File No: STD/1636

June 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Aspartic acid, *N,N′*-(2-methyl-1,5-pentanediyl)bis-, 1,1',4,4'-tetraethyl ester

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/1636	Convestro Pty Ltd and PPG Industries Australia Pty Ltd	Aspartic acid, *N,N'*-(2-methyl-1,5-pentanediyl)bis-, 1,1',4,4'-tetraethyl ester	No	≤ 40 tonnes per annum	Component of industrial coatings

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*
Acute toxicity (Category 3)	H402 – Harmful to aquatic life
Chronic toxicity (Category 3)	H412 – Harmful 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

REGULATORY CONTROLS

CONTROL MEASURES

Occupational Health and Safety

- 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:
  - Avoid contact with 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:
  - Protective clothing
  - Impervious gloves

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.

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of industrial 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)
Covestro Pty Ltd (ABN: 18 086 237 765)
Level 1, 700 Springvale Road
MULGRAVE VIC 3170

PPG Industries Australia Pty Ltd (ABN: 82 055 500 939)
14-20 McNaughton Road
CLAYTON VIC 3169

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: analytical 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 as follows: dissociation constant, flammability, oxidising properties, acute dermal toxicity and bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2007)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Desmophen® NH 1220

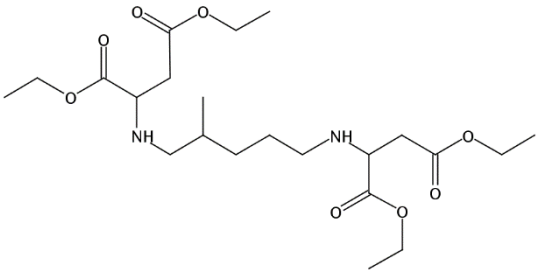
CAS NUMBER
168253-59-6

CHEMICAL NAME
Aspartic acid, *N,N'*-(2-methyl-1,5-pentanediyl)bis-, 1,1',4,4'-tetraethyl ester

OTHER NAME(S)
Aspartic acid, N,N'-(2-methyl-1,5-pentanediyl)bis-, tetraethyl ester
DL-Aspartic acid, N,N'-(2-methyl-1,5-pentanediyl)bis-, tetraethyl ester
Tetraethyl 2,2'-[(2-methylpentane-1,5-diyl)diimino]dibutanoate

MOLECULAR FORMULA
$C_{22}H_{40}N_2O_8$

STRUCTURAL FORMULA



MOLECULAR WEIGHT

460.56 g/mol

ANALYTICAL DATA

Reference FTIR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY

> 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -50 °C	Measured
Boiling Point	237 °C at 101.3 kPa	Measured
Density	1,066 kg/m^3 at 25 °C	Measured
Vapour Pressure	< 1 x 10^{-6} kPa at 20 °C	Measured
Water Solubility	4 – 6 g/L at 20 °C	Measured; significant hydrolysis was observed in the water solubility test.
Hydrolysis as a Function of pH	$t_{1/2}$ = 0.98 h at pH 9 and 50°C; $t_{1/2}$ = 1.48 h at pH 7 and 50°C; $t_{1/2}$ = 34.92 h at pH 4 and 50°C; $t_{1/2}$ = 13.47 h at pH 4 and 60°C; $t_{1/2}$ = 5.29 h at pH 4 and 70°C	Measured
Partition Coefficient (n-octanol/water)	log P_{ow} = 3.7	Measured
Surface Tension	49.58 mN/m at 20.1 °C	Measured
Adsorption/Desorption	log K_{oc} = 2.7	Measured
Dissociation Constant	Not determined	Contains cationic functionalities and is likely to be ionised in the environmental pH range.
Flash Point	105°C at 101.3 kPa	Measured
Flammability	Not determined	Not expected to be highly flammable based on the measured flash point
Autoignition Temperature	305 °C	Measured
Explosive Properties	Not explosive	Measured
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties
Viscosity	129 mPas at 20°C	Measured

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, but will undergo hydrolysis in water.

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 in Australia. It will be imported into Australia either as a component of formulations at ≤ 50% concentration for reformulation into industrial coatings or as a component of finished coatings at 30-50% concentration.

