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September 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

2-Propanone, reaction products with 5-amino-1,3,3-trimethylcyclohexanemethanamine, reduced

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

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1656	PPG Industries Australia Pty Ltd	2-Propanone, reaction products with 5-amino-1,3,3-trimethylcyclohexanemethanamine, reduced	Yes	≤ 40 tonnes per annum	Component of industrial automotive coatings

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Acute toxicity, dermal (Category 3)	H311 – Toxic in contact with skin
Skin corrosion/irritation (Category 1B)	H314 – Causes severe skin burns and eye damage
Serious eye damage (Category 1)	H318 – Causes serious eye damage
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction
Specific target organ toxicity (repeated exposure) (Category 2)	H373 – May cause damage to organs through prolonged or repeated exposure

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

Hazard classification	*Hazard statement*
Acute toxicity (Category 2)	H401 – Toxic to aquatic life
Chronic toxicity (Category 2)	H411 – Toxic to aquatic life with long lasting effects

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

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

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

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Acute toxicity, dermal (Category 3): H311 – Toxic in contact with skin
  - Skin corrosion/irritation (Category 1B): H314 – Causes severe skin burns and eye damage

- Skin sensitisation (Category 1): H317 – May cause an allergic skin reaction
- Serious eye damage/eye irritation (Category 1): H318 – Causes serious eye damage
- Specific target organ toxicity, repeated exposure (Category 2): H373 – May cause damage to organs through prolonged or repeated exposure

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

Health Surveillance

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

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation and end use:
  - Enclosed, automated processes, where possible
  - Sufficient ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical for reformulation and during end use:
  - Avoid contact with skin and eye
  - Avoid inhalation of mists or aerosols

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during reformulation and end use:
  - Impervious gloves
  - Boots
  - Coveralls
  - Safety glasses
  - Respiratory protection

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

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

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

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

Disposal

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

Storage

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

Emergency procedures

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

Transport and Packaging

- Due to the corrosive properties of the notified chemical, introducers of the chemical should consider their obligations under *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG code) (NTC, 2017).

Regulatory Obligations

Secondary Notification

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

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

(1) Under Section 64(1) of the Act; if
  - the composition of the chemical has changed, or is likely to change significantly, contributing to changes in its toxicology profile;

or

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

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

Safety Data Sheet
The SDSs of the notified chemical and a product containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDSs remains the responsibility of the applicant.

ASSESSMENT DETAILS

This notification has been conducted under the cooperative arrangement with Canada. The health and environmental hazard assessment components of the Canadian report were provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
PPG Industries Australia Pty Ltd (ABN: 82 055 500 939)
14 – 20 McNaughton Road
CLAYTON VIC 3168

NOTIFICATION CATEGORY
Standard (reduced fee notification): Chemical other than polymer (more than 1 tonne per year) – Approved Foreign Scheme – Canada

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: spectral data, degree of purity, impurities, use details and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for dissociation constant and bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2005)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
JEFFLINK® 754

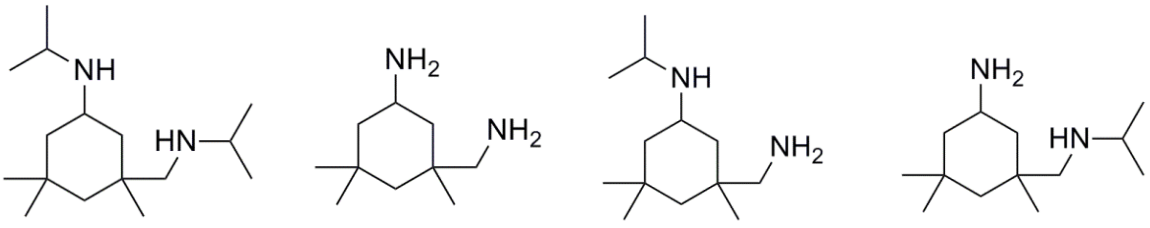
CAS NUMBER
156105-38-3

CHEMICAL NAME
2-Propanone, reaction products with 5-amino-1,3,3-trimethylcyclohexanemethanamine, reduced

MOLECULAR FORMULA
Unspecified

The notified chemical is a substance of Unknown, of Variable Composition, or of Biological Origin (UVCB).

