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November 2019

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1,2-Ethanediol, 1,2-dibenzoate

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/1688	Nouryon Chemicals Australia Pty Ltd	1,2-Ethanediol, 1,2-dibenzoate	No	≤ 20 tonnes per annum	Component of surface coatings for industrial use

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

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*
Chronic (Category 2)	H411 – 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.

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

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 during mixing of the notified chemical:
  - Enclosed systems

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during transfer to the enclosed system:
  - Avoid contact with eyes and skin

- 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 transfer to the enclosed system, cleaning and maintenance:
  - Protective clothing
  - Goggles
  - Impervious gloves
  - Respiratory protection (if inhalation exposure is expected)

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.

Emergency procedures

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

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.

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

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

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

ASSESSMENT DETAILS

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)
Nouryon Chemicals Australia Pty Ltd (ABN: 64 621 806 273)
8 Kellaway Place
WETHERILL PARK NSW 2164

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include other names, analytical data, degree of purity, impurities, additives/adjuvants and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for hydrolysis as a function of pH, dissociation constant, flash point, autoignition temperature, explosive properties, oxidising properties, acute inhalation toxicity and bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2018)

2. IDENTITY OF CHEMICAL

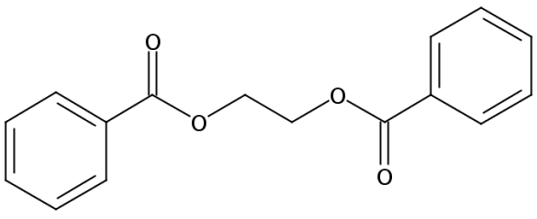
MARKETING NAME(S)
Perkadox® GB-50 (product containing ~50% notified chemical)

CHEMICAL NAME
1,2-Ethanediol, 1,2-dibenzoate

CAS NUMBER
94-49-5

MOLECULAR FORMULA
$C_{16}H_{14}O_4$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
270.28 g/mol

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

3. COMPOSITION

DEGREE OF PURITY
> 99%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: White powder

Property	*Value*	*Data Source/Justification*
Melting Point*	70 °C	Measured
Boiling Point*	365 °C at 101.3 kPa	Measured
Density*	1,340.4 kg/m^3 at 20 °C	Measured
Vapour Pressure*	5.6 × 10^{-9} kPa at 25 °C	Measured
Water Solubility*	2.3 × 10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities but significant hydrolysis is not expected in environmental pH range of 4-9
Partition Coefficient (n-octanol/water)*	log Pow = 3.75	Measured
Adsorption/Desorption	log Koc = 3.1 – 3.8 at 20 – 25 °C	Measured
Dissociation Constant	Not determined	Contains no dissociable functionalities
Particle Size*	Inhalable fraction (< 100 μm): 5.2% Respirable fraction (< 10 μm): 0.48% Respirable fraction (< 5 μm): 0.22%	Measured
Flammability	Not highly flammable	Measured
Autoignition Temperature	Not flammable	Not expected to auto-ignite based on measured flammability results
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties

* Assessed by Canada

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 is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured within Australia. It will be imported into Australia at ~50% concentration as a component of organic peroxide formulations for industrial use.

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

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

PORT OF ENTRY
Melbourne and Sydney

IDENTITY OF RECIPIENT(S)
Nouryon Chemicals Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The product Perkadox® GB-50 containing ~50% notified chemical will be imported in 24 kg cartons and transported within Australia by road.

USE
The notified chemical will be used as a component of organic peroxide formulations which will be used as a catalyst for the curing of resin-based road line marking.

OPERATION DESCRIPTION
The imported product Perkadox® GB-50 will be added manually into one of the reservoirs of the purpose-designed two-component road marking machine. It will be dosed in-line and mixed with resins inside the road marking machine just before the coating is sprayed (airless spray) onto the road surface. The concentration of the notified chemical in the end-use coating is expected to be ≤ 1.5%.

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 Warehousing	2-4	12
Road Marking	8	250

EXPOSURE DETAILS

Transport and storage
Transport, storage and trade sale workers are not expected to be exposed to the notified chemical except in the unlikely event of accidental rupture of the packaging.

