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December 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

PVE-EX

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

TABLE OF CONTENTS

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
LTD/2011	Cintox Australia Pty Ltd	PVE-EX	Yes	≤ 2 tonnes per annum	Industrial synthetic refrigerant lubricant/compressor oil

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified polymer 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*
Specific target organ toxicity – repeated exposure (Category 2)	H373: May cause damage to organs (pancreas) through prolonged or repeated exposure (oral)

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

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

Environmental risk assessment
On the basis of the low toxicity to aquatic life and the reported use pattern, the notified polymer 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 to the notified polymer:
  - Enclosed systems (service readiness-equipment)

- 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 polymer:
  - Avoid skin and eye contact

- 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 polymer:
  - Impervious gloves
  - Coveralls
  - Safety glasses or goggles

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

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

- If products and mixtures containing the notified polymer 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 polymer in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Storage

- The handling and storage of the notified polymer 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 polymer 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 polymer is listed on the Australian Inventory of Chemical Substances (AICS).

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

(1) Under Section 64(2) of the Act; if
  - the function or use of the polymer has changed from industrial synthetic refrigerant lubricant/compressor oil, or is likely to change significantly;
  - the amount of polymer being introduced has increased, or is likely to increase, significantly;
  - the polymer has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the polymer 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.

No additional secondary notification conditions are stipulated.

Safety Data Sheet
The SDS of the notified polymer (and products containing the notified polymer) provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Cintox Australia Pty Ltd (ABN: 63 122 874 613)
Suite 1, Level 2, 38 – 40 George Street
PARRAMATTA NSW 2150

NOTIFICATION CATEGORY
Limited: Synthetic polymer with Mn ≥ 1,000 g/mol

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, polymer constituents, residual monomers, impurities, and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
The endpoints for which a variation of the scheduled data requirements is being claimed include: melting point/boiling point, vapour pressure, partition co-efficient, absorption/desorption, dissociation constant, flammability limits, auto-ignition temperature, explosive properties, oxidising properties and reactivity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
PVE-EX

MOLECULAR WEIGHT
Number Average Molecular Weight (Mn) is > 1,000 g/mol

ANALYTICAL DATA
Reference IR and GPC spectra were provided

3. COMPOSITION

DEGREE OF PURITY
> 99%

DEGRADATION PRODUCTS
No degradation products expected under normal conditions of use

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	Expected to be < 0 °C
Boiling Point	Not determined	Expected to undergo decomposition prior to the boiling.
Density	970 kg/m^3 at 15 °C	SDS
Vapour Pressure	Not determined	Expected to be low based on the relatively high molecular weight
Water Solubility	> 3 g/L at 40 °C	Measured
Hydrolysis as a Function of	Hydrolytically stable at	Measured

pH	pH 1.2, 4, 7, 9 at 40 °C	
Partition Coefficient (n-octanol/water)	Not determined	Based on the relatively high water solubility of the notified polymer and the calculated log P_{ow} of the monomers, the log P_{ow} for the notified polymer is expected to be in the range of 0 – 1
Adsorption/Desorption	Not determined	Based on the relatively high water solubility, the notified polymer is not expected to bind strongly to soils and sediments
Dissociation Constant	Not determined	Contains no functional groups that would imply dissociable functionality
Flash Point	204 °C (Open Cup)	SDS
Flammability	Not determined	Not expected to be a flammable liquid based on flash point
Autoignition Temperature	Not determined	–
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

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

Reactivity
The notified polymer 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 polymer 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 polymer will not be manufactured in Australia. It will be imported in a lubricant formulation at a concentration > 90% or in neat form (100% concentration) to be used directly in refrigeration applications. No local reformulation will occur.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.1 – 2	0.1 – 2	0.1 – 2	0.1 – 2	0.1 – 2

PORT OF ENTRY
Sydney

TRANSPORTATION AND PACKAGING
The notified polymer (in neat form) or the lubricant product containing the notified polymer (at > 90% concentration) will be imported in various container sizes ranging from 1 L steel cans to 205 L steel drums and distributed to industrial end users by road or railway.

USE
The notified polymer (in neat form) or the product containing the notified polymer (at > 90% concentration) will be used as a synthetic refrigerant lubricant, and as compressor oil for commercial air conditioning systems. The notified polymer or the lubricant formulation containing the notified polymer will be distributed to industrial end-users for injection into commercial hydrofluorocarbon (HFC) compressors as well as heating, ventilation, and air conditioning (HVAC) equipment for buildings. The notified polymer is soluble in process fluids and is miscible with HFC refrigerants.