STRUCTURAL FORMULA



Component 1 Component 2 Component 3 Component 4

Representative structures of the notified chemical

MOLECULAR WEIGHT
170.3 – 254.46 g/mol

ANALYTICAL DATA
Reference NMR, IR, GC-MS and UV-Vis spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 98%

The notifier provided the following:

Component 1: > 90%
Component 2: < 1%
Combined Components 3 and 4: 1 – 10%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless liquid

Property	Value	Data Source/Justification
Freezing Point	< -78 °C	Assessed by Canada
Boiling Point	276 – 278 °C	Assessed by Canada
Density	860 kg/m^3 at 20 °C	Assessed by Canada
Vapour Pressure	1.12 × 10^{-2} kPa at 20 °C	Assessed by Canada
Water Solubility	4.1 g/L at 20 °C	Assessed by Canada
Hydrolysis as a Function of pH	t ½ > 1 year at pH 4, 7 and 9	Assessed by Canada
Partition Coefficient (n-octanol/water)	log Pow = 4.5 – 4.6 at 23.5 °C	Assessed by Canada
Surface Tension	35.7 mN/m at 20 °C	Measured; regarded as surface active
Adsorption/Desorption	log K_{oc} > 5.63 at 35 °C	Assessed by Canada
Dissociation Constant	pKa = 10.15 - 11	Assessed by Canada
Flash Point	103.5 °C (closed cup)	Measured
Flammability	Combustible liquid[#]	Based on measured flash point and boiling point
Flammability in contact with water	Not flammable in contact with water	Measured
Autoignition Temperature	260 °C	Measured
Explosive Properties	Not explosive	Based on the chemical structure
Oxidising Properties	Not oxidising	Based on the chemical structure
Pyrophoric Properties	Not pyrophoric	Based on the chemical structure

Based on *Australian Standard AS1940 definitions*

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties that were not assessed by Canada, refer to Appendix A.

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

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical may not be recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*, as adopted for industrial chemicals in Australia. However, due to corrosive properties of the notified chemical, it is considered a dangerous good (Class 8, UN 2735, amines, liquid, corrosive, not otherwise specified (N.O.S.)) under *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG Code) (NTC, 2017).

The notified chemical has a flash point of 103.5 ºC which is greater than 93 °C but less than its boiling point (276 – 278 ºC). Based on *Australian Standard AS1940* definitions for combustible liquid, the notified chemical is considered to be a Class C2 combustible liquid.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. The majority of the notified chemical will be imported as a component of a finished two-part coating system at ≤ 30% concentration. The notified chemical may also be imported in the neat form for local reformulation into coatings.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	10 – 40	10 – 40	10 – 40	10 – 40	10 – 40

PORT OF ENTRY
Melbourne and Sydney

IDENTITY OF RECIPIENT
PPG Industries Australia Pty Ltd

TRANSPORTATION AND PACKAGING
Finished coatings containing the notified chemical at ≤ 30% concentration will be imported in 20 L cans or 205 L drums. The notified chemical in the neat form will be imported in lined 205 L drums, and will be distributed for local reformulation into end-use coatings. The notified chemical and products containing the notified chemical will be transported by road and rail for distribution.

The notified chemical is considered to be a dangerous good and introducers of the notified chemical will follow their obligations under the ADG code (NTC, 2017).

USE
The notified chemical will be used as a component of industrial automotive coatings at ≤ 30% concentration.

OPERATION DESCRIPTION

Reformulation
The notified chemical will be added into 10,000 L blending tanks with other components using automated equipment and hoses. The mixtures will be mixed by high speed dispersion. Additional solvents and binders will be then added to form the finished coating products. Quality assurance (QA) workers will transfer small samples of the coating products for testing. The finished coatings will be pumped into filling machines and filled into 0.5 to 20 L metal cans or 205 L drums for end-use distribution.

The mixing and filling processes of the coating products containing the notified chemical are expected to be automated in enclosed systems with local exhaust ventilation.

End Use
The finished two-part coating products containing the notified chemical at concentration of ≤ 30% will be applied by spray using specialised painting equipment in industrial settings, such as vehicle repair shops and vehicle manufacturing facilities. For a typical use, the two parts of the coating system will be mixed in-line at the application nozzle and the coating will then be sprayed onto the automotive surface. The application will be carried out in designated spray booths with ventilation to capture any mists or overspray formed.

The spray equipment used to apply the coating products will be cleaned with solvents. Professional automotive body shops will use special enclosed cabinets for spray equipment cleaning. Any rinse-off and cleaning cloths used to absorb the waste will be collected and disposed of in accordance to the environmental regulations.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage	1 – 2	2 – 4
Reformulation	2 – 4	5 – 10
QA	0.5	1 – 2
Spray painting	4 – 12	10 – 50

EXPOSURE DETAILS

Transport and Storage

Transport and storage workers may come into contact with the notified chemical only in the unlikely event of an accident, breaching the containers.