End-use
Dermal or ocular exposure to the notified chemical at ≤ 50% concentration may occur during manual transfer into road marking machine reservoir and road marking operations, and during cleaning and maintenance of equipment. Exposure will be mitigated by the use of engineering controls (including enclosed purpose-designed road marking machines) and personal protective equipment (PPE: goggles, impervious gloves and protective clothing), as anticipated by the notifier. Inhalation exposure is not expected to be significant as spray will be airless, conducted with good ventilation (outdoors), and directed towards the ground and hence droplets are unlikely to reach the breathing zone to a significant extent. Once the coating is cured and dried, the notified chemical will be bound into the coating matrix and will not be available for exposure.

6.1.2. Public Exposure
The product containing the notified chemical (at ≤ 50% concentration) is intended for industrial use and will not be made available to the public. The public may have dermal contact with the coated road surface containing the notified chemical at ≤ 1.5% concentration. However, once the coating is cured and dried, the notified chemical will be bound into the coating 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*
Acute oral toxicity – rat*	LD50 > 2000 mg/kg bw; low toxicity
Acute dermal toxicity – rat*	LD50 > 2000 mg/kg bw; low toxicity
Skin irritation – rabbit*	non-irritating
Skin irritation – *in vitro* human skin model*	non-irritating
Eye irritation – rabbit*	slightly irritating
Eye irritation – *in vitro* EpiOcular cornea epithelial model*	non-irritating
Skin sensitisation – mouse local lymph node assay*	no evidence of sensitisation (up to 25% concentration)
Skin sensitisation – *in chemico DPRA test*	inconclusive
Combined repeat dose oral toxicity with reproductive/developmental toxicity screening test – rat, 90 days*	systemic NOAEL = 300 mg/kg bw/day reproductive NOAEL = 1000 mg/kg bw/day developmental NOAEL = 300 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*	non genotoxic
Genotoxicity – *in vivo* mammalian erythrocyte micronucleus test*	non genotoxic

* Assessed by Canada

Toxicokinetics
Based on the low molecular weight (< 500 g/mol), water solubility (2.3×10^{-3} g/L at 20 °C) and partition coefficient (log Pow = 3.75 at 20 °C) of the notified chemical, there is some potential for the chemical to cross biological membranes.

Acute Toxicity
In an acute oral toxicity test in rats for the notified chemical, two groups of three female animals received the test substance at 2000 mg/kg bw by oral gavage. No mortalities occurred. Hunched position and piloerection were noted for all animals on Days 1 and/or 2. No abnormalities were found at macroscopic post mortem examination. The test substance showed low acute oral toxicity with an LD50 > 2000 mg/kg bw.

In an acute dermal toxicity test in rats for the notified chemical, 5 male and 5 female animals received a single dermal application of 2000 mg/kg bw to clipped skin for 24 hours. No mortalities occurred. Chromodacryorrhea was noted for one male animal on Day 2. Scabs or general erythema were noted for four female animals. No abnormalities were found at macroscopic post mortem examination. The test substance showed low acute dermal toxicity with an LD50 > 2000 mg/kg bw.

Irritation
In a skin irritation test in New Zealand rabbits for the notified chemical, three animals were exposed to 0.5 g of the test substance moistened with water by application onto clipped skin for 4 hours using a semi-occlusive dressing. Skin reactions were assessed 1, 24, 48 and 72 hours after exposure. No skin reactions were noted and the test substance is considered to not be a skin irritant.

Skin irritation of the notified chemical was also evaluated on a human three-dimensional epidermal model (EPISKIN-SM). The possible skin irritation potential was tested through topical application for 15 minutes. After a 42 hours post-incubation period, determination of the cytotoxic (irritancy) effect was performed. The relative mean tissue viability obtained after 15 minutes treatment with the test substance compared to the negative control tissue was 96%. Since the mean relative tissue viability for the test substance was above 50%, the test substance is considered to not be an irritant.

