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June 2008

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Rhodiasolv IRIS

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

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

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

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Director
NICNAS

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Rhodiasolv IRIS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Rhodia Australia Pty Ltd (ABN: 24 050 029 000)
Building 25, 270 Ferntree Gully Road
Notting Hill VIC 3168

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical Name; Other Names; CAS Number; Molecular Formula; Structural Formula; Molecular Weight; Purity; Residual Monomers/Impurities; Additives/Adjuvants; Import Volume; Use Details

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Dissociation constant; Hydrolysis as a function of pH; Acute inhalation toxicity

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
US EPA

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Rhodiasolv® IRIS (70-100% notified chemical)

MOLECULAR WEIGHT
<500 Da

ANALYTICAL DATA
Reference NMR, IR, UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 80%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Clear odourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -75°C	Measured
Boiling Point	215.5°C at 100.1 kPa	Measured
Density	1055 kg/m^3 at 20 ± 0.1°C	Measured
Vapour Pressure	0.01 kPa at 25°C 0.0063 kPa at 20°C	Measured
Water Solubility	25.2 ± 0.2 g/L at 20 °C	Measured

Hydrolysis as a Function of pH	Not determined	Stable at neutral pH, slowly hydrolysed at low pH, and rapidly hydrolysed at high pH.
Partition Coefficient (n-octanol/water)	Log P_{ow} = 0.89	Measured
Surface Tension	64.0 mN/m at 20.7°C	Measured
Adsorption/Desorption	Log Koc < 1.25 which is equal to a Koc value < 18	Measured
Dissociation Constant	Not determined	The notified chemical does not contain dissociable groups.
Particle Size	Not applicable	The notified chemical is a liquid.
Flash Point	98°C at 101.1kPa	Measured
Flammability	Not expected to be flammable	Based on flash point.
Autoignition Temperature	430°C	Measured
Explosive Properties	Not explosive	Measured
Oxidising Properties	Not oxidising	Estimated

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

The notified chemical is classified as a C1 combustible liquid according to *National Standard for the Storage and Handling of Workplace Dangerous Goods* [NOHSC:1015(2001)].

Reactivity
Stable under normal conditions of use. Avoid strong oxidising agents. Hazardous decomposition products may include carbon dioxide and carbon monoxide.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported as a component of Rhodiasolv® IRIS at concentrations of 70-100%.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	<200	<200	<200	<200	<200

PORT OF ENTRY
Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Cleaning solvent formulators

TRANSPORTATION AND PACKAGING
The notified chemical will be imported by ship in 200L plastic lined steel drums. The drums will then be transported by truck.

The finished cleaning solvent products containing the notified chemical will be packaged in 1L, 4L and 10L steel cans and 200L drums that will be transported to end users by road.

USE
The notified chemical will be used as an additive in cold cleaning solvents in a wide range of applications including:

- Automotive cleaning (i.e. cleaning overspray in spray booths) (30%)
- Cleaning of vessels and tanks - resin and paint manufacturers (60%)
- Cleaning of shoe sole injection moulding machines (5%)
- Cleaning of printed circuit boards (5%)

OPERATION DESCRIPTION

Reformulation

The imported product containing the notified chemical at concentrations of 70-100% will be transferred, together with other ingredients, into a mixing vessel using metered dosing. The vessel will be sealed during mixing and a local ventilation system will be used. Following quality checks and necessary batch adjustments, the resulting product (5-100% notified chemical) will be dispensed into cans or drums using an automated filling machine.

End use

Finished products containing the notified chemical (5-100%) will be supplied to various industries around Australia. Typically, such processes will generally involve either: (i) flushing of equipment with the product (for large equipment); or (ii) spraying the product onto surfaces or cloths followed by wiping the surfaces with a rag.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency*
Transportation and storage			
Dock to formulator's site	3	2-3	10-15 days/year
Formulator's site to end-use customers	6	2-3	10-15 days/year
Reformulation			
Weighing and mixing operations	6	30 min to 6 hrs	16 days/year
Filling cans of solvent	4	3	16 days/year
Quality control/chemists and technical service	4-8	1	16 days/year
Cleaning operations	2	30 min	16 days/year
End use			
Automotive cleaning (spraying)	> 500	1	260 days/year
Vessel and tank cleaning	50	2-3	1-2 days/year
Shoe sole injection moulding machine cleaning (spraying)	20	1	260 days/year
Cleaning of printed circuit boards	20	1	260 days/year

EXPOSURE DETAILS

Reformulation

Dermal, ocular and inhalation exposure of workers to the notified chemical (concentrations up to 100%) may occur during charging of the mixer, quality control checks and batch adjustment, and dispensing of the reformulated product into end use containers. Exposure is expected to be low given the exhaust ventilation system in place, the automated systems used, the enclosed mixing vessel, and the wearing of personal protective equipment (PPE), including coveralls, goggles and impervious gloves.