Reformulation

For coating product reformulations, dermal and ocular exposure of workers to the notified chemical in neat form may occur when mixing and transferring materials containing the chemical or during QA laboratory testing, equipment cleaning and maintenance. Given that the notified chemical has relatively low vapour pressure, significant inhalation exposure is not expected, unless aerosols or mists are formed during the mixing processes. Exposure to the notified chemical is expected to be minimised through the use of enclosed and automated systems, local exhaust ventilation and suitable personal protective equipment (PPE) capable of protecting workers from exposure to the notified chemical, including impervious rubber gloves, safety glasses with side protection or goggles, protective clothing and respiratory protection if necessary.

End use

Professional workers will apply coatings containing the notified chemical at ≤ 30% in a controlled industrial setting, and may be exposed (dermal, ocular and inhalation) to the notified chemical during the spray application of finished coatings. Exposure should be minimised through the recommended use of engineering controls such as spray booths, specialised cleaning equipment and local exhaust ventilations, and PPE for workers as described on the product safety data sheets (SDS) including coveralls, gloves, goggles, and respiratory protection.

Once the coatings are cured, the notified chemical will be bound within the coating matrix and will not be available for exposure.

6.1.2. Public Exposure

Coatings containing the notified chemical will not be available to the general public. The finished coatings will require a high level of equipment and expertise to be applied successfully and will be used exclusively by professional workers.

Members of the public may come into contact with coated articles; however, once the coatings are cured, the notified chemical is expected to be bound into the inert matrix and will not be available for exposure.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of tests on human health effects that were not assessed by Canada, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity*	LD50 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity*	LD50 = 50 – 400 mg/kg bw (in female rats); fatal
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw (in male rats); low toxicity LD50 < 2,000 mg/kg bw (in female rats)
Rabbit, skin irritation	corrosive
Eye irritation (*in vitro*)	expect to be severely irritating
Mouse, skin sensitisation – Local lymph node assay*	evidence of sensitisation, EC3 = 1%

Endpoint	*Result and Assessment Conclusion*
Rat, repeat dose oral toxicity – 28 days*	NOAEL = 50 mg/kg bw/day
Mutagenicity – bacterial reverse mutation*	non mutagenic
Genotoxicity – *in vitro* chromosome aberration*	non genotoxic
Genotoxicity – *in vitro* mammalian gene mutation	non genotoxic

* Assessed by Canada

Toxicokinetics
Based on the low molecular weight (< 500 g/mol), water solubility (4.1 g/L at 20 °C) and partition coefficient (log Pow = 4.5 – 4.6 at 23.5 °C) of the notified chemical, there is some potential for the chemical to cross biological membranes.

Acute toxicity
The notified chemical was tested in an acute oral toxicity study. Female rats were gavaged with the test substance diluted in water at 300 and 2,000 mg/kg bw, with 6 animals tested in each dose group. Symptoms of treatment included flat gait and piloerection, which resolved within three days. No abnormalities were noted at necropsy. Base on the results of this study, the notified chemical is of low acute toxicity via the oral route.

An acute dermal toxicity study was conducted on female rats using the notified chemical, in a stepwise manner. The test substance was applied dermally to one female rat at 1,000 mg/kg bw, resulting in lethargy, hunched posture, chromodacryorrhea, ptosis, leanness and hypothermia. Severe skin necrosis was noted on Days 2 and 3 and the animal was euthanised on Day 3. The test substance was then applied dermally to another rat at 400 mg/kg bw, resulting in lethargy, flat and hunched posture, laboured respiration, piloerection, chromodacryorrhea and severe necrosis of the skin. The animal was euthanised on Day 2. Subsequently, the test substance was applied dermally to another fresh rat at 50 mg/kg bw, resulting in flat or hunched posture, ptosis, chromodacryorrhea and piloerection up to Day 4. The test substance was applied to 4 additional female rats and 5 additional male rats at 50 mg/kg bw. Noted erythema, scales, scabs and necrosis resolved slowly and only scarring was noted in the animals on Day 15. Body weight changes were normal. Thickened and necrotic skin was noted up to necropsy but no other abnormalities were noted. The LD50 was established to be 50 – 400 mg/kg bw.