In an eye irritation test in New Zealand rabbits for the notified chemical, approximately 0.1 mL of the test substance was instilled into one eye of each of three animals. Observations were made 1, 24, 48 and 72 hours and 7 days after instillation. Instillation of the test substance resulted in irritation of the conjunctivae, which consisted of redness, chemosis and discharge. The irritation had completely resolved within 7 days in all animals. No iridial irritation or corneal opacity were observed, and treatment of the eyes with 2% fluorescein 24 hours after test substance instillation revealed no corneal epithelial damage. The maximum average irritation score was calculated to be 1.7 which is considered to be indicative of mild irritation.

Eye irritation of the notified chemical was also evaluated on the reconstructed human EpiOcular model. The possible eye irritation potential was tested through topical application for 6 hours. After an 18 hours post-

incubation period, determination of the cytotoxic (irritancy) effect was performed. The relative mean tissue viability obtained after 6 hours treatment with the test substance compared with the negative control tissue was 96%. Since the mean relative tissue viability for the test substance was above 60%, the test substance is not considered to be an irritant.

Sensitisation
In an *in chemico* Skin Sensitisation: Direct Peptide Reactivity Assay (DPRA), the skin sensitisation of the notified chemical was inconclusive due to precipitation and co-elution of the test substance.

Dermal sensitisation of the notified chemical was evaluated in female CBA/J mice using the local lymph node assay. Three groups were treated with 5%, 10% or 25% on three consecutive days by open application on the ears. Five vehicle control animals were similarly treated with the vehicle only (acetone/olive oil 4:1). No erythema was observed in any of the animals. The majority of auricular lymph nodes were considered normal in size, except for one node in one animal treated at 25%. No macroscopic abnormalities of the surrounding area were noted for any of the animals. The SI values calculated for 5%, 10% and 25% were 1.7, 1.0 and 1.5 respectively. Since there was no indication that the test substance elicits a SI $\geq$ 3 when tested up to 25%, it is not considered to be a skin sensitiser under the conditions of this study.

Repeated dose toxicity combined with reproductive/developmental toxicity screening
Sub-chronic toxicity of the notified chemical was evaluated in male and female rats. The test substance was administered daily by oral gavage 7 days a week for a minimum of 90 days. Male animals were treated for 92 days up to and including the day before scheduled necropsy (i.e. 8 weeks prior to mating, during the mating period and at least 2 weeks post mating). Female animals that delivered were treated for 93-98 days (i.e. 8 weeks prior to mating, the variable time to conception, the duration of pregnancy and 14-15 days after delivery, up to and including the day before scheduled necropsy).

In female animals treated at 1000 mg/kg bw/day microscopic examination revealed an increased incidence of follicular cell hypertrophy (minimal or slight) in the thyroid. This was accompanied by a decrease of thyroid hormone T4 (on average 19%). In male animals treated at 1000 mg/kg bw/day serum levels of thyroid hormone T4 were also decreased (on average 57%), unaccompanied by treatment related changes in thyroid weight or morphology. For both male and female animals no corroborative findings were observed in TSH levels. No other biologically significant adverse effects were noted for parental animals. No effect on fertility was observed up to the highest dose level tested. A statistically significant skewed sex ratio towards female animals was noted at 1000 mg/kg bw/day (66% female pups versus 43% in the control group). This was strengthened by the finding that the percentage of female pups was about 70-80% in 5/8 litters of normal size at 1000 mg/kg bw/day versus 1/9 in the control group. There were no treatment-related changes in nipple retention in male pups, anogenital distance in male and female pups, or reproductive organs of parental animals. Therefore, it was considered unlikely that the skewed sex ratio resulted from an endocrine-mediated effect; however, the possibility cannot be ruled out.

Live birth index at 1000 mg/kg bw/day was lower compared to controls (91% versus 100%). In total, 9 pups of the 1000 mg/kg bw/day group were found dead at first litter check (7/9 of one litter) and one male pup in two other litters. Additionally, a slight increase in postnatal loss was noted (4 pups in three litters died between PND 1 and 4). Furthermore, decreased mean pup weights were note at 1000 mg/kg bw/day on PND 1 (11% relative to control). Mean pup weights at 1000 mg/kg bw/day remained slightly lower at PND 4 and 7, but were close to control values at PND 13.

