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September 2007

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)**

# FULL PUBLIC REPORT

## XP 338

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 and Water Resources.

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:


| | |
|---|---|
| Street Address: | 334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA. |
| Postal Address: | GPO Box 58, SYDNEY NSW 2001, AUSTRALIA. |
| TEL: | + 61 2 8577 8800 |
| FAX | + 61 2 8577 8888 |
| Website: | www.nicnas.gov.au |


**Director**
**NICNAS**

# TABLE OF CONTENTS

# FULL PUBLIC REPORT

## XP 338

### 1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Rhodia Australia Pty Ltd. (ABN 24 050 029 000) of Building 25, Omnico Business Park, 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, CAS number, Molecular formula, Structural formula, Molecular weight, Spectral data, Purity, Identity of toxic or hazardous impurities, %Weight of toxic or hazardous impurities, Non-hazardous impurities, Identity of additives/adjuvants, %Weight of additives/adjuvants, and Manufacture/import volume

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:

Water solubility, Partition coefficient, Absorption/desorption, Dissociation constant, Particle size, Flash point, Flammability limits, and Explosive properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
UK HSE (2004)

### 2. IDENTITY OF CHEMICAL

OTHER NAME(S)
None

MARKETING NAME(S)
XP 338

MOLECULAR WEIGHT
<500 Da

ANALYTICAL DATA
Reference NMR, IR, and UV spectra, and microanalysis data were provided.

### 3. COMPOSITION

DEGREE OF PURITY
>95%

## 4. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance at 20ºC and 101.3 kPa** Pale yellow crystalline solid

| Property | Value | Data Source/Justification |
|---|---|---|
| Melting Point | ~300ºC (with decomposition) | Measured |
| Boiling Point | 359ºC at 102.57 kPa | Calculated |
| Density | 1,210 kg/m$^3$ at 21ºC | Measured |
| Vapour Pressure | $2.5\times10^{-16}$ kPa at 25ºC | Measured |
| Water Solubility | Not determined | Rapidly hydrolysable in water |
| Hydrolysis as a Function of pH | t½ < 1 hour (pH 4, 7, and 9) | Measured |
| Partition Coefficient (n-octanol/water) | Not determined | Rapidly hydrolysable in water |
| Adsorption/Desorption | Not determined | Rapidly hydrolysable in water |
| Dissociation Constant | Not determined | Rapidly hydrolysable in water, and has no known modes of dissociation |
| Particle Size | Not determined | Imported only as a solution in petroleum distillates (bp ~250°C) |
| Flash Point | Not determined | The notified chemical is a solid with a low vapour pressure |
| Flammability | Not highly flammable | Measured |
| Autoignition Temperature | No self-ignition occurred below the melting temperature. | Measured |
| Explosive Properties | Not expected to be explosive | Calculated |

**Discussion of Observed Properties**

For full details of the physical-chemical properties tests please refer to Appendix A.

*Reactivity*

From experience in use and from the chemical structure, the notified chemical does not lead to the development of dangerous amounts of flammable gases in contact with water or moist air, and is not flammable in contact with air (pyrophoric).

The notified chemical does not possess oxidising properties on the basis of experience in use and from its chemical structure. The oxygen balance for the representative structure of the notified chemical is -164, and it does not contain any functional groups that might indicate an oxidant.

*Dangerous Goods classification*

Based on the available physico-chemical properties the notified chemical is not classified as a Dangerous Good according to the Australian Dangerous Goods Code (FORS, 1998).

## 5. INTRODUCTION AND USE INFORMATION

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

The notified chemical will not be manufactured in Australia, but imported as a ~50% formulation in a petroleum distillate.

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

| *Year* | *1* | *2* | *3* | *4* | *5* |
|---|---|---|---|---|---|
| *Tonnes* | 10-50 | 10-50 | 10-50 | 10-50 | 10-50 |

PORT OF ENTRY

The notified notified chemical will be imported through Melbourne by wharf.