OPERATION DESCRIPTION
Manufacture, reformulation and repacking of the notified polymer or products containing the notified polymer will not occur in Australia.

The notified polymer (in neat form) or the product containing the notified polymer (at > 90 % concentration) will be used by trade equipment suppliers and original equipment manufacturers (OEMs). The notified polymer or the product containing it will be injected into apparatus either at air conditioner factories or building construction sites. In a typical use scenario, refrigeration/air conditioning technicians will connect hoses and pumping equipment to fill the reservoir inside the commercial air conditioning unit with the notified polymer or the product containing it. This will be followed by charging the unit with the refrigerant gas. After charging the unit, the valves will be closed prior to decoupling the charging lines. The notified polymer or the product containing the notified polymer is expected to be enclosed in pressurised air conditioning units during normal use. When the lubricant oil is spent, it will be manually drained from the unit and collected for disposal.

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 – 24
Refrigeration/air conditioning technicians	0.5 – 4	12 – 24

EXPOSURE DETAILS
Transport and warehousing
Transport and warehouse workers are not expected to be exposed to the notified polymer except in the unlikely event of an accident, as the notified polymer will be sealed in original containers during transport and storage.

Refrigeration/air conditioning technicians
The notified polymer or the product containing the notified polymer will be used in commercial air conditioning applications. Exposure of workers to the notified polymer up to 100% concentration may occur during installation, filling, topping-up and emptying air conditioning units especially when the operations involve the use of pressurised systems. In particular, dermal and ocular exposure can occur during connecting and disconnecting transfer hoses. Workers may also be potentially exposed to the notified polymer at 100% concentration if leakages occur. As stated by the notifier, engineering controls in place, including the use of enclosed systems (service readiness-equipment) comprising of hoses, couplings, valves and pressure gauges, are expected to minimise worker exposure. The use of appropriate personal protection equipment (PPE), including impervious gloves and safety glasses, will also reduce the potential for exposure during the operations.

6.1.2. Public Exposure
The notified polymer and products containing it will not be made available to the general public. These will only be used by workers within enclosed systems and in building areas which will not be accessible to the general public. It is unlikely that the public will come into contact with the notified polymer under normal use conditions.

6.2. Human Health Effects Assessment
The results from toxicological investigations conducted on the notified polymer are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, repeat dose oral toxicity – 28-day	NOAEL 40 mg/kg bw/day*
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* chromosome aberration in *Chinese Hamster* Lung Cells	non genotoxic

* Conclusion of study authors

Toxicokinetics, metabolism and distribution
No information on the toxicokinetics, metabolism and distribution was provided. Based on the high molecular weight of the notified polymer (Mn > 1,000 g/mol) it is not expected to be readily absorbed across biological membranes.

Acute toxicity
No information on acute toxicity via any route was provided for the notified polymer.

Irritation and sensitisation
No information on the irritation and sensitisation potential of the notified polymer was provided. No particular structural alert was identified for skin sensitisation.

Mutagenicity/Genotoxicity
The notified polymer tested negative in a bacterial reverse mutation assay and in an *in vitro* chromosomal aberration test in *Chinese hamster* lung cells.

Repeated dose toxicity
A repeated dose oral (gavage) toxicity study on the notified polymer was conducted in rats (see Appendix B.1.). In a dose range finding study (report not submitted), one animal administered at 1,000 mg/kg bw/day was found deceased on Day 5. Therefore, in the main study the test substance was administered at 40, 160 and 640 mg/kg bw/day for 28 consecutive days with a 14 day recovery period. The 640 mg/kg bw/day dose was further reduced to 320 mg/kg bw/day during the study from Day 12, because 4 female animals were found dead or in moribund state. Clinical effects observed in these 4 females included staining of the abdomen, decreased spontaneous locomotion, decreased respiratory rate, emaciation, subnormal temperature and eyelid closure.

At the low dose of 40 mg/kg bw/day, statistically significant effects were noted in both male and female animals. The effects in males include increase in total protein, increases in relative liver and kidney weights, and decrease in seminal vesical weight. In females, increase in total cholesterol and bilirubin were observed. However, these changes were considered incidental by the study authors.