Although an LD50 of > 2,000 mg/kg bw was established for rats in another acute dermal toxicity study with the notified chemical, a significant difference in mortality was noted between males (0/5 died) and females (4/5 died). Dermal LD50 is < 2,000 mg/kg bw for female rats in this study, and it could be similar to the LD50 established in the previous dermal toxicity study on female rats (see above).

The notified chemical has been classified as acute dermal toxicity (Category 3) by the notifier in the application dossier, consistent with the classification on the ECHA C&L inventory.

Irritation
The notified chemical was tested in a skin irritation study. The notified chemical was found to be corrosive to the skin with severe erythema, oedema and skin necrosis observed in all animals when the test substance was applied. The notified chemical is expected to be a severe eye irritant, based on the results of *in vitro* bovine eye and chicken chorioallantoic membrane assays.

Sensitisation
A Local Lymph Node Assay was conducted in 6 groups of mice (5 female mice per group) for the notified chemical. The test substance was mixed with acetone and olive oil (4:1) and applied to the dorsal surface of the ears for 3 days. Test substance concentrations were 0, 0.25%, 0.5% and 1%. Nodes were increased in size in 1 animal treated at 0.25% concentration and 1 control animal (left side). No other abnormalities of the nodes were noted. Disintegrations per minute (dpm) was measured to be 251, 233 and 878 for 0.25%, 0.5% and 1% respectively. Based on the findings, two additional groups were treated at 5% and 10% concentrations respectively. Radioactivity in these groups was 22,812 and 29,340 dpm respectively. Increased size of the mandibular lymph nodes was noted in animals treated at 1%, 5% and 10% concentrations. The vehicle control group had a mean dpm value of 626. Based on the dose-related increased radioactivity detected in animals tested at 1%, 5% and 10% concentrations, the test substance was concluded to be a sensitizer with an EC3 = 1%.

Repeated dose toxicity
A repeated dose oral toxicity was conducted in Wistar rats (28 day test, 5 male and 5 female animals per dose level) for the notified chemical. Doses of the test substance administered were 0, 50, 150 and 450 mg/kg bw/day (water was used as the vehicle).

In the 450 mg/kg bw/day dose group, all animals were dead or sacrificed moribund within 3 – 5 days. Death was attributed to severe corrosion of the gastrointestinal tract (from necropsy findings). Enlarged liver of unspecified grade or severity was noted in all animals.

All rats in the 150 mg/kg bw/day dose group survived. Body weight gain was lower in all males and females compared to the control (17 – 18% less, however this was variable and was not found to be statistically significant due to a large standard deviation in weight gain values). All female animals showed enlarged liver (average enlargement was 36% absolute liver weight, compared to controls, and 48% relative to body weight, compared to controls) with isolated instances of necrotic cells. Elevated levels of some white blood cells and altered haematological parameters such as elevated cholesterol, reduced chloride, elevated potassium were found in the serum. Liver enzymes were elevated in female animals (ALT, AST (each 4-fold elevated) and AP) and clotting times were reduced (by 2 seconds) for male and female rats. Albumin and total protein levels were reduced (4 – 6% in males and females; statistically different from control values ($P < 0.05$) in males only). The reduced weight gain, hepatomegaly associated with biochemical and isolated instances of hepatocyte necrosis were together considered adverse. The other serum changes were not toxicologically relevant.

All rats in the 50 mg/kg bw/day dose group survived. Albumin and total protein levels were reduced (2 – 4%; not significantly different from control values). In the absence of significant adverse effects, the NOAEL was determined to be 50 mg/kg bw/day in rats.

Mutagenicity/Genotoxicity
A bacterial reverse mutation test was performed in *S. typhimurium* strains TA98, TA100, TA1535 and TA1537, and *E. coli* strain WP_2uvrA for the notified chemical. A plate incorporation assay was used, whereas a pre-incubation assay (Prival modification) might have been more specific and appropriate for this category of substance. Duplicate experiments were performed, altering only the amount of metabolic enzymes (S9 mix) added to the top agar mixture – 5% in the first experiment and 10% in the second experiment. The concentrations of the test substance were 100, 333, 1,000, 3,330 and 5,000 µg/mL. The test substance precipitated at 3,330 and 5,000 µg/plate. Cytotoxicity (detected as a decrease in background lawn) was noted in TA1537 at 5,000 µg/plate only (Experiment 1) or in TA98 and TA1537 at 5,000 µg/plate and TA100 at 3,330 and 5,000 µg/plate (Experiment 2). All cytotoxicity was noted only in the absence of metabolic activation. No increase in revertant number was noted at any of the tested concentrations. The notified chemical was not considered mutagenic to bacteria under the conditions of this study.