End use

Dermal, ocular and inhalation exposure of workers to the notified chemical (concentrations up to 100%) are expected to be high due to the nature of the manual handling of products containing high concentrations of the notified chemical and generation of aerosols, especially during cleaning of automotive equipment, shoe sole moulding machines, and printed circuit boards. EASE modelling of the spraying process was performed to estimate dermal exposure of workers to the notified chemical. The following assumptions were used for these estimates: direct handling, wide dispersive use (uncontrolled exposure) and intermittent contact level (assumed to be 2 -10 events per day). The predicted dermal exposure to the notified chemical is 1 - 5 mg/cm^2/day. This is equivalent to 12 - 60 mg/kg bw/day, based on assumptions outlined by the European Commission (EC, 2003). It is noted that exposure is expected to be lowered by the use of personal protective equipment that is likely to include anti-static overalls and footwear, respirators, goggles and gloves.

6.1.2. Public exposure

Products containing the notified chemical will only be used in industrial settings. Therefore, public exposure is expected to be negligible.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	low oral toxicity LD50 >2000 mg/kg bw
Rat, acute dermal toxicity	low dermal toxicity LD50 >2000 mg/kg bw
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Rat, repeat dose oral toxicity with reproduction/developmental toxicity screening	NOAEL 300 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	non genotoxic
Genotoxicity – in vivo mammalian erythrocyte micronucleus test	inconclusive
Genotoxicity – in vivo mammalian erythrocyte micronucleus test (in conjunction with the repeat dose oral toxicity study)	non-genotoxic

Toxicokinetics, metabolism and distribution
The notified chemical may be absorbed from the gastrointestinal tract or dermally, given its low molecular weight, high water solubility, moderate lipophilicity, and its low vapour pressure.

No data was submitted on the inhalation toxicity of the notified chemical. Given its low volatility, inhalation as a vapour is not expected to occur. If it were inhaled as an aerosol, it would be expected to diffuse/dissolve into the mucus lining of the respiratory tract and then have the potential to be absorbed directly across the respiratory tract epithelium (log P>0). It may also be absorbed through aqueous pores (MW < 500) or retained within the mucus (as it is hydrophilic) and transported out of the respiratory tract (EC, 2003).

Acute toxicity
The notified chemical was found to be of low acute oral and dermal toxicity (LD50 >2000mg/kg bw). In addition, it was slightly irritating to the eyes and skin of test animals and was not found to display any evidence of skin sensitisation effects. It is also noted that the notified chemical has been shown to induce hypothermia in mice (see below).

Repeated dose toxicity and toxicity for reproduction
There were some toxicologically significant changes observed in the 28 day repeat dose oral toxicity study, including the death of one female animal that may be test item related, and significant increases in the weight of the kidneys of female animals that had been treated with 1000 mg/kg/day of the notified chemical. As such, the NOAEL was established as 300 mg/kg/day for this study. The study also examined effects on reproduction/development, resulting in no significant toxicological observations to offspring.

Mutagenicity
The notified chemical was negative in the bacterial reverse mutation assay and the in vitro mammalian chromosome aberration test. Several in vivo mammalian erythrocyte micronucleus tests were performed in order to confirm the nature of the potential genotoxicity of the notified chemical. The first test resulted in increases in the micronucleated bone marrow cells of mice, which may be consistent with genotoxic effects of the notified chemical. However, in subsequent studies, such effects were not observed when repeated under similar conditions. One such test examined the rectal temperature of mice in conjunction with the micronucleus assay. Whilst effects suggestive of clastogenicity were not observed, it was shown that the notified chemical can induce hypothermia in mice. It is known that hypothermia can result in increases in micronucleated cells in the bone marrow that are unrelated to the intrinsic genotoxicity of a chemical (Tweats, 2007). In conclusion, the notified

chemical is not considered to be mutagenic, given that effects observed during testing were not reproducible, and the effects that were observed in the initial testing are likely to be due to the induction of hypothermia in mice.