Based on the combination of a decrease live birth index, a slight increase in postnatal loss and decreased mean pup weights at PND 1, a treatment-related effect on the early viability of the pups could not be excluded. In conclusion, the systemic no-observed-adverse-effect-levels (NOAEL) was established as 300 mg/kg bw/day, based on decreased T4 levels at 1000 mg/kg bw/day. The reproductive NOAEL was established as 1000 mg/kg bw/day, based on no treatment-related adverse effects were observed at any dose tested. The developmental NOAEL was established as 300 mg/kg bw/day, based on the findings including a skewed sex ratio towards female animals, a reduced live birth index, increased postnatal loss and decreased body weights at 1000 mg/kg bw/day. Since these effects were observed at maternally toxic levels, it is unclear if they are secondary to maternal toxicity.

Overall, the test substance shows low sub-chronic toxicity and potentially moderate developmental toxicity. However, the effects observed indicate the test substance may be a potential endocrine disruptor.

Mutagenicity/Genotoxicity
Mutagenicity of the notified chemical was tested in five strains of *Salmonella typhimurium* TA1535, TA1537, TA98, TA100 and TA102. In experiment 1, the test substance was tested up to 5000 µg/plate in the presence and absence of metabolic activation using the plate incorporation method. In experiment 2, the test substance was tested up to 2500 µg/plate without metabolic activation and up to 5000 µg/plate with metabolic activation using the pre-incubation method. Precipitation and toxic effects were noted for most strains in both experiments. No biologically relevant increase in revertant colony numbers of any of the five tester strains were observed at any concentrations, neither in the presence nor absence of metabolic activation. The test substance is considered to be negative for *in vitro* mutagenicity under the conditions of this study.

Mutagenicity of the notified chemical was tested in L5178Y mouse lymphoma cells. In the first experiment, the test substance was tested up to 500 µg/mL in the presence and absence of metabolic activation. The incubation time was 3 hours. No toxicity was observed at this dose level in the presence and absence of metabolic activation; however, the test substance precipitated in the culture medium. In the second experiment, the test substance was tested up to 500 µg/mL in absence of metabolic activation. The incubation time was 24 hours. The test substance precipitated in the culture medium at this dose level. The test substance is considered to be negative for *in vitro* mutagenicity under the conditions of this study.

Clastogenicity of the notified chemical was tested in cultured peripheral human lymphocytes. In the first assay, the test substance was tested up to 250 µg/mL for a 3-hour exposure time and a 24-hour fixation time in the presence and absence of metabolic activation. In the second assay, the test substance was tested up to 250 µg/mL for a 24-hour continuous exposure time and a 24-hour fixation time in the absence of metabolic activation. It was also tested up to 500 µg/mL for a 48-hour continuous exposure time and a 48-hour fixation time in the absence of metabolic activation. The test substance did not induce any statistically significant or biologically relevant increase in the number of cells with chromosome aberrations in the presence and absence of metabolic activation. In either of the two independently performed experiments. No biologically relevant effects on the number of polyploid cells and cells with endoreduplicated chromosomes were observed both in the presence and absence of metabolic activation. The test substance is considered to be negative for *in vitro* clastogenicity under the conditions of this study.

Genotoxicity of the notified chemical was evaluated in male NMRI mice. Five animals received two doses of 1000 mg/kg bw by oral gavage, using split doses, at a 24-hour interval. No treatment-related clinical signs or mortality were noted in any animal. Bone marrow was sampled 48 hours after the first dosing. No increase in the mean frequency of micronucleated polychromatic erythrocytes was observed in the bone marrow of animals. No decrease in the ratio of polychromatic to normochromatic erythrocytes compared to the concurrent vehicle control was observed indicating a lack of toxic effects of this test substance on erythropoiesis. The test substance is not considered to be genotoxic *in vivo* under the conditions of this study.

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

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on available toxicological studies on the notified chemical, the notified chemical is expected to be of low acute toxicity, presenting only as a mild eye irritant. The notified chemical is not a skin sensitiser up to 25% concentration. Potential risk through prolonged or repeated exposure cannot be ruled out.

Workers handling the organic peroxide formulations containing notified chemical may come into contact with the chemical at ≤ 50% concentration during manual transfer into the road marking machine reservoir and road marking operations, and during cleaning and maintenance of equipment. However, the exposure is expected to be limited by the use of enclosed, purpose-designed road line marking machine and PPE (goggles, impervious gloves and protective clothing).