A chromosome aberration study was conducted in cultured peripheral human lymphocytes for the notified chemical. Based on a range-finding assay, cytogenetic assay 1 was conducted using 100, 333, 420, 580, 720 and 860 µg/mL of the test substance (3 hours exposure and 24 hours fixation, in the presence or absence of metabolic activation (S9 mix)). To reach a better final cytotoxicity, cytogenetic assay 1A (3 hours exposure and 24 hours fixation) was carried out at 400, 500, 600, 650, 700 and 750 µg/mL (in the absence of metabolic activation) and at 400, 600, 700, 750, 800 and 850 µg/mL (in the presence of metabolic activation). The dose levels selected for scoring of chromosomal aberrations were 400, 500 and 600 µg/mL (in the absence of metabolic activation 9) and 400, 600 and 700 µg/mL (in the presence of metabolic activation).

In cytogenetic assay 2, cells were continuously exposed to the test substance in the absence of metabolic activation for 24 or 48 hours. Concentrations used were 10, 33, 66, 100 and 166 µg/mL (24 hours exposure and 24 hours fixation), or 33, 100, 166, 333, 400, 500 and 600 µg/mL (48 hours exposure and 48 hours fixation). In the presence of metabolic activation, concentrations used were 100, 333, 420, 580, 720 and 860 µg/mL (3 hours exposure and 48hours fixation). In both experiments, the test substance did not induce an increase in the number of cells with chromosomal aberrations and was not considered to be clastogenic.

However, polyploidy was noted for all experiments. For experiment 1A, 4, 11 and 10 polyploid cells out of 200 scored cells were noted at 400, 500 and 600 µg/mL, respectively (in the absence of metabolic activation). Three, 5 and 6 polyploid cells out of 200 scored cells were noted at 400, 600 and 700 µg/mL, respectively (in the presence of metabolic activation). For experiment 2, at 166 µg/mL (24 hours exposure and 24 hours fixation, in the absence of metabolic activation), 2 out of 200 cells were polyploid. At 166 µg/mL (48 hours exposuree and 48 hours fixation, in the absence of metabolic activation), 5 out of 200 cells were polyploid. At 580, 720 and 860

µg/mL (3 hours exposure and 48 hours fixation, in the presence of metabolic activation), there were 2, 2 and 1 polyploid cells per 200 scored cells, respectively, compared to 2 polyploid cells out of 200 cells in the negative (ethanol) control group. Although the test substance was concluded to be negative for chromosomal aberration induction *in vitro*, it induced polyploidy in the cells when applied at relatively high dose levels. Polyploidy is not considered a chromosomal aberration and is considered to be a biological event with a threshold.

The notified chemical was negative in an *in vitro* mammalian cell gene mutation test.

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

Hazard classification	*Hazard statement*
Acute toxicity, dermal (Category 3)	H311 – Toxic in contact with skin
Skin corrosion/irritation (Category 1B)	H314 – Causes severe skin burns and eye damage
Serious eye damage (Category 1)	H318 – Causes serious eye damage
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction
Specific target organ toxicity (repeated exposure) (Category 2)	H373 – May cause damage to organs through prolonged or repeated exposure

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available information, the notified chemical presents a concern for a number of acute and chronic health effects, including acute toxicity, corrosion and eye damage, sensitisation and damage to organs with repeated exposure. Therefore, exposure via any route to the notified chemical should be avoided.

During reformulation and application of coatings containing the notified chemical, dermal, ocular and inhalation exposure of workers is expected to be limited by the use of engineering controls and PPE. Once the coating has dried and cured, the notified chemical will be bound within an inert solid matrix and is not expected to be available for exposure.

Therefore, given the expected low exposure under the conditions of the occupational settings, the risk to workers from use of the notified chemical is not considered to be unreasonable.

6.3.2. Public Health
The notified chemical will be used in industrial settings only and will not be made available to the public. Members of the public may come into contact with coated articles containing the notified chemical; however, once the coating has dried and cured, the notified chemical is expected to be bound into an inert matrix and will not be available for exposure.

Based on the assessed use patterns, the risk to the public from use of the notified chemical is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The release of the notified chemical to the environment during importation, storage, and transport is unlikely. Release during reformulation in Australia is expected to arise from spills, formulation equipment cleaning and residues in import containers. Accidental spills during transport or reformulation are expected to be captured in a solvent. The solvent is recycled with residue being disposed of to landfill. Import containers will either be recycled or disposed of through an approved waste management facility. Less than 0.5% of the import volume is estimated to be released to landfill as a result of reformulation in Australia.