IDENTITY OF MANUFACTURER/RECIPIENTS
Rhodia Australia Pty Ltd.
Building 25, Omnico Business Park
270 Ferntree Gully Road
Notting Hill VIC 3168

TRANSPORTATION AND PACKAGING
The notified chemical is imported into Australia only as a formulation in a petroleum distillate (boiling point ~250°C). The import containers are 55 US gallon (205 L) steel drums. The notified chemical will be transported from the point of importation to the recipients by road.

USE
The notified chemical will be used as a viscosity control agent to formulate ink vehicles (also known as "varnishes") for the production of lithographic printing inks. The notified chemical will typically be added to ink vehicles at a concentration of <2%. During formulation of the vehicle, the notified chemical reacts with other ink vehicle components, losing its chemical identity.

The ink vehicles will be used to produce lithographic printing inks, which are typically used in the printing of high quality, high gloss magazines.

OPERATION DESCRIPTION
*Formulation of ink vehicles (varnishes)*
Typically, the petroleum distillate preparation containing the notified chemical at ~50% would be pumped from a drum into a pre-dilution tank, or directly into the varnish kettle. A typical varnish kettle is a closed reactor-type tank, with a condenser to catch any volatiles. The varnish is typically composed of drying oils, petroleum oils, and various rosin/phenolic and alkyd resins. During formulation of the ink vehicles, the chemical identity of the notified chemical is lost by reaction, and the chemical itself is therefore not present during the subsequent processes of ink manufacturing and printing.

## 6. HUMAN HEALTH IMPLICATIONS

### 6.1. Exposure assessment

#### 6.1.1. Occupational exposure

*Number and Category of Workers*

| *Category of Worker* | *Number* | *Exposure Duration* | *Exposure Frequency* |
|---|---|---|---|
| Process operator | 1 | 15 min | 1/day |

*Exposure Details*
The exposure of transport and storage workers is only expected in the unlikely event of a significant industrial accident, where rupture of the steel drums occurred.

The only significant exposure of workers might occur to the imported notified chemical solution (~50% concentration) during hose attachment/detachment and pumping operations for ink vehicle formulation. This exposure is expected to be primarily dermal or ocular, arising from spills or leaks. During these procedures, appropriate personal protective equipment (PPE) will be worn by workers, such as chemical resistant gloves (eg neoprene), chemical goggles and overalls. Appropriate industrial hygiene procedures are expected to be implemented during these operations.

The remainder of the formulation process will occur in an enclosed chemical reactor, where very low or no exposure to workers will occur. During formulation, the notified chemical is consumed in the reaction, so no exposure to the notified chemical is expected from subsequent steps in ink vehicle formulation and use.

Ink vehicles (and therefore inks) may contain the hydrolysis products of the notified chemical. Therefore, ink manufacturing and lithographic printing workers may also be exposed to these chemicals (at <2% in ink vehicles). This exposure is likely to primarily dermal and possibly ocular. In addition, traces of these hydrolysis products may remain on printed media, which might result in dermal exposure of other workers such as printed media distributors and retailers. These species are

volatile, and therefore dry printed pages are not expected to contain significant levels.

### 6.1.2. Public exposure

The notified chemical will not be sold directly to members of the public, but will be used in the formulation of ink vehicles that in turn will be used for printing media for use by members of the public. However, the notified chemical will be consumed during the industrial process of ink vehicle formulation, and it is therefore not expected to be present in either the printing inks or in any printed media that is available to the public.

Ink vehicles (and therefore inks) may contain the hydrolysis products of the notified chemical (at <2%), and traces of these may remain on printed media available for public use. These species are volatile, and therefore dry printed pages are not expected to contain significant levels.