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

6.3.2. Public Health

The notified chemical is intended for industrial use only and will not be made available to the public. The public may have dermal contact with the coated road surface containing the notified chemical at ≤ 1.5% concentration. However, once the coating is cured and dried, the notified chemical will be bound into the coating matrix and will not be available for exposure.

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

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia as a component of peroxide powder. It will not be repackaged or reformulated in Australia. Accidental spills of the product containing the notified chemical during transport or storage are expected to be collected for disposal of, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The imported peroxide powder containing the notified chemical will be used as a catalyst for curing of cold applied road paint used to mark lines on the road surface. The paint will be applied using a purpose-designed machine, where the catalyst is mixed in-line with the paint, which starts the curing reaction. The paint is then applied by airless spray at close proximity to the road surface. This will minimise the potential for any aerosol formation and overspray drift. Once the paint has cured, the coating will be in a cured form and the notified chemical will be bound within the coating and will not be available for release to the environment.

Accidental spills of the product containing the notified chemical during use and wastes from equipment maintenance (estimated by the notifier as < 3% import volume) are expected to be collected for disposal in accordance with local government regulations. Potential release to the environment could occur from overspray and line marking errors. However, even during spraying the notified chemical is incorporated within the developing polymer matrix of the paint at low concentrations (≤ 1.5 %). Therefore, overspray and line marking errors will lead to diffuse release of the paint but the notified chemical is expected to be retained within the polymer matrix and will not be bioavailable.

RELEASE OF CHEMICAL FROM DISPOSAL

Empty import containers containing residues of the notified chemical are expected to be disposed of to landfill in accordance with local government regulations.

7.1.2. Environmental Fate

Two biodegradability studies conducted on the notified chemical show that it is readily biodegradable (81 and 90% biodegradation after 28 days).

After applying to the road surface, the notified chemical will be bound within the cured coating and will not be available for release to the environment. A very small portion of the import volume of the notified chemical may be disposed of to landfill as collected spills. Based on its low solubility in water, very low volatility and moderate log Koc, the notified chemical is expected to have low mobility in landfill. Potential release to the environment could occur from overspray and line marking errors. However, the notified chemical is expected to be retained within the polymer matrix and will not be bioavailable. At longer timescales, the notified chemical is expected to be slowly released from road line-markings by erosion, diffusion and/or leaching. When released by these mechanisms the notified chemical is expected to bind irreversibly to soil within close proximity to the road surface (based on the results of an adsorption/desorption study) and eventually degrade via biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated since no significant release of the notified chemical to the aquatic environment is expected based on the reported use pattern.

7.2. Environmental Effects Assessment

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

Endpoint / Method	*Result*	*Assessment Conclusion*
Acute Fish Toxicity* (OECD TG 203)	96 h LL50 > 100 mg/L (nominal, saturated solution) 96 h LC50 > 0.43 mg/L (measured)	Not harmful to fish up to its water solubility limit
Acute Fish Embryo Toxicity (OECD 236)	96 h EL50 = 10 – 100 mg/L 96 h LOELR = 10 mg/L (nominal, WAF)	Survival of zebrafish embryos reduced significantly at 10 mg/L WAF at 96 hours.
Fish Early Life Stage* (OECD 210)	34 d NOEC = 0.073 mg/L (larvae survival, measured)	Abnormal appearances or behaviour were observed in embryos and larvae at the 0.124 and 0.345 mg/L test concentrations.
Acute Daphnia Toxicity* (OECD TG 202)	48 h EL50 > 100 mg/L (nominal, saturated solution) 48 h EC50 > 2.4 mg/L (measured)	Not harmful to aquatic invertebrates up to its water solubility limit
Daphnia Reproduction* (OECD TG 211)	21 d NOEC = 0.65 mg/L (measured)	The 1.44 mg/L test concentration showed a statistically significant difference from the control after 21 days in terms of producing no live young per adult.
Algal Toxicity* (OECD TG 201)	72 h E_rL50 > 100 mg/L (nominal, saturated solution) 72 h E_rC50 > 0.87 mg/L (measured) 72 h NOEC = 0.045 mg/L (measured)	Not harmful to algae up to its water solubility limit
Inhibition of Bacterial Respiration (OECD TG 209)	3 h IC50 > 1,280 mg/L (nominal)	Not inhibitory to microbial respiration in STPs
Earthworm Reproduction and Growth (OECD TG 222)	28 d NOEC for mortality and mean body weight > 1,000 mg/kg dry soil (nominal) 56 d NOEC for the number of juvenile worms = 555.6 mg/kg dry soil (nominal)	The 1,000 mg/kg dry soil treated group had significantly fewer juveniles than the control.