RELEASE OF CHEMICAL FROM USE

During application by spray, it is expected that up to 20% of the notified chemical will be released as overspray, which will be collected, allowed to cure and disposed of to landfill. Residues containing the notified chemical on brushes and rollers are expected to be rinsed into containers and then allowed to cure before disposal as solid wastes to landfill. Less than 2% of the notified chemical may remain as residues in product containers and these will be disposed of to landfill or recycled. Equipment used to apply the coating formulations may be rinsed with solvent. The solvent is expected to be recycled with residue being disposed of to landfill. It is estimated that less than 1% of the import volume of the notified chemical will be collected from cleaning of equipment, which is expected to be treated and disposed of by a licensed waste contractor.

RELEASE OF CHEMICAL FROM DISPOSAL

The majority of the notified chemical will be cured into an inert matrix with other chemical substances as part of the coating process and hence will be immobilised within a film on coated articles. The articles coated with the notified chemical, at the end of their useful life, are expected to either go to metal recyclers or be disposed of to landfill.

7.1.2. Environmental Fate

The notified chemical is not to be readily biodegradable (7% biodegradability over 29 days; assessed by Canada). When used as one component of a two-part system for industrial coating of steel, the majority of the notified chemical is expected to cross-link to form an inert polymer film after its application. The notified chemical will share the fate of the coated articles, which are expected to be eventually disposed of to landfill or be subjected to metal reclamation. In its cured form, the notified chemical is not expected to be bioavailable or mobile in the environment. The notified chemical will eventually degrade in landfill via biotic or abiotic pathways, or by thermal decomposition during metal reclamation processes, to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The notified chemical is not expected to be present at significant concentrations in the aquatic environment because of the very low potential for direct release to surface waters when used in automotive coating or metal surfaces coating for industrial applications. Therefore, a predicted Environmental concentration (PEC) has not been calculated.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. For full details of the studies that were not assessed by Canada, refer to Appendix C.

Endpoint	*Result (mg/L)*	*Assessment Conclusion*
Fish Toxicity	LC50 (96 h) > 100 mg/L	Not harmful to fish
Daphnia Toxicity	EC50 (48 h) = 16 mg/L	Toxic to aquatic invertebrates
Algal Toxicity	E_rC50 (72 h) = 8.5 mg/L	Toxic to algae
Inhibition of Bacterial respiration	EC50 (3 h) > 100 mg/L	Not inhibitory to bacterial respiration

Based on the endpoints for fish, Daphnia and algal toxicity, the notified chemical is considered to be toxic to aquatic organisms on an acute basis, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009). Therefore, the notified chemical is formally classified as "Acute Category 2; Toxic to aquatic life" under the GHS. Based on the acute toxicity and potential for the notified chemical to persist in the environment, the chronic hazard of the notified chemical has been formally classified as "Chronic Category 2; Toxic to aquatic life with long lasting effects" under the GHS.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) for the notified chemical has been calculated and is presented in the table below. The PNEC is calculated based on the endpoint of the most sensitive species (Algae, 72 h EC50 = 8.5 mg/L). An assessment factor of 100 has been used as acute toxicity endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EL50 (Daphnia)	8.5	mg/L
Assessment Factor	100	
PNEC:	85	µg/L

7.3. Environmental Risk Assessment

A Risk Quotient is unable to be quantified as a PEC was not calculated. There is no significant aquatic release of the notified chemical anticipated based on its reported use pattern. Moreover, after curing, the majority of the notified chemical will be irreversibly incorporated into an inert matrix and it is not expected to be mobile, bioavailable or bioaccumulative. On the basis of the assessed use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Surface Tension 35.7 mN/m at 20 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions EEC Directive 92/69 A.5 Surface Tension
Remarks	Concentration: 1.06 g/L The notified chemical is considered surface active.
Test Facility	NOTOX (2004a)

Flash Point 103.5 °C

Method	EEC Directive 92/69 A.9 Flash Point
Remarks	Closed cup method
Test Facility	NOTOX (2004b)

Flammability in Contact with Water Not flammable in contact with water

Method	EEC Directive 92/69 A.12 Flammability (Contact with Water)
Remarks	No development of dangerous amount of (flammable) gas was noted.
Test Facility	NOTOX (2004c)

Autoignition Temperature 260°C

Method	EEC Directive 92/69 A.15 Auto-Ignition Temperature (Liquids and Gases)
Test Facility	NOTOX (2004d)