Related chemicals
A number of studies have been performed on chemicals with structures that are closely related to the notified chemical. Many such studies have investigated the effects of their inhalation. These related chemicals have been shown to induce mild degeneration of the olfactory epithelium of the rat nasal cavity (mild olfactory cytotoxicity), mainly following enzyme metabolism. However, further studies suggest that such effects are likely to be much less significant in humans compared to rats due to a reduced rate of enzymatic hydrolysis. Other toxicologically significant effects upon acute and repeated inhalation exposure of these related chemicals were observed, such as decreases in serum testosterone concentrations and increased epididymal sperm counts in male rats. However, it is noted that the severity of these effects does not meet the criteria for hazard classification. Moreover, the notified chemical has a vapour pressure approximately ten-fold lower than that of the related chemicals. Therefore, the effects of the structurally similar chemicals via inhalation exposure may not be relevant to the notified chemical.

Classification
Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Exposure of workers to the notified chemical at concentrations of up to 100% are expected to occur, particularly during end use processes. Such exposure may be dermal, ocular, or by inhalation of aerosols (unlikely to be inhaled as a vapour due to its low volatility).

Upon dermal/ocular contact with the notified chemical, the risk of slight irritation exists. However, the personal protective equipment (PPE) worn by workers when handling products containing the notified chemical should prevent such effects from occurring.

Whilst the acute dermal toxicity of the notified chemical was found to be low, health effects resulting from repeated dermal exposure to the notified chemical cannot be ruled out, particularly on the basis of effects observed in test animals following repeated oral exposure. During end use spray operations, dermal exposure of worker is estimated to be 12 - 60 mg/kg bw/day. A dermal NOEL/NOAEL was not determined, however, a NOAEL of 300 mg/kg bw/day was established in a 28 day oral study in the rat. This results in a margin of exposure (MOE) of 5, which suggests that the risk is not acceptable if workers are exposed to the notified chemical repeatedly on the skin. However, the PPE worn by workers should lower dermal exposure levels.

The effects of inhalation of aerosols of the notified chemical have not been studied. However, based on its low vapour pressure and rapid transportation out of the respiratory tract, together with comparison to the structurally similar chemicals (see Section 6.2), the risk of effects via inhalation of aerosols of the notified chemical is considered to be low. In addition, the presence of exhaust ventilation during reformulation, and the wearing of respirators during end use spray operations are likely to reduce inhalation exposure.

Overall, the notified chemical is not considered to pose an unacceptable risk to workers, given the use conditions described. However, employers should implement appropriate control measures to minimise skin, eye and inhalation exposure.

6.3.2. Public health
As the public are not expected to be exposed to the notified chemical, the risk to public health is considered to be negligible.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured in Australia. Local operations will include transport and storage, formulation, filling and packaging and application by end-users (i.e. industrial cleaners).

RELEASE OF CHEMICAL FROM USE

During formulation of the solvent cleaning products it is estimated that < 5400 kg per annum of notified chemical waste will be generated. This is derived from:

Release from accidental spill:	0.2% (400 kg/annum)
Residues in import containers:	0.5% (1000 kg/annum)
Release from formulation of cleaning solvent:	1.0% (2000 kg/annum)
Release from cleaning of formulation equipment:	1.0% (2000 kg/annum)

It is anticipated that spills of the notified chemical and blended cleaning solvents will be contained within the plant through the bunding systems in place. Spills will be collected using absorbent material and removed by a licensed industrial waste contractor to a licensed waste landfill site. Formulation equipment will be cleaned using solvent and licensed hazardous liquid waste contractors will dispose waste from this process by incineration.

Release from end-use products:

Given the use pattern of the notified chemical, initial release is entirely expected to occur to the aquatic compartment. Assuming the maximum importation volume of 200 tonnes and that all cleaning operations using the notified chemical occur throughout the year, the average daily release is expected to be 550 kg. This release is expected to be relatively diffuse.

There may be localised release to soil in the event that cleaning solutions are discarded directly to this compartment, but this is not expected to be significant.

Residues in end-use containers are expected to be < 400 kg/annum. There is unlikely to be much residual product in containers as they will probably be flushed with water prior to being disposed of. It is expected that end use containers will normally be disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

It is expected that emptied import drums containing residual chemical will be used to collect liquid waste and when full will be collected by a licensed hazardous waste contractor. The liquid contents will be treated and disposed of and the drums will be disposed of to a licensed waste landfill site. The majority of the notified chemical will be disposed of through the sewer as a result of its use as an industrial cleaner.

7.1.2 Environmental fate

The two ready biodegradability tests submitted showed that the notified chemical achieved >70% biodegradation after 28 days. Therefore, the notified chemical can be considered to be readily biodegradable, indicating that it would not be expected to persist in the environment.

Data on bioaccumulation of the notified chemical is not available. However, based on the log K_{OW} value of the notified chemical (0.89), the potential to bioaccumulate is expected to be low.