For animals treated at dose levels of ≥ 160 mg/kg bw/day, treatment-related adverse effects on specific organs were noted, including apoptosis of acinar cells of the pancreas, diffuse hyperplasia of hepatocytes, and increases in relative liver weight together with increases in total cholesterol and bile acids. At the end of the recovery period, the effects on the pancreas were fully reversed in males, and decreased in severity in females. The toxic effects on the liver were also reversible with the changes disappearing in males, and the severity of the changes decreasing in females. However, in females increased total cholesterol and bile acid levels were still present after the recovery period. This effect was considered by the study authors to be associated with the increase in relative liver weight.

The No Observed Adverse Effect Level (NOAEL) was determined by the study authors as 40 mg/kg bw/day, based on the treatment-related adverse effects observed on the pancreas and liver at ≥ 160 mg/kg bw/day.

Based on the above toxicity investigation the notified polymer is considered to cause adverse effects in pancreas and liver upon repeated or prolonged exposure. Detailed histopathological investigation may be required to gain further insight into the organ specific toxicity.

Health hazard classification
Based on Paragraphs 3.9.2.9.5 and 3.9.2.9.7 of the GHS (United Nations, 2009), significant toxic effects observed in a 28-day oral repeated dose study conducted in experimental animals and seen to occur within 30 to 300 mg/kg bw/day (being the guidance values for 90-day study increased by a factor of 3) should be considered for Category 2 classification for specific target organ toxicity.

Therefore, based on the NOAEL of 40 mg/kg bw/day with specific organ toxicity observed in the pancreas at ≥ 160 mg/kg bw/day, the notified polymer is recommended for classification in accordance with 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***
Specific target organ toxicity – repeated exposure (Category 2)	H373: May cause damage to organs (pancreas) through prolonged or repeated exposure (oral)

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Only limited hazard information on the notified polymer is available. Based on the studies provided, the notified polymer may have potential to cause adverse effects on pancreas and liver if prolonged or repeated oral exposure occurs at high doses. However, systemic absorption of the notified polymer through dermal exposure is expected to be limited due to its relatively high molecular weight. No data are available on acute toxicity and irritation effects of the notified polymer.

Throughout end-use workers may be exposed to the notified polymer up to 100% concentration during applications. Workers may also be potentially exposed to the notified polymer at 100% concentration if leakages occur. The main exposure routes are expected to be dermal and ocular. The proposed use of engineering controls including enclosed systems (service readiness-equipment) comprising of hoses, couplings, valves and pressure gauges, and appropriate personal protection equipment (PPE), including impervious gloves and safety glasses, will reduce the potential for exposure during the operations, hence reduce the risk of any adverse effects.

Provided that the work place controls are being adhered to, under the conditions of the occupational settings described, the notified polymer is not considered to pose an unreasonable risk to the health of workers.

6.3.2. Public Health

The notified polymer will only be used by workers within enclosed systems and in areas which will not be accessible to the general public.

When used in the proposed manner, the notified polymer 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 polymer will be imported into Australia in neat form or in lubricant products. Manufacture, reformulation and repacking of the notified polymer will not occur in Australia. Accidental spills of the notified polymer during import, transport or storage are expected to be adsorbed onto suitable materials and collected for disposal in accordance with local regulations.

RELEASE OF CHEMICAL FROM USE

The notified polymer in the neat form or in the lubricant products will be used as synthetic refrigerant lubricant and as compressor oil for commercial HFC compressors and HVAC equipment by original equipment manufacturers and trade equipment suppliers. The notified polymer will be injected into the apparatus either at air conditioner factories or in buildings. In a typical use scenario, refrigeration/air conditioning technicians will connect hoses and pumping equipment to fill the reservoir inside the commercial air conditioning unit with the notified polymer or the product containing it. This will be followed by charging the unit with the refrigerant gas. After charging the unit, the valves will be closed prior to decoupling the charging lines.

As estimated by the notifier, up to 2% of the import volume of the notified polymer may remain as residues in empty containers, which are expected to be disposed of in accordance with local regulations. Up to 1% of the import volume of the notified polymer, as estimated by the notifier, may be released as accidental spills or leaks during charging of units, which are also expected to be collected and disposed of in accordance with local regulations.

RELEASE OF CHEMICAL FROM DISPOSAL

When the lubricant and compressor oil is spent, it will be manually drained from the unit and collected for recycling or disposal of by an approved waste management facility.