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

TRANSPORTATION AND PACKAGING
The notified chemical will be imported at ≤ 50% concentration in 205 L drums. Finished products containing the notified chemical at 30-50% concentration will be imported in 20 L cans or 205 L drums.

USE
The notified chemical will be used as a component of a two-part coating system at 30-50% concentration for aftermarket vehicle body repairs.

OPERATION DESCRIPTION

Reformulation
The imported formulations containing the notified chemical at ≤ 50% concentration will be transferred to the mixing vessel using automated dosing equipment and hoses where it will be blended with other ingredients in the presence of local exhaust ventilation. Following blending, samples of the finished products will be taken for quality control testing. The finished coatings containing the notified chemical at 30-50% concentration will be filled into containers in a variety of pack sizes from 0.5 to 205 L metal cans or 205 L drums through a filling machine.

End-use
The two-part coating system containing the notified chemical at 30-50% concentration will be applied using specialised spray painting equipment. The two parts of the coating will be mixed in-line at the application nozzle before the coating is sprayed on the surface. Coatings containing the notified chemical will mainly be applied in purpose-built spray booths with ventilation and directional air flow (down draft) to capture and filter any mists and overspray.

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
Quality control	0.5	1 – 2
End-use (spray painting)	4 – 12	10 – 50

EXPOSURE DETAILS
Transport and storage workers are not expected to be exposed to the notified chemical except in the unlikely event of an incident.

Reformulations
Dermal and ocular exposure of workers to the notified chemical at ≤ 50% concentration may occur when connecting or disconnecting transfer hoses, cleaning or maintaining equipment and testing for quality control. Inhalation exposure to the notified chemical may also occur if aerosols are formed. Exposure will be minimised through the use of enclosed and automated systems, local exhaust ventilation and personal protective equipment (PPE: respirators, impervious gloves, goggles and coveralls) as stated by the notifier.

End-use
Dermal, ocular and inhalation exposure of workers to the notified chemical at 30-50% concentration may occur during spray application of coatings. As stated by the notifier, the potential for exposure will be minimised through the use of PPE (full-face, self-contained breathing apparatus, impervious gloves, coveralls, and safety boots) by workers. Inhalation exposure will be further mitigated through the use of exhaust ventilation and spray booths. Once the coating is dried, the notified chemical will be trapped within the coating film and will not be available for exposure.

6.1.2. Public Exposure
Coatings containing the notified chemical at 30-50% concentration will be used for industrial and professional purposes and will not be made available to the public. Once the coating is dried, the notified chemical will be trapped within 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 the studies that were not assessed by Canada, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute inhalation toxicity	LC50 > 4923 mg/m^3; low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	non irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days	NOAEL = 200 mg/kg bw/day
Rat, repeat dose oral toxicity – 93 days	NOAEL = 200 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian cell gene mutation test	non mutagenic
Genotoxicity – *in vivo* mouse micronucleus	non genotoxic
Rat, prenatal development toxicity	NOAEL (maternal toxicity) = 1000 mg/kg bw/day NOAEL (developmental toxicity) = 1000 mg/kg bw/day

Toxicokinetics
Based on the low molecular weight (< 500 g/mol), water solubility (4 – 6 g/L at 20 °C) and partition coefficient (log Pow = 3.7) of the notified chemical, there is potential for the chemical to cross biological membranes.

Acute toxicity
An acute oral toxicity study was carried out using the notified chemical in rats. No treatment-related deaths or clinical signs were noted. Growth of the surviving animals was not affected. None of the animals showed any noticeable gross pathological findings at necropsy. The notified chemical showed low toxicity via the oral route.

An acute inhalational toxicity study was carried out using the notified chemical in rats (5 animals of each sex) at a concentration of 4923 mg/m^3 for four hours. Control animals (5 of each sex) were exposed to conditioned air. The animals were observed for 14 days. No treatment-related mortality was noted. Clinical signs included reduced motility, piloerection, ungroomed hair-coat, bradypnea, laboured breathing pattern, hypothermia and

decreased body weight in male animals. Rectal temperature in male and female animals was reduced by 3 °C (measured 30 mins after cessation of exposure). The decreased weight gain in males could be explained by the differences in ages of the animals tested – male animals were approximately 6.5 weeks old whereas female animals were 9-10 weeks old. The notified chemical showed low toxicity via inhalation.