For the details of the environmental fate studies please refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

Given the use pattern of the notified chemical, the majority will be released to the aquatic compartment through the sewer. Assuming the maximum importation volume of 200 tonnes and all cleaning operations using the notified chemical occur all year, the average daily release is expected to be around 550 kg. As a worst case scenario it has been assumed that the entire import volume will be discharged to the sewers across Australia and that no removal occurs as a result of the passage through the sewage treatment plant. The result of the PEC calculations using an STP model are summarised below:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	200,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	200,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	547.95	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River:	129.47	µg/L
PEC - Ocean:	12.95	µg/L

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	46 < LC50 < 100 mg/L	Harmful to fish.
Daphnia Toxicity	EC50 > 100 mg/L	Not harmful to *Daphnia magna*
Algal Toxicity	EC50 > 60 mg/L	Not harmful to algae (at maximum concentration tested, 60 mg/L)
Inhibition of Bacterial Respiration	EC50 >1000 mg/L	Not harmful to bacteria.

7.2.1 Predicted No-Effect Concentration

The Predicted No-Effect Concentration has been calculated from the most sensitive fish toxicity (96 h LC50 = 46 mg/L) to the notified chemical. As the results are available for three trophic levels, the assessment factor of 100 has been used.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish)	46	mg/L
Assessment Factor	100	
PNEC:	460	µg/L

7.3. Environmental risk assessment

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	*PEC/PNEC*
Q - River:	129	460	0.281
Q - Ocean:	12.9	460	0.028

The unmitigated Risk Quotients (PCE/PNEC) are <1 for both the river and ocean disposal scenarios. Given that the notified chemical is readily biodegradable, the amount of notified chemical entering receiving waters would be reduced as a result of degradation in sewage treatment plants. Consequently, the risk quotients would be even smaller. Therefore, the notified chemical is not expected to pose an unacceptable risk to the aquatic environment based on the current use pattern and the maximum import volume of 200 tonnes/year.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

and

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	*Hazard statement*
Acute hazards to the aquatic environment	Category 3	Harmful to aquatic life

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

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

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the reported use pattern, the notified chemical is not considered to pose a risk to the environment.

Recommendations
CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Enclosed vessels, automated systems and exhaust ventilation during reformulation procedures.
  - Engineering controls to minimise exposure to eye, skin and respiratory system during end use.

- Employers should implement the following safe work practices to minimise occupational exposure during handling of products containing the notified chemical:
  - Avoid contact with eyes and skin.
  - Avoid inhalation of aerosols.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Gloves, safety glasses, coveralls, footwear.
  - Respirators when inhalation of aerosols containing the notified chemical may occur.

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Environment

- The notified chemical should be disposed of to landfill.
- Spills or accidental release of the notified chemical should be collected on to absorbing material and stored in appropriately labelled container for disposal.

Storage

- The notified chemical should be stored and handled in accordance with the *National Standard for the Storage and Handling of Workplace Dangerous Goods* [NOHSC:1015(2001)].

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
- Information becomes available as to the inhalation effects of the notified chemical;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from an additive in cold cleaning solvents in a wide range of applications, or is likely to change significantly;
- the amount of chemical being introduced has increased from 200 tonnes per annum, or is likely to increase, significantly;
- if the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

Material Safety Data Sheet
The MSDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Freezing Point < -75 ºC

Method OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Visual test
Test Facility RCC (2008a)

Boiling Point 215.6 ± 0.1ºC at 100.1 kPa

Method OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Calorimeter. Onset temperature was used.
Test Facility RCC (2008a)

Density 1055 kg/m^3 at 20 ± 0.1ºC

Method OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Remarks Oscillating densitimeter
Test Facility RCC (2007a)

Vapour Pressure 0.01 kPa at 25ºC
0.0063 kPa at 20ºC

Method OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Gas saturation method
Test Facility RCC (2007b)

Water Solubility 25.2 g/L at 20ºC

Method OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Flask Method/Column Elution Method
Test Facility RCC (2008b)

Hydrolysis as a Function of pH Stable at neutral pH, slowly hydrolysed at low pH and rapidly hydrolysed at high pH.

Remarks Stability testing of the notified chemical in distilled water showed negligible hydrolysis over a 14 d period at 20°C. In contrast, ~ 75% hydrolysis was observed at pH 1.5 over the 14 d period and hydrolysis was rapid under basic conditions. Therefore, the notified chemical would be expected to undergo hydrolysis, but only under extreme pH conditions that are not observed in the environment.