7.1.2. Environmental Fate

The stability test conducted on the notified polymer indicates that it is stable to hydrolysis under environmental conditions. For details of the stability study, please refer to Appendix A. The other tests conducted on the notified polymer showed that it is not readily biodegradable (no degradation after 28 days in the OECD TG 301C test) and not bioaccumulative (Bioaccumulation Factor (BCF) < 65), for details of the biodegradability and bioaccumulation study, please refer to Appendix C. The notified polymer is not expected to be released to the air compartment at significant quantities based on its expected low vapour pressure and the reported use pattern. The notified polymer is expected to neither be released into nor partition to the aquatic compartment in ecologically significant quantities based on its reported use pattern. The notified polymer is expected to 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 as release of the notified polymer 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 polymer are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h EC50 > 100 mg/L	Not harmful to fish
Daphnia Toxicity	48 h EC50 > 100 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity	72 h EC50 > 100 mg/L	Not harmful to alga

Based on the above ecotoxicological endpoints for the notified polymer, it is not expected to be harmful to aquatic life. Therefore, the notified polymer is not formally classified under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) for acute and chronic toxicities (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) for the aquatic compartment has not been calculated as the notified polymer is not considered to be harmful to aquatic organisms.

7.3. Environmental Risk Assessment

The Risk Quotients (Q = PEC/PNEC) have not been calculated since the PEC and PNEC were not calculated. The notified polymer is not expected to be released to the air and aquatic environment at ecologically significant quantities, and it is not harmful to aquatic life. The notified polymer is not considered to be accumulative. Therefore, based on the low toxicity to aquatic life and the assessed use pattern as synthetic refrigerant lubricant, and as compressor oil for commercial HFC compressors and HVAC equipment, the notified polymer is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water solubility and stability Water Solubility: > 3 g/L at 40 °C
Stable at pH 1.2, 4, 7 and 9 at 40 °C

Method	OECD TG 120 Solution/Extraction Behaviour of Polymer in Water Guideline of Korean National Institute of Environmental Research
Results	Water Solubility: > 3 g/L at 40 °C The test substance (notified polymer) is stable at pH 1.2, 4, 7 and 9 at 40 °C with no sign of degradation occurring as determined by GPC and IR analyses.
Remarks	The test substance is in liquid form. OECD TG 120 is a modification of OECD TG 105 Shake Flash Method. The test was conducted using one sample size with TOC analysis followed by estimation by Tosoh EcoSEC HLC-8320 Gel Permeation Chromatograph (GPC) and JASCO 4100 Fourier Transform Infra-red Spectrometer (FT-IR).
Test Facility	KOPTRI (2017)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Repeat dose toxicity

TEST SUBSTANCE	Notified polymer
METHOD	Ministry of Health, Labour and Welfare, Japan, 28-day Repeated Dose Toxicity Study in Mammalian Species (Testing Methods for New Chemical Substances) (Comparable to OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents)
Species/Strain	Rat/Crl:CD(SD)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	Olive oil
Remarks - Method	The methodology was comparable to the OCED Test Guideline 407. No significant deviations of protocols were noted. A 7-day dose range finding study on the notified polymer was conducted prior to the main study. One animal administered at 1,000 mg/kg bw/day was found deceased on Day 5. Therefore, in the main study the test substance was administered at 40, 160 and 640 mg/kg bw/day. Due to the severe toxicity effects observed, 640 mg/kg bw/day dose level was further reduced to 320 mg/kg bw/day from Day 12.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
control	10 (5M/5F)	0	0/10
low dose	10 (5M/5F)	40	0/10
mid dose	10 (5M/5F)	160	0/10
high dose	10 (5M/5F)	640 (→ 320)*	4/10
control recovery	10 (5M/5F)	0	0/10
high dose recovery	10 (5M/5F)	640 (→ 320)*	1/10

* The high dose was reduced from 640 mg/kg bw/day to 320 mg/kg bw/day on Day 12 of dosing because of deceased and moribund female animals in the high dose group. The reduced dose of 320 mg/kg bw/day was also applied to the recovery group from Day 12.

Mortality and Time to Death

One female animal in the high dose group died on Day 10 of dosing. Two female animals in the high dose group died on Days 11 and 12. One female animal was found moribund on Day 12. No further mortality was noted after Day 12 when the dose level was reduced from 640 to 320 mg/kg bw/day. The new dose (320 mg/kg bw/day) was continued till the end of the dosing period.

One male animal in the high dose group died on Day 28. The study author asserted that there were no general clinical changes prior to the death and attributed the death to an error in dosing.