Acute dermal toxicity data were not provided.

Irritation
The notified chemical was tested for skin irritation in rabbits, using 0.5 mL undiluted test substance under semi-occlusive dressing for four hours, on shaved unabraded skin. Following patch removal, the unwashed site was observed for a further 72 hours. Barely perceptible erythema was noted in two animals, which resolved by 72 hours. The primary irritation index was calculated to be 1.25. Based on the results of this study, the notified chemical is slightly irritating to the skin.

The notified chemical was tested for eye irritation in rabbits by instilling 0.1 mL of undiluted test substance into the conjunctival sac of rabbits. No treatment-related effects were noted and the cornea, iris and conjunctivae were unaffected. A transparent film was noted and persisted until 24 hours after instillation. No findings were noted at the 24-hour fluorescein test. Based on the results of this study, the notified chemical is not irritating to the eyes.

Sensitisation
The notified chemical was tested in a Magnusson-Kligman guinea pig maximisation test. The induction test was conducted using an injection with the test substance at 1%, followed by 100% topical induction. Challenge using 25% of the test substance was applied by topical application. No treatment-related mortality occurred. All animals gained weight during the study. No skin reaction was noted for treated or control animals at the 48- and 72-hour observations following challenge. The notified chemical showed no evidence of skin sensitisation.

Repeated dose toxicity
The notified chemical was tested in a repeated-dose toxicity study in Wistar rats (5 males and 5 females per group), using test substance diluted in corn oil and administered by oral gavage for 28 days at 0 (corn oil), 40, 200 and 1000 mg/kg bw/day. Recovery groups were included for the 0 and 1000 mg/kg bw/day dose levels, which were allowed to recover for a further 14 days after the treatment.

No test substance-related mortality was noted. Mean feed intake, functional observations, grip strength, haematological parameters, clinical chemistry parameters were not altered with increasing administrations of the test substance.

Significant reduction in mean body weight and body weight gain was noted in high-dose male animals from day 14 onwards. Male animals in the high-dose recovery group had a mean weight that was 10% lower than control animals in the recovery group. This effect was not noted at other dose levels or in female animals.

No change in absolute or relative organ weights was noted in comparison to control animals at any dose level, for male animals.

Male animals in the high-dose recovery group showed lower mean absolute thymus and testes weight; however, no differences were noted compared to the control group when organ weight was expressed relative to body weight. In female animals, mean absolute heart, spleen and kidney weight was statistically significantly higher in the high dose group but only spleen weight was statistically significantly different from the corresponding control when compared to body weight. No changes were evident between the treatment and recovery groups upon recovery.

Slight to moderate cytoplasmic vesiculation of the epithelium of the cortical tubules of kidneys in 1000 mg.kg bw/day males was noted. Slight increases in basophilic tubules were observed for four male animals, compared to two control animals. Recovered animals did not show these effects.

The No Observed Adverse Effect Level (NOAEL) was established to be 200 mg/kg bw/day based on kidney effects and reduced body weights in males at 1000 mg/kg bw/day.

Another repeated dose oral (gavage) toxicity study on the notified chemical was conducted in rats (n=10/sex/dose), in which the test substance was administered at 40, 200 and 1,000 mg/kg bw/day for 93 consecutive days.

The NOAEL was established as 200 mg/kg bw/day in this study, based on treatment-related findings were noted for kidneys (including cortical tubular vacuolation, very slight tendency for increase of ketone bodies and urobilinogen, and slightly but statistically significantly increased absolute and relative weight of kidneys in female animals) at 1000 mg/kg bw/day.

Mutagenicity/Genotoxicity
The notified chemical was tested in a bacterial reverse mutation test (plate incorporation procedure) at concentrations up to 5000 µg/plate, using *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535 and TA1537. Dimethyl sulfoxide was used as the vehicle. The test substance at concentrations up to 5000 µg/plate did not cause cytotoxicity. No precipitate was noted at any concentration tested. None of the strains showed any concentration-related or statistically significant increase in revertants. The notified chemical was not mutagenic to bacteria under the conditions of the test.

The notified chemical was also negative in an *in vitro* mammalian cell gene mutation test in Chinese hamster V79 cells.