## 6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical or on a structurally related analogue ("XP 339") are summarised in the table below. The notifier stated that the rat acute oral $LD_{50}$ of XP 339 was >2,500 mg/kg – identical to that of the notified chemical. In addition, the differences between the two chemicals were analysed in relation to their expected physicochemical properties and toxicological profiles. The two chemicals were found to be sufficiently similar for assessment by analogy. The details of the toxicological investigations can be found in Appendix B.

| *Endpoint* | *Test substance* | *Result and Assessment Conclusion* |
|---|---|---|
| Rat, acute oral toxicity | Notified chemical | Low toxicity, $LD_{50}$ >2,500 mg/kg bw |
| Rat, acute dermal toxicity | XP 339 | Low toxicity, $LD_{50}$ >2,000 mg/kg bw |
| Rabbit, skin irritation | XP 339 | Slightly irritating |
| Rabbit, eye irritation | XP 339 | Slightly irritating |
| Mouse, Local Lymph Node Assay (LLNA) | XP 339 | No evidence of sensitisation. |
| Rat, oral repeat dose toxicity - 90 days | XP 339 | NOAEL = 1,000 mg/kg bw/day (NOEL not established) |
| Mutagenicity (bacterial reverse mutation) | Notified chemical | Non-mutagenic |
| Genotoxicity (*in vitro* chromosome aberration) | XP 339 | Non-genotoxic |

***Toxicokinetics, metabolism and distribution***

Given its reactive nature, the notified chemical is not likely to be significantly absorbed following exposure by any route. Any absorption would result in rapid hydrolysis to yield simple, well-defined chemicals (see below for some information on the general toxicity of these).

Due to its reactivity, the toxicity of the notified chemical is expected to be restricted to local irritative effects, where it might be expected to react with surface molecules of skin or mucous membranes. The production of hydrolysis products may also contribute to its irritative properties.

The analogue of the notified chemical, "XP 339", is expected to hydrolyse at an equivalent rate to the notified chemical upon administration and/or contact with water.

***Acute and repeated dose toxicity***

Generally, the notified chemical or its analogue was found to be of low acute oral and dermal toxicity. No signs of toxicity were observed after an acute exposure.

In a 90-day oral repeated-dose toxicity study, the analogue of the notified chemical induced minor effects or no significant effects. Most of the observed effects can be related to the irritant nature of the analogue of the notified chemical.

***Irritation and sensitisation***

Slight irritation was observed upon acute administration of the analogue of the notified chemical to eye or skin. Irritant effects were also observed in the repeat dose toxicity study upon microscopic

examination of the stomach and trachea of gavage-treated rats. The analogue of the notified chemical might be expected to be more irritating than the notified chemical, based on the available toxicological data determined for the hydrolysis products of each.

The analogue of the notified chemical was not sensitising in a mouse LLNA assay.

***Mutagenicity and Genotoxicity***
The weight of evidence from the two *in vitro* studies suggests that the notified chemical is not likely to be mutagenic or genotoxic.

***Observations on human exposure***
No human health conditions have been reported to be associated with exposure to the notified chemical.

***Hydrolysis products***
The from the data available in the literature, the hydrolysis products of the notified chemical are generally of low toxicity, and their toxic effects are expected to be limited to mild-moderate irritative effects on skin and eye. This hypothesis is supported by the toxicological data available for the notified chemical and its analogue, XP 339. Based on the known toxicological data for the hydrolysis products of the analogue of the notified chemical, it is expected to perhaps higher toxicity (though still low), and possibly more severe irritative characteristics.

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

### 6.3. Human health risk characterisation

#### 6.3.1. Occupational health and safety
The only significant occupational exposure to the notified chemical is likely to occur during the formulation of ink vehicles, during hose attachment and pumping operations. During these procedures, the use of appropriate PPE and good industrial hygiene procedures should ensure that exposure is minimal. The toxicological profile of the notified chemical and its analogue is suggestive of a probable low hazard. Therefore, the notified chemical is unlikely to pose a significant risk to process operators involved in ink vehicle formulation.

The risk to ink manufacturing or lithographic printing workers from the notified chemical is negligible, as the chemical will not be present in ink vehicles after formulation. These workers may experience exposure to the hydrolysis products of the notified chemical. The risk from these hydrolysis products in ink vehicles is likely to be low, due to their low concentration (<2%). The possibility of irritant effects to workers may be significant, but given the other components of the ink vehicles this would be a known hazard in the use of such products. Appropriate measures (eg appropriate PPE and physical containment) are expected to be implemented where these inks will be used. Therefore, the overall risk to workers from the use of ink vehicles is expected to be acceptable.