Partition Coefficient (n-octanol/water) log Pow = 0.89 at 20ºC

Method OECD 107 Partition Coefficient (n-octanol/water): Shake Flask Method
OECD TG 117 Partition Coefficient (n-octanol/water), HPLC Method.
EC Directive 92/69/EEC A.8 Partition Coefficient
Test Facility RCC Ltd (2008b)

Surface Tension 64.0 mN/m at 20.7ºC

Method OECD TG 115 Surface Tension of Aqueous Solutions.
EC Directive 92/69/EEC A.5 Surface Tension.
Remarks Concentration: 90% of saturation concentration.
The notified chemical is not surface active.

Test Facility RCC (2007c)

Adsorption/Desorption – screening test Log Koc < 1.25 which is equal to a Koc value < 18

Method OECD 121 Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography

EC Directive 2001/59/EC C.19 Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography.

Remarks This value indicates the notified chemical will not be adsorbed by organic carbon in soil. The notified chemical can be classified to be of very high mobility.

Test Facility RCC (2008c)

Dissociation Constant Not determined

Remarks The notified chemical does not contain groups that may undergo dissociation.

Flash Point 98°C at 101.1 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Pensky-Martens flash point apparatus

Test Facility Rhodia (2006)

Autoignition Temperature 430°C

Method EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).

Test Facility Rhodia (2006)

Explosive Properties Not explosive

Method EC Directive 92/69/EEC A.14 Explosive Properties.

Remarks The notified chemical was determined not to have shock or thermal sensitivity to explosion.

Test Facility Rhodia (2006)

Oxidizing Properties Not oxidising

Method UN recommendation on the Transport of Dangerous Goods (Manual of Tests and Criteria, Fourth revised edition, 2003, Appendix 6, "Orange book") – screening procedure for oxidising properties

Remarks Based on the structure and oxygen balance of the notified chemical, it is not expected to have oxidising properties (expert statement).

Test Facility RCC (2007d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure.
Species/Strain	Rat/Wistar
Vehicle	None
Remarks - Method	No significant protocol deviations.
RESULTS	
LD50	>2000 mg/kg bw
Remarks - Results	No mortality, signs of toxicity, or adverse effects in organs were observed at the dose level of 2000 mg/kg bw.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	RCC (2007e)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity.
Species/Strain	Rat/Wistar
Vehicle	None
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.
RESULTS	
LD50	>2000 mg/kg bw
Remarks - Results	No mortality, signs of toxicity, or adverse effects in organs were observed at the dose level of 2000 mg/kg bw. On test day 5, one animal displayed slight local erythema. The same animal also had slight scaling from day 5 to day 8.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	RCC (2007f)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	1 male, 2 females
Vehicle	None
Observation Period	10 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.7	1	0.3	1	10 days	0
Oedema	0	0.3	0	1	48 hr	0

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

Remarks - Results: Very slight erythema was noted in all treated animals at the 1 hour observation point, which persisted until 24 hour, 48 hour, or day 7. In one animal very slight oedema was present at the 24 hour observation.

CONCLUSION: The notified chemical is slightly irritating to the skin.

TEST FACILITY: RCC (2008d)

B.4. Irritation – eye

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain: Rabbit/New Zealand White
Number of Animals: 1 male, 2 females
Observation Period: 72 hr
Remarks - Method: No significant protocol deviations.

RESULTS

Remarks - Results: Moderate reddening of the conjunctivae was observed at the 1 hour time point in all animals. This persisted in two of the animals at the 24 hour observation at a lesser severity and disappeared by the 48 hour observation. Slight reddening of the sclerae was noted in two of the animals at the 1 hour observation only.

CONCLUSION: The notified chemical is slightly irritating to the eye.

TEST FACILITY: RCC (2008e)

B.5. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 429 Skin Sensitisation: Local Lymph Node Assay

Species/Strain: Mouse/CBA/CaOlaHsd
Vehicle: Acetone/olive oil (4:1)
Remarks - Method: No significant protocol deviations. Historic positive control data were used.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	717	-
5	807	1.12
10	702	0.98

25	546	0.76
50	438	0.61
100	397	0.55

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY RCC (2007g)

B.6. Repeat dose toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test.
OECD TG 474 Mammalian Erythrocyte Micronucleus Test.

Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage
Exposure Information	Total exposure: - Males: 28 days - Females: 4 days post partum (40-45 days) Dose regimen: 7 days per week Post-exposure observation period: 0 days Pairing: Day 14
Vehicle	Purified water
Remarks - Method	No significant protocol deviations.