An *in vivo* mouse micronucleus test was conducted on the notified chemical. Maximum tolerated dose of 2500 mg/kg was chosen for male animals (used in the main test) based on a pilot test. The test substance was suspended in corn oil (vehicle) and administered as two intraperitoneal injections, 24 hours apart. No unscheduled deaths occurred. Animals were examined 24 hours after the last injection. A dose-related increase in the ratio of polychromatic erythrocytes (PCE) to normochromatic erythrocytes was noted. This was considered as an indication of cytotoxicity and that the test substance reached the marrow. Micronucleated PCE did not increase in any dose group, except for the positive control. No increase in normochromatic erythrocytes containing micronuclei was noted for any group. The notified chemical was not clastogenic under the conditions of the test.

Toxicity for reproduction
In a prenatal developmental toxicity study in female rats (n=25/dose), the notified chemical was administered at 0, 100, 300 and 1000 mg/kg bw/day in corn oil daily by gavage from day 6 to day 20 post coitum. The foetuses were delivered on day 21 of gestation. The NOAEL for developmental and maternal toxicity was established as 1000 mg/kg bw/day, the highest dose tested, based on no treatment-related adverse effects observed.

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
The notified chemical is slightly irritating to the skin.

Reformulation
During reformulation, workers may be at risk of mild skin irritation when handling the notified chemical as introduced at ≤ 50% concentration and in reformulated products at 30-50% concentration. The notifier states that worker exposure will be limited through the use of engineering controls such as enclosed systems and local exhaust ventilation. The use of appropriate personal protective equipment (PPE) will also limit worker exposure.

End-Use
Workers may be at risk of mild skin irritation when handling coatings containing the notified chemical (30-50% concentration). The notifier states that worker exposure will be limited through the use of engineering controls such as spray booths. The use of appropriate PPE (protective clothing, imperious gloves, safety glasses and respirators) will also limit worker exposure.

Exposure is not anticipated for workers who might make dermal contact with the notified chemical when handling dried end products, as the notified chemical will be incorporated into a solid matrix and will not be available for exposure.

Overall, 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 use in industrial and professional applications only. The public may come into dermal contact with substrates on which the coating containing the notified chemical is applied. However, once the coating is dried, the notified chemical will be incorporated into a solid matrix and will not be available for exposure. Therefore, there is not unreasonable risk to public.

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 either as a component of industrial coatings or as a component of formulations for reformulation into the end-use products. The reformulation processes involve automated blending operation in an enclosed environment, followed by automated filling of the end-use products into containers. The empty import containers and reformulation equipment containing up to 0.5% of the import volume of the notified chemical will be cleaned with suitable solvent which is collected and recycled where possible. Any spills containing the notified chemical will also be collected and recycled where possible. If it is not suitable to recycle, the spills will be collected using a suitable absorbent material and disposed of to landfill in accordance with local government regulations. Accidental spills of the notified chemical during import, transport and storage are also expected to adsorb onto a suitable material and collected for disposal in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be used as a component of a two-part coating system for aftermarket vehicle body repairs. The two parts of the coating will be mixed in-line at the application nozzle before the coating is sprayed on the surface. The main release of the notified chemical is likely from overspray during use, estimated by the notifier to account for up to 20% of the total import volume. As the coatings will be applied within a purpose-designed spray booth, the overspray is collected within the vent system and trapped onto filters. The spent filters will be disposed of to landfill in accordance with local government regulations. The solvent waste from cleaning of the application equipment, will be collected by an approved waste contractor, and be disposed of in accordance with local government regulations. During use, the notified chemical may also be released to the environment as accidental spills. These releases are expected to be collected and disposed of to landfill in accordance with local government regulations.

RELEASE OF CHEMICAL FROM DISPOSAL

Most of the notified chemical is expected to share the fate of the article to which it has been applied, either subjected to metal reclamation or being disposed of to landfill at the end of their useful lives. Residual notified chemical in empty end-use containers, estimated by the notifier to account for up to 2% of the total import volume, is expected to be cured into an inert solid matrix and be disposed of to landfill along with the empty containers.