The likelihood of exposure of distribution and retail workers to the hydrolysis products of the notified chemical from printed media is expected to be negligible, given the volatile nature and low toxicity of these species. Their potential for irritant effects are not likely to be a concern from dried, printed pages at the concentrations proposed.

#### 6.3.2. Public health
The notified chemical will be used in the formulation of ink vehicles that will be used for printing media that is intended for public consumption. However, the notified chemical will be consumed during the industrial process of ink vehicle formulation, and it is therefore not expected to be present in the printing inks or in any printed media that is available to the public.

The hydrolysis products may be present in formulated ink vehicles, and thus may remain on printed surfaces. However, these species will be present at low concentrations in the ink vehicles (<2%), are volatile, and are of low toxicity. The potential for irritant effects are not likely to be a concern from dried, printed pages at the concentrations proposed.

Therefore, due to the negligible public exposure to the notified chemical in the proposed use, it is not considered to pose a significant risk to public health.

# 7. ENVIRONMENTAL IMPLICATIONS

## 7.1. Environmental Exposure & Fate Assessment

### 7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical in petroleum distillate (~50%) will be imported from overseas and is used in the formulation of the printing ink vehicles.

During the formulation process, the notified chemical reacts with the resins resulting in the irreversible formation of acylate linkages. On this basis, the notified chemical is not present in the preparation following formulation of the vehicles. There is scope for accidental spillage to occur while loading the notified chemical into the formulation kettle, which is a closed reactor-type tank with a condenser to catch any volatiles. Should a spill occur it would be contained to the plant by bunding.

It is expected that up to 2% of the residues will remain in the imported container. The residues in the container will be cleaned with aqueous media resulting in the hydrolysis of the notified chemical to its components. When cleaned with solvents, the residues would be expected to be incinerated. Empty drums may be returned to the supplier or be sent for cleaning and re-conditioning.

RELEASE OF CHEMICAL FROM USE

As the notified chemical is not present in the final printing ink, there are no further environmental implications from the proposed use.

RELEASE OF CHEMICAL FROM DISPOSAL

It is anticipated that up to 2% of the notified chemical will be lost as residues in imported container, which are primarily disposed of by incineration.

### 7.1.2 Environmental fate

For the details of the environmental fate studies, please refer to Appendix C. The notified chemical is not soluble in water, but rapidly hydrolyses upon contact with water. It is readily biodegradable. As the notified chemical is not present in the formulated product, the only environmental release is prior to the formulation process. Such releases may result from incineration, resulting in the formation of oxides of carbon and aluminium and water, or from hydrolysis of the notified chemical.

### 7.1.3 Predicted Environmental Concentration (PEC)

As the notified chemical is not present in the formulated product, there is no aquatic release from the proposed use. Therefore, a PEC value cannot be calculated.

## 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 | 96 h $EC_{50}$ >100 mg/L | Non-toxic |
| *Daphnia* Toxicity | 48 h $EC_{50}$ = 35 mg/L | Harmful |
| Algal Toxicity | 72 h $ErC_{50}$ >320 mg/L | Non-toxic |
| Inhibition of Bacterial Respiration | $EC_{50}$ >1,000 mg/L | Non-toxic |

These results indicate that the notified chemical or its hydrolysed products are harmful to *Daphnia magna*.

### 7.2.1 Predicted No-Effect Concentration (PNEC)

The Predicted No-Effect Concentration has been calculated from the most sensitive *Daphnia magna* toxicity (48 h $EC_{50}$ = 35 mg/L) of the notified chemical. As the results are available for three trophic levels, an assessment factor of 100 has been used.

| PNEC for the Aquatic Compartment | | |
|---|---|---|
| 48 h $EC_{50}$ for *Daphnia magna* | 35 | mg/L |
| Assessment Factor | 100 | |
| Mitigation Factor | 1.00 | |
| PNEC | 350 | µg/L |

### 7.3. Environmental risk assessment

The majority of the notified chemical will be consumed during the formulation process and will not be present in the formulated product. Therefore, minimal environmental exposure is likely to occur. Its use in industrial settings and consumption in the industrial process is unlikely to have an adverse effect on aquatic organisms.