* Assessed by Canada
WAF: Water Accommodated Fraction

Since the chronic NOEC for algae is 0.045 mg/L, the notified chemical is classified as "Chronic Category 2; Toxic to aquatic life with long lasting effects" under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated based on the most sensitive endpoint for algae as shown in the table below. An assessment factor of 10 was used given the acute and chronic endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
72 h NOEC for algae	0.045	mg/L
Assessment Factor	10	
Mitigation Factor	1	
PNEC:	4.5	µg/L

7.3. Environmental Risk Assessment

A Risk Quotient (PEC/PNEC) has not been calculated as no significant release of the notified chemical to the aquatic environment is expected based on the reported use pattern. The notified chemical is expected to be slowly released from the solid polymer matrix of the paint in which it is bound by erosion, leaching and/or diffusion. When released by these mechanisms the notified chemical is expected to irreversibly bind to soil where it will

ultimately degrade to water and oxides of carbon by biotic and abiotic processes. Therefore, on the basis of this assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Adsorption/Desorption log Koc = 3.1 – 3.8 at 20-25 °C

Method OECD TG 106 Adsorption – Desorption Using a Batch Equilibrium Method

Soil Type	*Organic Carbon Content (%)*	*pH*	*Log Koc*
Red soil (sandy clay)	0.77	5.48	3.7
Black soil (sandy loam)	4.32	6.54	3.1
Paddy soil (sandy clay loam)	1.96	6.88	3.3
Moisture soil (sandy clay)	1.22	7.87	3.8
Aquic-brown soil (sandy loam)	2.06	5.47	3.5

Remarks The test substance was determined by GC-MS/MS; based on desorption results, adsorption was considered as irreversible.
Test Facility SRICI (2018)

Flammability Not highly flammable

Method EC Council Regulation No 440/2008 A.10 Flammability (Solids)
Remarks The test substance melted and did not ignite within 2 minutes applying a flame.
Test Facility Akzo Nobel (2017a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Skin Sensitisation – *In Chemico* Direct Peptide Reactivity Assay

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 442c *In Chemico* Skin Sensitisation: Direct Peptide Reactivity Assay (DPRA) (2015)
Vehicle	Acetonitrile
Remarks – Method	No significant protocol deviations. The test was run in triplicates. In each replicate cinnamic aldehyde and the vehicle (acetonitrile) were included as a positive and negative control, respectively. Co-elution controls were set up in parallel to sample preparation but without the respective peptide solution.

RESULTS

Sample	*Cysteine Peptide Depletion (% ± SD)*	*Lysine Peptide Depletion (% ± SD)*
Vehicle	0	0
Test Substance	0.03 ± 0.05	0^ ± 0
Positive Control	78.9 ± 0.58	57.48 ± 1.25

SD = Standard Deviation
^ Value was set to 0 due to negative result

Remarks – Results	Significant precipitation was observed for the test substance and co-elution controls in both cysteine and lysine tests. Centrifugation was carried out for the test substance samples prior to HPLC analysis. Co-elution of the test substance with cysteine peak was observed. The study authors stated that in combination with the observed precipitation, possible underestimation of the reactivity (the sensitising potential of the test substance) could not be predicted and the test result must be considered as inconclusive. The positive and reference controls fulfilled all quality criteria confirming the validity of the test.
CONCLUSION	The test result was inconclusive.
TEST FACILITY	Eurofins (2017)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Ecotoxicological Investigations

C.1.1. Acute Toxicity to Fish Embryo

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 236 Fish Embryo, Acute Toxicity Test – Semi-static
Species	*Danio rerio* (zebrafish)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	Not provided
Analytical Monitoring	None
Remarks – Method	No major deviations from the test guidelines were reported. The test solution was prepared in a covered glass and stirred slowly for 3 days. The solution was then allowed to stand for 1 hour before the water accommodated fraction (WAF) was tapped directly from the vessel to fill the well plate. The test solutions were renewed daily. A positive control with 3,4-dichloro aniline was run. As the positive control being prepared with acetone, a solvent control of 100 µL/L acetone was also run.