Clinical Observations

In females of the high dose group, suppressed weight gains were observed during the treatment period. No significant body weight changes were noted in males in any of the treatment groups.

Clinical effects attributed to the notified polymer were noted in males and females of the high dose groups (including the high dose recovery group). Staining of the abdomen was observed in 6/10 females of the high dose groups on and after Day 5. In addition, decreased spontaneous locomotion in 9 animals; decreased respiratory rate in 7 animals; staining of the lower abdomen and tremor in 5 animals; staining around the nose and mouth in 4 animals; emaciation and subnormal temperature in 2 animals; eyelid closure, crouching and prone position in 1 animal were observed on and after Day 9 of dosing. Salivation just after dosing on and after Day 4 was also observed in 9/10 animals in males of the high dose groups.

No treatment-related toxic effects were observed in the detailed clinical observations, sensorimotor function examinations, urinalyses or haematological examinations in the mid and low dose groups. No clinical signs were observed for any animal in the low dose group.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Serum chemistry
At the low dose of 40 mg/kg bw/day, statistically significant effects were noted in both male and female animals. The effects in males include increased total protein, and in females increases in total cholesterol and bilirubin were observed. However, these changes were considered incidental by the study authors.

A statistically significant increase in total cholesterol and bile acids in females in the mid and high dose groups (≥ 160 mg/kg bw/day) were observed. The change was associated with increased liver weight.

A dose dependent statistically significant increase in total bilirubin was noted in male rats in the mid and high dose groups.

Haematology
Animals in the high dose group showed decrease in mean corpuscular volume and haemoglobin. An increase of white blood cell count in males and an increase of reticulocyte count ratio in females were also observed in the high dose groups. There were no changes in the other parameters in the haematological examinations. The study authors concluded that the observed changes were treatment-related but were of no toxic relevance.

Effects in Organs

Pancreas
The treatment-related toxic effects on the pancreas were recorded. Apoptosis of acinar cells of the pancreas was observed in males in the high dose group and in females in the mid and high dose groups (≥ 160 mg/kg bw/day) at the end of the dosing period. The change on the pancreas was fully reversed in male animals and decreased in severity in females at the end of the recovery period.

Liver
Treatment-related changes on the liver were noted. Diffuse hyperplasia of hepatocytes and increased relative weight of the liver in both sexes in the high dose groups, increased relative weight of the liver in females in the mid dose group (160 mg/kg bw/day) were observed at the end of the dosing period. It was concluded by the study authors that the changes in relative liver weight in females of the mid and high dose groups were associated with increased total cholesterol and bile acids. The increased relative liver weight and total cholesterol in females in the high dose group were not fully reversed at the end of the recovery period.

Other effects
Decreased (but not statistically significant compared to control groups) absolute epididymis weight, increased relative weights of the heart, kidneys and prostate in males, and decreased absolute adrenal weight and increased heart weight in females were observed in high dose groups. These changes were considered by the study authors to be incidental and within the histological control range.

Remarks – Results
Exposure to ≥ 160 mg/kg bw/day of the notified polymer resulted in signs of toxicity including apoptosis of acinar cells of the pancreas, diffuse hyperplasia of hepatocytes, increases in relative liver weight associated with increases in total cholesterol and bile acids.

There were statistically significant effects including increased total protein, increased relative liver and kidney weight and decreased seminal vesical weight for male animals, and increased total cholesterol and bilirubin in female animals were reported at 40 mg/kg bw/day. The study authors concluded these were incidental.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) for the notified polymer was established as 40 mg/kg bw/day by the study authors, based on the adverse effects observed in the pancreas in animals treated at ≥ 160 mg/kg bw/day.

TEST FACILITY CERI (2016a)

B.2. Genotoxicity – bacteria

TEST SUBSTANCE Notified polymer

METHOD OECD TG 471 Bacterial Reverse Mutation Test
Pre incubation procedure
Species/Strain *Salmonella typhimurium*: TA1537, TA1535, TA100, TA98
Escherichia coli: WP2*uvr*A
Metabolic Activation System Phenobarbital (PB) and 5,6-benzoflavone (BF) induced rat liver S9 mix
Concentration Range in Main Test a) With metabolic activation: 313 – 5,000 µg/plate
b) Without metabolic activation: 10 – 5,000 µg/plate
Vehicle Acetone
Remarks - Method Concentrations for main test were chosen based on the preliminary test conducted on TA100, TA1535 and WP2*uvr*A (base-pair substitution type) and on TA98 and TA1537 (frameshift type) results.