The likely route of environmental exposure is from accidental spillage and washing of the used import container. In the case of spillage, it would be contained to the plant by bunding. The residues from the washing of containers will be collected and eventually be incinerated with the generation of oxides of carbon and metal and water or be hydrolysed in aqueous media.

Given its limited environmental exposure, the notified chemical is unlikely to pose an environmental risk under the proposed use pattern.

## 8. CONCLUSIONS – SUMMARY OF RISK ASSESSMENT FOR THE ENVIRONMENT AND HUMAN HEALTH

### 8.1. Hazard classification

Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances*.

and

As a comparison only, the classification of 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*** |
|---|---|---|
| Environmental Hazard | Acute III | Harmful |

### 8.2. Human health risk assessment

#### 8.2.1. Occupational health and safety

Under the conditions of the occupational settings described, the risk to workers is considered to be acceptable.

#### 8.2.2. Public health

When used in the proposed manner, the risk to the public is considered to be acceptable.

### 8.3. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

## 9. MATERIAL SAFETY DATA SHEET

The MSDS of the notified chemical, provided by the notifier, is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

## 10. RECOMMENDATIONS

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical solution as introduced:
  - *Avoid spills and skin or eye contact*

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical solution as introduced:
  - *Chemical resistant gloves, chemical goggles and overalls*

  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*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of by landfill.

Emergency procedures

- Prevent leakage of large quantities into the drainage system by bunding with sand or other absorbent material. In the event of large spills contact emergency services and the local authorities.

- Ventilate area and try to contain spill by diking with sand or other absorbent material. Collect spill for disposal by scooping up liquids, using a vacuum pump, or absorbing with sand or other approved absorbent materials and place in suitably labelled container for disposal in accordance with local and national regulations. Contact authorities and wastewater treatment plant as appropriate if significant contamination occurs.

## 11. REGULATORY OBLIGATIONS

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

(1) Under Section 64(1) of the Act; if
  - The notified chemical is imported in a solid physical state. If importation of a solid is intended, particle size data should be provided.

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of ink vehicle

formulations, or is likely to change significantly;
- the amount of chemical being introduced has increased from 50 tonnes, 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.

## APPENDIX A: PHYSICO-CHEMICAL PROPERTIES

**Melting Point** ~300ºC (with decomposition)

METHOD EC Directive 92/69/EEC A.2 Melting/Freezing Temperature.
Remarks Measured by Differential Scanning Calorimetry (DSC) at 102.57 kPa
TEST FACILITY SafePharm (2004a)

**Boiling Point** ~359ºC at 102.57 kPa

METHOD Calculation.
Remarks The test material decomposed, no value for boiling temperature could be determined by DSC.
TEST FACILITY SafePharm (2004a)

**Density** 1,210 kg/$m^3$ at 21ºC

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Determined using a gas comparison pycnometer.
TEST FACILITY SafePharm (2004a)

**Vapour Pressure** $2.5\times10^{-16}$ kPa at 25ºC

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Determined by worst-case extrapolation from experimental (vapour pressure balance) data with low correlation.
TEST FACILITY SafePharm (2004b)

**Hydrolysis as a Function of pH**

METHOD EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH.

| *pH* | *T (°C)* | *$t_{½}$ (hours)* |
|---|---|---|
| 4 | 50 | <1 |
| 7 | 50 | <1 |
| 9 | 50 | <1 |

Remarks It was necessary to pre-dissolve the notified chemical in acetone. The notified chemical was added to de-ionised water preheated to 50ºC at pH 4.0, 7.0 and 9.0. Samples were periodically removed, microfiltered and analysed by gas chromatography. The hydrolysis was measured by analysing for its hydrolysed products.