Explosive Properties Non-explosive

Method	EEC Directive 92/69 A.14 Explosive Properties.
Remarks	The molecular structure of the notified chemical does not contain oxygen or any chemically instable or highly energetic groups that might lead to an explosion.
Test Facility	NOTOX (2004e)

Oxidizing Properties Non-oxidising

Method	EEC Directive 92/69 A.21 Oxidizing Properties (Liquids)
Remarks	The molecular structure of the notified chemical does not contain oxygen or any group that might act as an oxidising agent.
Test Facility	NOTOX (2004f)

Pyrophoric Properties Non-pyrophoric

Method	EEC Directive 92/69 A.13 Pyrophoric Properties of Solids and Liquids
Remarks	The molecular structure of the notified chemical does not contain any chemical groups that might lead to spontaneous ignition a short time after coming into contact with air. The non-pyrophoric property was also supported by experience in handling the notified chemical.
Test Facility	NOTOX (2004g)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity
Species/Strain	Rat/Sprague-Dawley
Vehicle	None
Type of dressing	Semi-occlusive
Remarks - Method	Five male and 5 female animals were treated with the test substance dermally at 2000 mg/kg bw. It is recommended in the OECD TG 402 that females should normally be used.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	10 (5F, 5M)	2,000	4/10 (all F)

LD50	> 2,000 mg/kg bw in male rats and < 2,000 mg/kg bw in female rats
Signs of Toxicity - Local	Severe erythema and oedema were observed in 1 animal, while all other animals showed skin necrosis at all application sites.
Signs of Toxicity - Systemic	4/5 female animals were found dead on Days 4 and 5. Clinical signs noted in the surviving animals on Days 2 – 15 included abnormal gait and stance, decreased activity, decreased body tone, piloerection, discoloured fur around eyes, prostration and/or thin body condition. 5/6 surviving animals (4 male and 1 female) gained body weight over Days 8 – 15. The remaining male animal lost weight during the study.
Effects in Organs	Lesions were noted in the stomach and intestines of the animals found dead on Days 4 and 5. No visible lesions were noted in the surviving animals.
Remarks - Results	The established LD50 > 2,000 mg/kg bw in this study was based on 4/10 animals died. However, a significant difference in mortality was noted between male (0/5 died) and female animals (4/5 died). According to the OECD TG 402, in the cases where differences are noted, females are generally slightly more sensitive. Therefore, there is some uncertainty with the established LD50 in this study.
CONCLUSION	A LD50 was established as > 2,000 mg/kg bw in this study. However, there is some uncertainty with the established LD50 due to a significant difference in sensitivity between female and male animals.
TEST FACILITY	Calvert (2011)

B.2. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	3 days
Type of Dressing	Semi-occlusive
Remarks - Method	Three application sites were used on each animal, with exposure periods of 3 minutes, 60 minutes and 4 hours respectively.

RESULTS

3 Minutes Exposure Time

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	2.3	4	4	4	72 h	4
Oedema	1	4	4	4	72 h	4

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

60 Minutes Exposure Time

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	3.3	4	4	4	72 h	4
Oedema	3.7	4	4	4	72 h	4

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

4 Hours Exposure Time

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	4	4	4	4	72 h	4
Oedema	4	4	4	4	72 h	4

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

Remarks - Results: No skin corrosive responses were noted at the 3-minute exposure site within the 1-hour observation period. Necrosis was noted in 2 animals at the 3-minute exposure site on Day 3, in 2 animals at the 60-minute exposure site on Day 2, and in all animals at the 4 hour exposure site on Day 2.

CONCLUSION: The notified chemical is corrosive to the skin.

TEST FACILITY: Calvert (2005)

B.3. Irritation – eye (*in vitro* bovine eye and chicken chorioallantoic membrane assays)

TEST SUBSTANCE: Notified chemical

METHOD: Based on methods described by Luepke N.P. (1985) and Weterings, P.J.J.M. and van Erp, Y.H.M. (1987)

Bovine eye (BE) assay: 8 bovine eyes were equilibrated with saline for 5 minutes. The test substance was applied to the cornea of 5 bovine eyes. One bovine eye was left untreated and the two control bovine eyes received toluene and acetone respectively. The treated bovine eyes were rinsed after 0.5 minute exposure and incubated for 10 minutes. Corneal injuries were assessed by evaluating the opacity and epithelial detachment, followed by application of sodium fluorescein to examine the integrity of the corneal epithelium.