Tests with vehicle control and positive controls were run concurrently. Positive controls were:

- With metabolic activation: 2-aminoanthracene (TA1535, WP2*uvr*A) and benzo[*a*]pyrene (TA98, TA100, TA1537)
- Without metabolic activation: sodium azide (TA1535); 2-methoxy-6-chloro-9-[3-di-(2-chloroethyl)aminopropylamino]acridine dihydrochloride (TA1537), 2-furanacetamide, α-[(5-nitro-2-furanyl)methylene]- (TA98, TA100, WP2*uvr*A).

No significant protocol deviations were noted.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 313	≥ 156	> 5,000	negative
Test 2	–	≥ 156	> 5,000	negative
Present				
Test 1	> 5,000	> 5,000	> 5,000	negative
Test 2	–	> 5,000	> 5,000	negative

Remarks - Results The test substance did not result in an increase of more than twice the number of revertant colonies in comparison to the negative control. In addition, no dose-related response was observed in any strains of base-pair substitution type or frame-shift type, with or without metabolic activation.

The positive and negative controls provided a satisfactory response confirming the validity of the test system.

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

TEST FACILITY BML (2015)

B.3. Genotoxicity – *in vitro*

TEST SUBSTANCE Notified polymer

METHOD OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test
Species *Chinese hamster* lung cells

Cell Type/Cell Line	CHL/IU
Metabolic Activation System	S9 fraction from phenobarbitone/5,6-benzoflabone induced rat liver
Vehicle	Acetone
Remarks - Method	The negative control was the vehicle acetone and the positive controls were mitomycin C (without metabolic activation) and 3,4-benzopyrene (with metabolic activation). No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1 (preliminary)	0, 39.1, 78.1, 156, 313, 625, 1,250, 2,500, 5,000	6 h	18 h
Test 2 (preliminary)	0, 39.1, 78.1, 156, 313, 625, 1,250, 2,500, 5,000	24 h	24 h
Test 3 (main)	0*, 150*, 300*, 600*, 1,200, 1,500	6 h	18 h
Test 4 (main)	0*, 25*, 50*, 100*, 200, 250	24 h	24 h
Present			
Test 1 (preliminary)	0, 39.1, 78.1, 156, 313, 625, 1,250, 2,500, 5,000	6 h	18 h
Test 2 (main)	0*, 500*, 750*, 1,000*, 1,250, 1,500	6 h	18 h

* Cultures selected for metaphase 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 (preliminary)	≥ 1,140	–	≥ 313	negative
Test 2 (preliminary)	≥ 191	–	≥ 313	negative
Test 3 (main)	–	≥ 600	≥ 300	negative
Test 4 (main)	–	≥ 100	> 250	negative
Present				
Test 1 (preliminary)	≥ 1,363	–	> 313	negative
Test 2 (main)	–	≥ 1,000	≥ 500	negative

Remarks - Results	The test substance did not result in a statistically significant and/or dose dependent increase in the frequency of cells with chromosome aberrations compared to the vehicle control groups either with or without metabolic activation. The positive controls demonstrated the sensitivity of the assay and the metabolising activity of the rat liver S9 preparations.
CONCLUSION	The notified polymer was not clastogenic to *Chinese hamster* lung cells CHL/IU treated *in vitro* under the conditions of the test.
TEST FACILITY	SRICC (2016)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 301C Ready Biodegradability: Modified MITI Test (I) Ministry of Health, Labour and Welfare, Ministry of Economy, Trade and Industry, Japan, Method for Testing the Biodegradability of Chemical Substances by Microorganisms, Ministry of Environment
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Biochemical Oxygen Demand (BOD) using oxygen consumption apparatus, Dissolved Oxygen Concentration (DOC) using DOC analyser, and test substance using High Performance Liquid Chromatography (HPLC)
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance (30 g) was added to 300 mL of test medium to achieve a test concentration of 100 mg/L in the test vessels. A toxicity control was run.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation by BOD*	*Day*	*% Degradation by BOD*
7	1	7	79
14	-1	14	95
21	-1	21	95
28	-1	28	96

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound, aniline surpassed the threshold level of 60% within 14 days indicating the suitability of the inoculums. The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The BOD, DOC and HPLC results show that test substance was not degraded after 28 days.
CONCLUSION	The test substance is not readily biodegradable.
TEST FACILITY	CERI (2015)