7.1.2. Environmental Fate

A biodegradation test conducted on the notified chemical shows that it is not inherently biodegradable. For details of the biodegradation test, see Appendix C. As a result of its use pattern, most of the notified chemical is expected to share the fate of the article to which it has been applied, either subjected to metal reclamation or being disposed of to landfill at the end of their useful lives. During metal reclamation, the notified chemical will thermally decompose to form water vapour and oxides of carbon and nitrogen. In landfill, the notified chemical will be present as cured solids and will be neither bioavailable nor mobile. Therefore, release of the notified chemical to the aquatic environment is expected to be minimal. However, if any amounts or losses do end up in water, the notified chemical will rapidly hydrolyse and will not be available to biota. Therefore, the notified

chemical is not expected to be bioaccumulative. In landfill and water, the remaining notified chemical is expected to eventually degrade via biotic and abiotic processes to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated as release of the notified chemical to the aquatic environment will be limited based on its reported use pattern.

7.2. Environmental Effects Assessment

The results from the ecotoxicological investigation 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*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 > 100 mg/L nominal concentration (> 87 mg/L measured concentration)	Not harmful to fish
Daphnia Toxicity	48 h EC50 > 100 mg/L nominal concentration (> 96.9 mg/L measured concentration)	Not harmful to aquatic invertebrates
Algal Toxicity	72 h EC50 = 41.7 - 84.2 mg/L measured concentration	Harmful to alga
Inhibition of Bacterial Respiration	3 h IC50 > 10,000 mg/L nominal concentration	Not inhibitory to microbial activity at STPs

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS), the notified chemical is expected to be harmful to alga. Therefore, the notified chemical is formally classified as "Acute Category 3; Harmful to aquatic life" under the GHS. Based on the acute toxicity and lack of readily biodegradability, the notified chemical is formally classified as "Chronic Category 3; Harmful to aquatic life with long lasting effects" under the GHS (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The most sensitive endpoint from the above ecotoxicity tests on the notified chemical is 72h EC50 for alga, and this was selected for the calculation of the predicted no-effect concentration (PNEC). An assessment factor of 100 was used in this case given acute endpoints for three trophic levels are available as a general indication of potential toxicity.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
72 h EC 50 for alga	41.7	mg/L
Assessment Factor	100	
Mitigation Factor	1	
PNEC:	417	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (PEC/PNEC) has not been calculated as release of the notified chemical to the aquatic environment will be limited based on its reported use pattern. Therefore, based on the relatively low hazard and reported use pattern as a component of industrial coatings, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 4 - 6 g/L at 20 °C

Method EC Directive 92/69/EEC A.6 Water Solubility
Remarks Using Flask Method; due to degradation of the test substance in water under study conditions, the solubility range is reported.
Test Facility Bayer (1999a)

Hydrolysis as a Function of pH

Method EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation

pH	*T (°C)*	*$t_{½}$ (hours)*
4	70	5.29
4	60	13.47
4	50	34.92
7	50	1.48
9	50	0.98

Remarks The $t_{1/2}$ at pH 4 and 25°C = 530 hours, when extrapolated from the data above using the Arrhenius equation.
Test Facility Bayer (1999b)

Surface Tension 49.58 mN/m at 20.1 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions
EC Council Regulation No 440/2008 A.5 Surface Tension
Remarks Concentration: 1.0 g/L
Test Facility Bayer (1999c)

Adsorption/Desorption log K_{oc} = 2.7

Method OECD TG 121 Adsorption Coefficient
EC Council Regulation No 440/2008 C.19 Adsorption Coefficient
Remarks HPLC method
Test Facility Currenta (2010)

Flash Point 105 °C at 101.3 kPa

Method EC Council Regulation No 440/2008 A.9 Flash Point
Remarks A gas flame was used as the ignition source and ignitions were visually determined by the tester.
Test Facility Bayer (1999d)

Autoignition Temperature 305°C

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Test Facility Bayer (1999d)

Explosive Properties Not explosive

Method EC Council Regulation No 440/2008 A.14 Explosive Properties
Remarks Koenen test for thermal stability and BAM drop-weight test and BAM friction mill for mechanical sensitivity
Test Facility Bayer (1999d)

Viscosity 129 mPas at 20 °C

Method OECD TG 114 Viscosity of Liquids

Remarks	Determined by a rotational viscosimeter
Test Facility	Currenta (2012)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents
Species/Strain	Rat/Wistar (HsdRCCHan:Wist)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 93 days Dose regimen: 7 days per week
Vehicle	Corn oil
Physical Form	Liquid
Remarks - Method	No significant protocol deviations The dose selection was based on the results of a 28-day repeated dose study conducted on the notified chemical.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10M; 10F	0	1
low dose	10M; 10F	40	0
mid dose	10M; 10F	200	0
high dose	10M; 10F	1000	0

Mortality and Time to Death

No treatment-related mortality was observed. One male in the control group died during the test.