RESULTS

Nominal concentration (mg/L WAF)	*Number of embryos*	*Survival %*	*Hatch % of Total*
Negative control	48	92	83
1	25	92	92
10	25	84	84
100	25	32	32

EL50	10 – 100 mg/L WAF at 96 hours
LOELR	10 mg/L WAF at 96 hours
Remarks – Results	Oxygen concentration was not measured during the test. As all test medium was aerated continually prior to use and the control survival exceeded the validity requirements, this is not expected to negatively affect the test results. Other validity criteria for the test were satisfied. The positive control resulted in 92-100% mortality.
CONCLUSION	Survival of zebrafish embryos reduced significantly by 10 mg/L WAF of the test substance at 96 hours.
TEST FACILITY	Akzo Nobel (2017b)

C.1.2. Inhibition of Microbial Activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test
Inoculum	Activated sludge from a domestic STP
Exposure Period	3 hours
Nominal Concentrations	Control, 20.4, 42.2, 80, 161.4, 323, 641.6 and 1,280.4 mg/L
Remarks – Method	No major deviations from the test guidelines were reported. The test substance was added directly to the test vessels. A reference test with 3,5-dichlorophenol was run.
RESULTS	
IC50	> 1,280 mg/L at 3 hours
Remarks – Results	The oxygen uptake rate in the control was 16 mg O_2/g dry weight/h which was lower than the prescribed rate of > 20 mg O_2/g dry weight/h for the

control measurements. The authors explained this was because the inoculum was obtained from a STP which is operated at a low organic sludge load and as a consequence has a low oxygen uptake rate. This was not considered to influence the sensitivity of the activated sludge as the 3 h IC50 for activated sludge exposed to 3,5-dichlorophenol was 10 mg/L which was within the historical ranges. All other validity criteria for the test were satisfied.

CONCLUSION The test substance does not inhibit microbial respiration in STPs.

TEST FACILITY Akzo Nobel (2017c)

C.1.3. Earthworm Reproduction

TEST SUBSTANCE Notified chemical

METHOD OECD TG 222 Earthworm Reproduction Test

Species *Eisenia fetida*

Auxiliary solvent Acetone

Exposure Period 56 days

Remarks – Method The definitive test was conducted based on a preliminary test results with no significant deviations from the test guidelines. Each test solution was prepared in acetone and placed over dry sand. The treated sand was left for solvent to evaporate before being mixed with moist soil and water. After treatment on Day 1 and on Day 7, the soil was sampled for analysis of the test substance. A positive control with Ringer (active ingredient carbendazim) was run.

RESULTS

Nominal Concentration (mg/kg dry soil)	*No. of earthworms*	*Mortality (%) at 28 days*	*Mean body weight (mg) at 28 days*	*No. of juveniles at 56 days*
Water Control	40	0	549	315
Solvent Control	40	2.5	556	315
16.3	40	0	565	296
29.4	40	0	591	294
52.9	40	2.5	529	303
95.3	40	0	619	317
171.5	40	2.5	625	297
308.6	40	0	586	293
555.6	40	0	536	285
1,000	40	2.5	564	281

NOEC for mortality and mean body weight > 1000 mg/kg dry soil at 28 days

NOEC for the number of juvenile worms 555.6 mg/kg dry soil at 56 days

Remarks – Results All validity criteria for the test were satisfied. The positive control resulted in substantial and unequivocal toxic effects. The measured test concentrations were within ± 20 % of the nominal concentrations.

CONCLUSION The 1000 mg/kg dry soil treated group had significantly fewer juveniles than the control.

TEST FACILITY Envigo (2018)

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