RESULTS

Dose mg/kg bw/day	*Number and Sex of Animals*	*Mortality*
0	10M, 10F	0
100	10M, 10F	0
300	10M, 10F	0
1000	10M, 10F	2F

Effects on Parental (P) animals:

With the exception of two female animals treated with 1000 mg/kg, all male and female animals survived until scheduled necropsy. One female animal died due to an unperceived injury during intubation (died day 2 post partum) and displayed dark red discoloured thymus and dark red discoloured lungs that were not collapsed at necropsy, and congested thymus and lungs (with alveolar edema, hyaline membranes, alveolar macrophages, and mixed inflammatory cell foci) at histopathology. The other animal may have died as a result of prolonged parturition (died day 22 post coitum), although the possibility that the death was test item related cannot be ruled out.

No treatment related clinical observations were observed in the following parameters in treated animals: effects on food consumption, body weight, functional observations, fertility and mating performance, duration of gestation, corpora lutea count, implantation rate, post implantation loss, litter size, post natal loss, and qualitative staging of the testes.

Some statistically significant changes in haematology and clinical biochemistry parameters were observed in treated animals, particularly those treated with 1000 mg/kg. Such changes were not considered to be of toxicological significance as they were within the range of reference values for rats of this strain and age.

In female animals treated with 1000 mg/kg, the mean kidney weight (19% increase compared to control), as well as the kidney weight relative to body weight and to brain weight was statistically significantly increased. Such changes were not dose dependent.

No significant histopathological findings were observed.

Effects on 1st Filial Generation (F1)
No significant abnormal findings, sex ratios, pup weights, or necropsy findings were observed in the offspring of the treated animals.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 300 mg/kg bw/day in this study, based on the observed increases in kidney weights in female animals treated with 1000 mg/kg bw/day, and the one female animal that may have died as a result of treatment with the notified chemical.

TEST FACILITY	RCC (2007h)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure and Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 mix from Wistar rat liver induced with Phenobarbital and β-naphthoflavone
Concentration Range in Main Test	a) With metabolic activation: up to 5000 µg/plate b) Without metabolic activation: up to 5000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	2-Aminoanthracene was used as the sole indicator of the efficacy of the metabolic activation. The OECD Test Guideline recommends against this.

RESULTS

Remarks - Results	No precipitation or toxic effects were observed at any of the concentrations tested. In the plate incorporation test, reduced background growth was observed at concentrations of 333 µg/plate and upwards without metabolic activation and in all strains tested. No such effects were observed in the presence of metabolic activation in this test, or during the pre-incubation experiment. No mutagenic effects were observed during any of the experiments.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC (2007i)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test. EC Directive 2000/32/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.
Species/Strain	Human lymphocytes
Metabolic Activation System	Liver fraction (S9 mix) from rats pretreated with Phenobarbital/β-naphthoflavone
Vehicle	Deionised water

Remarks - Method No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period (hr)*	*Harvest Time (hr)*
Absent			
Test 1a	12.7 – 1950	4	22
Test 1b	12.7 – 1950	22	22
Test 2	38.8 – 1950	46	46
Present			
Test 1	12.7 – 1950	4	22
Test 2	38.8 – 1950	4	46

RESULTS

Remarks - Results No cytotoxicity or visible precipitation of the notified chemical was observed. There were no significant increases observed in the number of cells with structural chromosomal aberrations or in the frequencies of polyploid metaphases observed.

CONCLUSION The notified chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.

TEST FACILITY RCC (2008f)

B.9. Genotoxicity – in vivo

TEST SUBSTANCE Notified chemical

METHOD OECD TG 474 Mammalian Erythrocyte Micronucleus Test.

Species/Strain Mouse/NMRI

Route of Administration Intraperitoneal injection

Vehicle Corn oil

Remarks - Method No significant protocol deviations.

Dose mg/kg bw	*Number and Sex of Animals*	*Sacrifice Time hours*
vehicle control	6M, 6F	24
375	6M, 6F	24
750	6M, 6F	24
1500	6M, 6F	24
1500	6M, 6F	48
40*	6M, 6F	24

*positive control = cyclophosphamide.

RESULTS

Doses Producing Toxicity The mean number of polychromatic erythrocytes was slightly decreased after treatment with 1500 mg/kg bw of the notified chemical after 24 hr compared to the vehicle control. This indicated that the notified chemical had cytotoxic properties in the bone marrow.

Genotoxic Effects A statistically significant increase in the frequency of detected micronuclei was observed at the dose level of 1500 mg/kg bw in comparison to the control (24 hr sacrifice time). The increase was observed to be dose dependent.