The notified chemical hydrolysed rapidly on contact with water. At pH 9, >90% of a hydrolysis product was recovered within the first hour. At pH 7, again >90% of the hydrolysis product was recovered in less than one hour. The data obtained at pH 4 was very similar to that obtained at pH 7.0.

It was evident that 50% or more of the notified chemical had been hydrolysed within the 2.4 hour time limit of the test guideline, at 50ºC at pH 4, 7 and 9.
TEST FACILITY FedChem (2003c)

**Flammability (solids)** Not highly flammable.

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids)
Remarks The solid notified chemical ignited upon application of an air-rich bunsen flame, and propagated combustion over 200 mm in 34 min 42 sec.

The moisture content of the solid notified chemical was determined to be 3.8% by drying to constant weight at 105°C. This loss of mass may be attributed in part to

the loss of volatiles resulting from surface hydrolysis.
TEST FACILITY SafePharm (2004b)

**Autoignition Temperature** No self-ignition occurred below the melting temperature.

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks None.
TEST FACILITY SafePharm (2004b)

**Explosive Properties**

Remarks The notified chemical is not expected to be explosive on the basis of experience in use, its known thermal properties, and from its chemical structure. The oxygen balance for the representative structure is –164, and it contains no explosophores.

## APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

**Note:** Several studies were performed using a related chemical, "XP 339", that is an acceptable, structurally related analogue of the notified chemical.

### B.1. Acute toxicity – oral

| | |
|---|---|
| TEST SUBSTANCE | Notified chemical (solid) |
| METHOD | OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method. |
| Species/Strain | Rat/Sprague-Dawley CD |
| Vehicle | Arachis oil BP |
| Remarks – Method | No significant protocol deviations. |

RESULTS

| *Dose (mg/kg bw)* | *Number and Sex of Animals* | *Mortality* |
|---|---|---|
| 2,000 | 6F | 0 |

| | |
|---|---|
| $LD_{50}$ | >2,500 mg/kg bw |
| Signs of Toxicity | There were no signs of systemic toxicity. |
| Effects in Organs | No abnormalities were noted upon necropsy. |
| Remarks – Results | The $LD_{50}$ was set using the flow chart of Annex 2d of the test guideline, and was based on the absence of any deaths in the test animals. |
| CONCLUSION | The notified chemical is of low toxicity via the oral route. |
| TEST FACILITY | SafePharm (2004c) |

### B.2. Acute toxicity – dermal

| | |
|---|---|
| TEST SUBSTANCE | XP 339 |
| METHOD | OECD TG 402 Acute Dermal Toxicity.<br>EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal). |
| Species/Strain | Rat/Sprague-Dawley CD |
| Vehicle | Arachis oil BP |
| Type of dressing | Semi-occlusive |
| Remarks – Method | No significant protocol deviations. |

RESULTS

| *Dose (mg/kg bw)* | *Number and Sex of Animals* | *Mortality* |
|---|---|---|
| 2000 | 3M, 3F | 0 |

| | |
|---|---|
| LD50 | >2,000 mg/kg bw |
| Signs of Toxicity - Local | No signs of dermal irritation were observed. |
| Signs of Toxicity - Systemic | No signs of systemic toxicity. All test animals showed the expected gains in bodyweight over the study period. |
| Effects in Organs | No abnormalities were noted at necropsy. |
| Remarks – Results | |
| CONCLUSION | The analogue of the notified chemical is of low toxicity via the dermal route. |
| TEST FACILITY | SafePharm (2004d) |

### B.3. Irritation – skin

TEST SUBSTANCE XP 339 (solid)

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).

| | |
|---|---|
| Species/Strain | Rabbit/New Zealand White |
| Number of Animals | 3 |
| Vehicle | Arachis oil BP |
| Observation Period | 72 hours |
| 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* | 0.66 | 0.66 | 0.66 | 1 | 48 hours | 0 |
| *Oedema* | 0 | 0 | 0 | 0 | - | 0 |

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

Remarks – Results Primary irritation index of 0.5 (mild irritant on Draize classification).
No corrosive effects were noted.

CONCLUSION The notified chemical is slightly irritating to skin.