C.1.2. Bioaccumulation

TEST SUBSTANCE	Notified polymer
METHOD	Ministry of Health, Labour and Welfare, Ministry of Economy, Trade and Industry, Japan, Method for Testing the Degree of Accumulation of Chemical Substances in Fish Body, Ministry of Environment
Species	*Cyprinus carpio*
Exposure Period	Exposure: 28 days
Auxiliary Solvent	None
Concentration Range	Nominal: 0.1 mg/L (level 1) and 0.01 mg/L (level 2) Actual: 0.09 mg/L (level 1) and 0.009 mg/L (level 2)
Analytical Monitoring	Liquid Chromatography – Tandem Mass Spectrometry (LC-MS/MS)
Remarks - Method	This is a flow-through test with no depuration period. No significant deviations from the test guidelines were reported. A preliminary test confirmed that the test substance was stable under the testing conditions.

The test fish was analysed five times at intervals of ≥ 48 hours and at 28 days.

RESULTS

Bioconcentration Factor	BCF < 7 for level 1 test and BCF < 65 for level 2 test.
CT50	
Remarks - Results	All validity criteria for the test were satisfied. No abnormality in behaviour or appearance was observed.

CONCLUSION The test substance is not considered to be bioaccumulative.

TEST FACILITY CERI (2016b)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE Notified polymer

METHOD OECD TG 203 Fish, Acute Toxicity Test – Static
Ministry of Health, Labour and Welfare, Ministry of Economy, Trade and Industry, Japan, Fish Acute Toxicity Test, Ministry of Environment

Species	*Oryzias latipes*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	37 mg $CaCO_3$/L
Analytical Monitoring	High Performance Liquid Chromatography (HPLC)
Remarks – Method	No significant deviations from the test guidelines were reported. The test substance was added and mixed with the test medium to achieve a test concentration of 100 mg/L. The test substance was measured at the start and end of the test.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	Control	7	0	0	0	0	0
100	99.3	7	0	0	0	0	0

LC50	> 100 mg/L at 96 hours
Remarks – Results	All validity criteria for the test were satisfied. The test substance was stable under the testing conditions (97.8 – 101% of the nominal concentration).

CONCLUSION The test substance is not harmful to fish.

TEST FACILITY CERI (2016c)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified polymer

METHOD OECD TG 202 *Daphnia sp.* Acute Immobilisation Test and Reproduction Test – Static
Daphnia sp. Acute Immobilisation Test, Ministry of Environment, Ministry of Health, Labour and Welfare, Ministry of Economy, Trade and Industry, Japan

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None

Water Hardness	37 mg $CaCO_3$/L
Analytical Monitoring	High Performance Liquid Chromatography (HPLC)
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance was added and mixed with the test medium to achieve a test concentration of 100 mg/L. The test substance was measured at the start and end of the test.

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	Control	20	0	0
100	99.9	20	0	0

LC50	> 100 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. The test substance was stable under the testing conditions (99.7 – 100% of the nominal concentration).

CONCLUSION The test substance is not harmful to aquatic invertebrates.

TEST FACILITY CERI (2016d)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified polymer

METHOD OECD TG 201 Alga, Growth Inhibition Test
Ministry of Health, Labour and Welfare, Ministry of Economy, Trade and Industry, Japan, Algal Growth Inhibition Test, Ministry of Environment

Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 6.25, 12.5, 25, 50, 100 mg/L Actual: 6.25, 12.3, 24.6, 49.7, 100 mg/L
Auxiliary Solvent	None
Water Hardness	Not determined
Analytical Monitoring	High Performance Liquid Chromatography (HPLC)
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance was added and mixed with the test medium to achieve a test concentration of 100 mg/L. The test substance was measured at the start and end of the test.

RESULTS

Biomass		*Growth*	
EC50	*NOEC*	*EC50*	*NOEC*
mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
Not determined	Not determined	> 100	50

Remarks - Results	All validity criteria for the test were satisfied. The test substance was stable under the testing conditions (98.2 – 100% of the nominal concentration). NOEC was estimated as 50 mg/L because inhibition rate of 12.5 – 50 mg/L levels were all less than 2% which was very low for estimation of observed effect concentration.

CONCLUSION The test substance is not harmful to alga.

TEST FACILITY CERI (2016e)

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