Clinical Observations

No test substance-related clinical signs were observed during the treatment period. There was no significant difference in body weight gain and food and water consumption in the treated animals when compared to controls.

Some findings including decreased motility, increased salivation, resistance during handling and high stepping gait were observed only in few animals for a short period of time and were not considered to be of toxicological significance by the study authors.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

In the high-dose male animals, statistically significant increase in the aspartate aminotransferase activity was observed, which was regarded to be of no relevance due to the absence of any correlating findings in the liver morphology.

There were no treatment-related adverse effects reported in the clinical chemistry and haematological parameters. A slight tendency for increase of ketone bodies and urobilinogen; significantly shortened HQuick time in males and decreased number of basophils in the highest dose were not considered to be of toxicological relevance by the study authors.

Effects in Organs

Significant increase in mean absolute kidney weights (13.6% increase compared to the control group) was observed in females at the highest dose and a decrease in absolute mean uterus weight (22% decrease compared to the control group) at 200 mg/kg bw was reported. No mean uterus weight decrease was recorded at the highest dose.

There were no significant necropsy findings. Histopathological findings noted in kidneys of animals treated at 1000 mg/kg bw included cortical tubular vacuolation (proximal and distal convoluted tubules in 7/10 males and 8/10 females).

Remarks – Results
Survival and clinical parameters were not affected by the treatment.

Cortical tubular vacuolation at the proximal and convoluted renal tubules at 1000 mg/kg bw was considered by the study authors "to be due to a storage process". The statistically significant increase in absolute weight of kidneys in females and the very slight tendency for increase of ketone bodies and urobilinogen at 1000 mg/kg bw were assume to be correlated with the above findings.

The decrease in the mean absolute uterus weights at 200 and 1000 mg/kg bw/day was not dose dependant and had no histopathological evidence. Hence was assumed to be toxicologically irrelevant by the study authors,

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 200 mg/kg bw/day in this study, based on adverse effects observed in the histopathological parameters of the kidneys at the higher dose.

TEST FACILITY Bayer (2012)

B.2. Genotoxicity – *in vitro*

TEST SUBSTANCE Notified chemical

METHOD OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test

Species/Strain	Chinese hamster
Cell Type/Cell Line	V79
Metabolic Activation System	S9 mix from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	Ethanol
Remarks - Method	A dose range-finding test was carried out at 37.5-4800 µg/mL. The dose selection for the main tests was based on toxicity and phase separation noted in the range-finding test. Solvent control (ethanol) and positive controls (ethyl methanesulfonate and 7,12-dimethylbenz[a]anthracene) were run concurrently with the notified chemical.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	12.5, 25, 50*, 75*, 100*, 150*, 200*	4h	7 days	~15 days
Test 2	25, 50, 75*, 100*, 150*, 200*, 300*	4h	7 days	~15 days
Present				
Test 1	150*, 300*, 600*, 1200^, 2400*, 4800*	4h	7 days	~15 days
Test 2	75, 150*, 300*, 600*, 1200*, 2400*, 4800#	4h	7 days	~15 days

* Cultures selected for metaphase analysis
^ Not continued to avoid analysis of too many precipitating concentrations
# Not continued to avoid analysis of too many concentrations showing phase separation

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 4800	> 150	≥ 600	negative
Test 2		> 150	≥ 600	negative
Present				
Test 1	> 4800	> 4800	≥ 600	negative
Test 2		> 2400	≥ 600	negative

Remarks - Results In both main tests, no relevant and reproducible increases in the mutation frequency were observed in the presence or absence of metabolic activation.