Chicken chorioallantoic membrane (CAM) assay: eggs were incubated for 10 days at 37 ± 1 °C and turned once every hour. Eggs were placed in an upright position of the seventh day of incubation. On the tenth day, the chorioallantoic membrane (CAM) was exposed by removing the outer shell and shell membrane. The test substance was tested on 4 eggs. The effects on the blood capillaries were evaluated 30 seconds after application and 1.5 and 4.5 minutes later.

Vehicle	None
Remarks - Method	It was stated in the study report that the assays were considered to be valid when the scores obtained with the reference substances fall within the range of the historical data of the test laboratory (below) and no effects were noted in the negative control. Furthermore, the effects produced by acetone should exceed those noted with toluene in the same test. BE assay score: toluene 0.5-1.5; acetone 3.0-3.5 CAM assay score: toluene 1.0-2.5; acetone 2.0-3.5

RESULTS

Test material	*Bovine eye (BE) assay mean score*	*Chicken chorioallantoic membrane (CAM) assay mean score*
Negative control	0	0
Test substance	5.5	5
Positive control (Toluene)	1.5	1
Positive control (Acetone)	3.5	2

Remarks - Results	BE assay: the corneal epithelium in bovine eyes were absent after treatment with the test substance and therefore no judgement could be made on the opacity. Epithelial integrity was confluent and intense in all bovine eyes treated with the test substance. CAM assay: injection and haemorrhages were noted after 30 seconds in all eggs treated with the test substance. No coagulation was noted on the blood capillaries of the chorioallantoic membrane, although the protein of all eggs showed coagulation. The combined mean scores from BE and CAM assays indicated severe irritancy (severe would apply if > 3.5 for BE and > 5.0 for CAM). The positive and negative controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	The notified chemical is expected to be a severe eye irritant, based on the results of this study.
TEST FACILITY	NOTOX (2004h)

B.4. Mutagenicity – *in vitro* mammalian cell gene mutation

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test
Species/Strain	Mouse
Cell Type/Cell Line	Mouse lymphoma cells/L5178Y ($TK^{+/-}$-3.7.2C)
Metabolic Activation System	S9 mix from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	Dimethyl sulfoxide
Remarks - Method	No significant deviations of protocol were noted. A dose range-finding study was carried out. The dose selection for the main experiments was based on toxicity observed in a range-finding study carried out at 33 – 3330 μg/mL and a solubility test. Vehicle and positive controls (methyl methanesulfonate and cyclophosphamide) were run concurrently with the test substance.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			

Test 1	1, 5, 10*, 50*, 100*, 150, 200*, 250, 300*, 350*, 400*, 450*	3 h	2 days
Test 2	5, 10, 50*, 75*, 100*, 125*, 150*, 200*, 250*, 275*, 300, 350, 400	24 h	2 days
Present			
Test 1	10, 50*, 100*, 250*, 500*, 600*, 700*, 800*, 900*, 1000, 1250	3 h	2 days
Test 2	10, 50*, 100*, 250*, 500*, 600*, 650, 700*, 725, 750*, 775, 800*, 825, 850	3 h	2 days

*Cultures selected for mutation frequency analysis

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 100	> 200	≥ 3330*	Negative
Test 2	> 333	> 150	≥ 3330*	Negative
Present				
Test 1	> 33	> 600	≥ 3330*	Negative
Test 2		> 500		Negative

* Reported in the range-finding study

Remarks - Results

The test substance did not induce a statistically significant increase in the mutation frequency, either in the presence or absence of metabolic activation, at any concentration tested.

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

CONCLUSION

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

TEST FACILITY

NOTOX (2005)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sludge
Exposure Period	30 minutes
Concentration Range	Nominal: 100 mg/L.
Remarks – Method	The test was conducted in accordance with the test guideline without significant deviations. Good Laboratory Practice (GLP) was followed. In a preliminary test activated sewage sludge was exposed to the test substance at a nominal concentration 100 mg/L for a period of 30 minutes at 20 ± 1 °C with the addition of a synthetic sewage as a respiratory substrate. As no inhibition of respiration of the sludge was recorded, it was considered that no further testing was necessary. 3,5-Dicholoro phenol was used as a reference substance.
EC50	> 100 mg/L
Remarks – Results	All validity criteria for the test were satisfied. The blank control respiration rate was 35 mg O_2/L/h. The EC50 of the reference substance was 10 mg/L.
CONCLUSION	The notified chemical is not expected to inhibit microbial respiration
TEST FACILITY	NOTOX (2004i)

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