DISCUSSION A supplementary study was performed under identical conditions, though only with treatment at 1500 mg/kg bw. In the supplementary study, the mean micronucleus frequency was not increased in comparison to the control, and thus the results described in the current study were not reproduced.

The supplementary study also analysed the rectal temperature of the mice

	at regular intervals, on the basis of previous reports that suggest that hypothermia may induce micronuclei in mouse bone marrow cells (Asanami, 1997; Asanami, 1998). The supplementary study found that the rectal temperature of animals treated with the test item was significantly reduced compared to the pre-treatment value at all time points evaluated. As such, the notified chemical is considered to induce hypothermia, which may account for the changes in the frequency of micronuclei detected in the main study.
CONCLUSION	The results of this in vivo mouse micronucleus assay are considered to be inconclusive in terms of determination of the clastogenicity of the notified chemical.
TEST FACILITY	RCC (2008g&h)

B.10. Genotoxicity – in vivo

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
Remarks - Method	A micronucleus assay was performed in conjunction with the repeat dose oral toxicity study. Cyclophosphamide monohydrate was used as a positive control item for this test (single dose of 20 mg/kg). For all other animals, femora were collected on the day of necropsy.
RESULTS	The notified chemical had no cytotoxic effects in the bone marrow of the treated rats. In addition, there was no biologically relevant increase in the frequency of the detected micronuclei at any dose level.
CONCLUSION	The notified chemical was not clastogenic to bone marrow cells of rats.
TEST FACILITY	RCC (2007h)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1 (a) Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD Guidelines for the Testing of Chemicals. Proposal for a New Guideline 310. Ready Biodegradability – CO_2 in sealed vessels (Headspace Test). Oct 2001. International Organisation for Standardization (ISO). Reference No. ISO 14593: 1999. Water quality – Evaluation of ultimate aerobic biodegradability of organic compounds in aqueous medium – Method by analysis of inorganic carbon in sealed vessels (CO_2 headspace test). First edition 1999-03-15
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	Sodium benzoate
Remarks – Method	No deviation form standard protocols

RESULTS

Notified chemical		*Sodium benzoate*	
Day	*% degradation*	*Day*	*% degradation*

3	-	3	-
5	7.06	5	81.09
7	26.83	7	84.45
14	89.66	14	89.81
21	91.85	21	90.30
28	91.88	28	91.15

Remarks – Results: The mean cumulative net CO_2 evolved from the inhibition control was 91.94% in 28 days. This value indicates that the test substance was not toxic to the inoculum. The mean cumulative CO_2 evolved from the sodium benzoate procedural control was 91.15% of the theoretical amount in 28 days. In addition, the reference substance, sodium benzoate, passed the OECD "10-Day window" criterion. This rapid degradation of the reference material confirmed the presence of an acceptable microbial community and confirmed system integrity.

CONCLUSION: The notified chemical can be classed as readily biodegradable.

TEST FACILITY: Laboratório de Meio Ambiente (2006).

C.1.1(b) Ready biodegradability

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 301 B Ready Biodegradability: CO2 Evolution Test.
EC Directive 92/69/EEC C.4-C Biodegradation: Determination of the "Ready" Biodegradability: Carbon Dioxide Evolution Test

Inoculum	Aerobic activated sludge from a wastewater treatment plant
Exposure Period	28 dayds
Auxiliary Solvent	Sodium benzoate
Analytical Monitoring	
Remarks – Method	There were no amendments to the study protocol.

RESULTS

Notified chemical		*Sodium benzoate*	
Day	*% degradation*	*Day*	*% degradation*
2	1.9	2	37.5
7	26.1	7	64.9
14	57.3	14	73.9
19	69.1	19	-
28	74.4	28	77.1

Remarks – Results: The notified chemical was found to be biodegradable by 74% under the test conditions within the 28-day exposure period. Moreover, the pass level for ready biodegradability, i.e. a CO_2 formation of at least 60% of the TOC in a 10-day window within the 28-day period of the test, was reached. In the toxicity control 70.9% degradation was observed at the end of the study indicating that the test material was not inhibitory to activated sludge.

CONCLUSION: The notified chemical can be classed as readily biodegradable.

TEST FACILITY: RCC (2007i)

C.1.2. Bioaccumulation

Test report for notified chemical on bioaccumulation is not available. However, based on the log K_{ow} value of the notified chemical (0.89), the potential for bioaccumulation is expected to be low. Furthermore, the notified chemical is readily biodegradable, indicating that it is not

expected to persist in the environment.