	The positive and negative controls gave a satisfactory response confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to Chinese hamster V79 cells treated *in vitro* under the conditions of the test.
TEST FACILITY	Harlan (2010)

B.3. Developmental toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 414 Prenatal Developmental Toxicity Study
Species/Strain	Rat/Wistar (Hsd Cpb: WU)
Route of Administration	Oral – gavage
Exposure Information	Exposure days: days 6–20 post coitum, inclusive Post-exposure observation period: 1 day
Vehicle	Corn oil
Remarks - Method	No significant protocol variations

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	25F	0	0/25
2	25F	100	0/25
3	25F	300	0/25
4	25F	1000	0/25

Mortality and Time to Death

There were no unscheduled deaths in the study.

Effects on Dams

Appearance, behaviour, mean body weights, body weight gains, food and water consumption and faecal/urinary excretions for treated animals were not affected at doses up to 1,000 mg/kg bw/day.

No treatment-related gross pathological findings were observed at doses up to 1,000 mg/kg bw/day.

Effects on Foetus

Gestation rate, appearance and weights of placenta, post-implantation loss, corresponding number of foetuses, foetal weights and sex distribution were unaffected by treatment at all dose levels up to 1,000 mg/kg bw/day.

Foetal malformations including rudiment flat, situs inversus, cleft palate, reduction in eye ball size, folded retina, ventricular defect of the heart and malformation of vertebral arch were reported in 1-4 foetuses out of 341, 286, 308 and 281 foetuses at 0, 100, 300 and 1000 mg/kg bw/day, respectively.

Skeletal malformations (retarded ossification of 6^{th}-9^{th} caudal vertebral bodies, the parietal bones bilateral, distal phalanges of left and proximal digits and 2^{nd}-5^{th} cervical vertebral bodies) were noted in 44/162 foetuses at 0 mg/kg bw/day, 49/148 foetuses at 100 mg/kg bw/day, 62/161 foetuses at 300 mg/kg bw/day and 45/146 foetuses at 1000 mg/kg bw/day. These findings were reported as comparable to the historical controls.

External and visceral deviations including flat eye rudiment, slight dilation of lateral and 3^{rd} brain ventricle(s), reduced/enlarged thyroid gland, folded membranous part of the trachea, cranially extended thymus, pericardia/abdominal cavity/thoracic cavity/liver filled with brown mass, flat/stretched kidneys, cranially lying testes etc. were reported in 2-7 foetuses in all treated groups as compared to 2-10 foetuses in the control group.

Remarks - Results

Some foetal malformations were reported in this study, but were considered to be representative of spontaneous malformations in the rat strain used, with no statistical significance compared to the control group.

A few of foetuses with external and visceral deviations and skeletal deviations were observed in this study, but these were all considered by the study author to be of common types and comparable to spontaneous findings within the current and historical control groups, and within the normal range in the rat strain used.

CONCLUSION
The No Observed Adverse Effect Levels (NOAELs) for maternal toxicity and developmental toxicity were established as 1000 mg/kg bw/day by the study authors.

TEST FACILITY Bayer (2013)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Inherent biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 302C Inherent biodegradability: Modified MITI Test (II)
Inoculum	Activated sludge from two local municipal sewage treatment plants (STPs) and one industrial STP
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Biochemical Oxygen Demand (BOD) by OxiTop System
Remarks – Method	No significant deviations from the test guidelines were reported. The test substance was added to the test flasks and diluted with the test medium to achieve a test concentration of 30 mg/L. A toxicity control was run.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	15	7	78
14	18	14	77
21	20	21	72
28	18	28	69

Remarks – Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound, sodium benzoate surpassed the threshold level of 60 % within 14 days indicating the suitability of the inoculum. The toxicity control exceeded 25 % biodegradation after 14 days showing that toxicity was not a factor in inhibiting the biodegradability of the test substance. The degree of degradation of the notified chemical after 28 days was 18 %.
CONCLUSION	The test substance is not inherently biodegradable.
TEST FACILITY	Currenta (2011)

C.2. Ecotoxicological Investigations

C.2.1. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	
Exposure Period	3 hours
Concentration Range	Nominal: 1,000; 1,800; 3,200; 5,600; 10,000 mg/L
Remarks – Method	No significant deviations from the test guidelines were reported. The test substance was directly added to the test vessels.
RESULTS	
IC50	> 10,000 mg/L
Remarks – Results	All validity criteria for the test were satisfied.
CONCLUSION	The test substance does not inhibit bacterial activity in STPs.
TEST FACILITY	Bayer (1999e)

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