australian Drinking Water Guidelines 6. National Health and Medical Research Council, Canberra.

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edition [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NOTOX (2011a) Evaluation of the Mutagenic Activity of [Notified Chemical] in an In Vitro Mammalian Cell Gene Mutation Test with L5178Y mouse Lymphoma Cells (with Independent Repeat). NOTOX Project: 495792. NOTOX B.V., Netherlands.

NOTOX (2011b) Micronucleus Test in Bone Marrow Cells of the Mouse with [Notified Chemical]. NOTOX Project: 495791. NOTOX B.V., Netherlands.

NOTOX (2012) Combined 28-Day Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test of [Notified Chemical] in Rats by Oral Gavage Followed by a 14-Day and 28-Day Recovery Period (Report Number: 495981, 19 January 2012) NOTOX B.V., Netherlands.

NOTOX B.V. (2011a) Determination of Physico-chemical Properties of [notified chemical] (Project No. 495968, 05 Sep 2011). 's-Hertogenbosch, The Netherlands, NOTOX B.V. (Unpublished report submitted by 3M Australia Pty Ltd).

NOTOX B.V. (2011b) Determination of Physico-chemical Properties of [notified chemical] (Project No. 495988, 05 Jan 2011). 's-Hertogenbosch, The Netherlands, NOTOX B.V. (Unpublished report submitted by 3M Australia Pty Ltd).

NOTOX B.V. (2011c) Fresh Water Algal Growth Inhibition Test with [notified chemical] (Project No. 495945, 21 Jun 2011). 's-Hertogenbosch, The Netherlands, NOTOX B.V. (Unpublished report submitted by 3M Australia Pty Ltd).

NOTOX B.V. (2011d) Activated Sludge Respiration Inhibition Test (Carbon and Ammonium Oxidation) with [notified chemical] (Project No. 495987, 07 Nov 2011). 's-Hertogenbosch, The Netherlands, NOTOX B.V. (Unpublished report submitted by 3M Australia Pty Ltd).

NSF (2011) Test Report. Scotchkote Pipe Renewal Liner 2400. J-00102016. NSF International, MI, USA.

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia.

Springborn Laboratories (1995a) [Notified chemical] – Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) under Static Conditions (Report No.: 95-9-6114, 1995). Massachusetts, USA, Springborn Laboratories. (Unpublished report submitted by 3M Australia Pty Ltd).

Springborn Laboratories (1995b) [Notified chemical] – Acute Toxicity to Daphnia (*Daphnia magna*) under Static Conditions (Report No.: 95-9-6113, 1995). Massachusetts, USA, Springborn Laboratories. (Unpublished report submitted by 3M Australia Pty Ltd).

Springborn Laboratories (1995c) [Notified chemical] –Toxicity to the Freshwater Green Alga, *Selenastrum capricornutum* (Report No.: 95-9-6108, 1995). Massachusetts, USA, Springborn Laboratories. (Unpublished report submitted by 3M Australia Pty Ltd).

Springborn Laboratories (1996) [Notified chemical] –Toxicity to the Freshwater Green Alga, *Selenastrum capricornutum*, with the Addition of Humic Acid (Report No.: 95-9-6108, 1996). Massachusetts, USA, Springborn Laboratories. (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow (2005a) Estimation of the Adsorption Coefficient (K_{OC}) on Soil and on Sewage Sludge Using High Performance Liquid Chromatography (Study No.: 8912-05, 2005). 12852 Sugar Land, Texas, USA, Stillmeadow Inc. (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow (2005b) [Notified Chemical] Acute Oral Toxicity Study in Rats. Lab Study No.: 6436-01. Stillmeadow Inc., TX, USA (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow (2005c) [Notified Chemical] Acute Dermal Toxicity Study in Rats. Lab Study No.: 8913-05. Stillmeadow Inc., TX, USA (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow (2005d) [Notified Chemical] Acute Dermal Toxicity Study in Rats. Lab Study No.: 9021-05. Stillmeadow Inc., TX, USA (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow (2005e) [Notified Chemical] Skin Sensitisation: Local Lymph Node Assay in Mice. Lab Study No.: 8914-05. Stillmeadow Inc., TX, USA (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow (2005f) Activited Sludge, Bacterial Respiration Inhibition Test (Study No.: 9155-05, 2005). 12852 Sugar Land, Texas, USA, Stillmeadow Inc. (Unpublished report submitted by 3M Australia Pty Ltd).

Stillmeadow Inc (2005g) Activited Sludge, Bacterial Respiration Inhibition Test (Study No.: 9155-05, 2005). 12852 Sugar Land, Texas, USA, Stillmeadow Inc. (Unpublished report submitted by 3M Australia Pty Ltd).

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 >.

Water Quality Association (2011) 3M Company – Corrosion Protection Products Division Test Report. 3M Skotchkote Pipe Renewal Liner 2400. Water Quality Association, International headquarters, IL USA.

WRc-NSF (2011) Testing to AS/NZS 4020: 2005, Products for Use in Contact with Drinking Water. Report Number: MAT/ASN 021J. WRc-NSW Ltd, Swindon, Wiltshire UK.

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 >.