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test – 96-hour semi-static test with daily test medium renewal. EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - 96-hour semi-static test with daily test medium renewal.
Species	Rainbow trout *(Oncorhynchus mykiss)*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	175 mg $CaCO_3$/L
Analytical Monitoring	Yes – HPLC analysis with UV/VIS - detection
Remarks – Method	No deviation from standard protocol

RESULTS

Concentration mg/L		*Number of Fish*	*Number of abnormal and dead fish/number of dead fish* *Type of visible abnormalities*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control		7	0/0	0/0	0/0	0/0	0/0
4.6		7	0/0	0/0	0/0	0/0	0/0
10		7	0/0	0/0	0/0	0/0	0/0
22		7	0/0	0/0	0/0	0/0	0/0
46		7	0/0	0/0	7/0 AP, TS	7/0 AP, TS, BO, VF	7/1 AP, TS, BO, VF
100		7	0/0	7/6 AP, BO	7/7	-/-	-/-

-/-: all fish dead

LC50	46 < LC50 < 100 mg/L at 96 h.
NOEC	96-hour NOEC:22 mg/L
LOEC	96-hour LOEC:46 mg/L
Remarks – Results	There is insufficient partial mortalities at 96 h to determine the LC50 value using probit analysis. However, given that complete mortality occurred at 100 mg/L the LC50 is between 46 mg/L and 100 mg/L. Sub lethal effects observed included apathy (AP); fish mainly at the bottom of the aquarium (BO); fumbling during swimming (TS); and changed body colour (VF).

CONCLUSION The notified chemical is harmful to *Oncorhynchus mykiss*.

TEST FACILITY RCC (2008i)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – 48-hour static test.
EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia -48 hour static test

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC analysis with UV/VIS-detection
Remarks – Method	There were no amendments to the study protocol.

RESULTS

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

EC50	> 100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks – Results	No immobilization of *Daphnia* was observed during the study.

CONCLUSION The notified chemical is not harmful to *Daphnia magna*.

TEST FACILITY RCC (2008j)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Directive 92/69/EEC C.3 Algal Inhibition Test.
Species	Freshwater green algal (*Pseudokirchneriella subcapitata* – formerly *Selenastrum capricornutum)*
Exposure Period	72 hours
Concentration Range Nominal	4.6, 10, 22, 46 and 100 mg/L were tested in parallel to a control
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC analysis with UV/VIS-detection
Remarks – Method	No deviation for standard protocol

RESULTS

Biomass		*Growth*	
NOE_bC mg/L at 0-72 h	*E_bC50 mg/L at 72 h*	*NOE_rC mg/L at 0-72 h*	*E_rC50 mg/L at 72 h*
60 mg/L*	> 60 mg/L	60 mg/L	> 60 mg/L

* Mean observed concentration.

Remarks – Results	The notified chemical had no statistically significant inhibitory effect on the growth (growth rate and yield) of *Pseudokirchneriella subcapitata* after the test period of 72 hours up to and including the highest nominal test concentration of 100 mg/L (mean measured concentration of 60 mg/L). The nominal test concentration on 100 mg/L (mean measured concentration of 60 mg/L) was therefore determined to be the 72-hour NOEC (highest concentration tested without toxic effects after the test period of 72 hours). This value might even be higher, but nominal concentrations of the test item above 100 mg/L were not tested in accordance with the test guidelines. The 72-hour LOE_rC and the 72-hour E_rC10 and E_rC50 for the growth rate and yield could not be quantified due to the absence of a toxic effect of the notified chemical at the tested concentrations. Accordingly, these parameters were clearly higher than the nominal concentration of 100 mg/L (mean measured concentration of 60 mg/L).
CONCLUSION	The notified chemical is not harmful to algae at the maximum test concentration (mean measured concentration 60 mg/L).
TEST FACILITY	RCC (2008k)

C.2.4. 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	Aerobic activated sludge
Exposure Period	3 hours
Concentration Range Nominal	1000 mg/L

Remarks – Method	There were no amendments to the study protocol
RESULTS	
EC50	The notified chemical had no significant inhibitory effect (< 15%) on the respiration rate of activated sludge after the incubation period of 3 hours at the limit test concentration of 1000 mg/L.
NOEC	Thus, the 3-hour NOEC (EC15) of the notified chemical to activated sludge microorganisms was at least 1000 mg/L. This value might have been higher but concentrations above 1000 mg/L were not tested. The 3-hour EC20, EC50 and EC80 could not be calculated but were clearly higher than 100 mg/L
CONCLUSION	The notified chemical had no inhibitory effect on the respiratory rate of activated sludge after the incubation period of 3 hours at the test item concentration of 1000 mg/L
TEST FACILITY	RCC (2007j)

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