TEST FACILITY SafePharm (2004e)

### B.4. Irritation – eye

TEST SUBSTANCE XP 339 (solid)

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 | 3 |
| Observation Period | 72 hours |
| 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 | | | |
| *Conjunctiva: redness* | 0 | 0 | 0 | 1 | 1 hour | 0 |
| *Conjunctiva: chemosis* | 0 | 0 | 0 | 1 | 1 hour | 0 |
| *Conjunctiva: discharge* | 0 | 0 | 0 | 1 | 1 hour | 0 |
| *Corneal opacity* | 0 | 0 | 0 | 0 | 0 | 0 |
| *Iridial inflammation* | 0 | 0 | 0 | 0 | 0 | 0 |

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

Remarks – Results Minimal conjunctival irritation was observed one hour after treatment. All eyes appeared normal after 24 hours.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY SafePharm (2004f)

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

| | |
|---|---|
| TEST SUBSTANCE | XP 339 (solid) |
| METHOD | OECD 429 Skin Sensitisation: Local Lymph Node Assay |
| Species/Strain | Mouse/CBA/Ca (CBA/CaBkl) |
| Vehicle | 4:1 acetone:olive oil |
| Remarks – Method | There were no significant protocol deviations.<br>Groups of five female mice were tested for each concentration |

RESULTS

| *Concentration* | *Proliferative response (DPM/lymph node)* | *Stimulation Index (Test/Control Ratio)* |
|---|---|---|
| 0 (control) | 967 | 0 |
| 5 | 1658 | 1.72 |
| 10 | 2341 | 2.42 |
| 25 | 1938 | 2.00 |

| | |
|---|---|
| Remarks – Results | The most recent historical positive control (hexylcinnamaldehyde) used generated a positive response at a concentration of 25%. |
| CONCLUSION | There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical. |
| TEST FACILITY | SafePharm (2004g) |

### B.6. Repeat dose toxicity

| | |
|---|---|
| TEST SUBSTANCE | XP 339 (solid) |
| METHOD | OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents. |
| Species/Strain | Rat/Sprague-Dawley Crl:CD (SD) IGS BR |
| Route of Administration | Oral – gavage |
| Exposure Information | Total exposure days: 90 days<br>Dose regimen: 7 days per week.<br>There was no post-exposure observation period. |
| Vehicle | Arachis oil BP |
| Remarks – Method | No significant protocol changes. |

RESULTS

| *Dose (mg/kg bw/day)* | *Number and Sex of Animals* | *Mortality* |
|---|---|---|
| 0 (control) | 10M, 10F | 0 |
| 50 | 10M, 10F | 0 |
| 250 | 10M, 10F | 0 |
| 1,000 | 10M, 10F | 0 |

*Mortality and Time to Death*
No deaths were observed during the study period.

*Clinical Observations*
No clinically observable signs of toxicity were observed. Incidental findings at 250 and 1,000 mg/kg bw/day included hunched posture, noisy respiration and red/brown staining around the eyes. These effects were deemed to be due to oral administration of an unpalatable or irritant substance, and not indicative of systemic toxicity.

There were no treatment-related effects on behaviour, functional performance, sensory reactivity, bodyweight, or on food or water consumption.

*Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*
There were no treatment-related changes detected in the haematological parameters measured, or in blood chemistry. Females treated with 1,000 mg/kg bw/day showed statistically significant reductions in inorganic phosphorus levels, mean corpuscular volume and mean cell haemoglobin levels, but in isolation these changes were considered not to be of significance. Similarly, a statistically significant increase in plasma glucose was observed in females of the 250 mg/kg bw/day group, but was considered incidental due to the lack of this effect in the higher dose group.

*Effects in Organs*
No treatment-related organ-weight changes were detected.

No macroscopic abnormalities were detected at terminal kill.

Tracheal epithelial deciliation was observed microscopically in males treated with 250 mg/kg bw/day and all animals treated with 1,000 mg/kg bw/day. Associated epithelial hyperplasia and inflammatory cell infiltrates were also observed. These changes were considered to be due to accidental tracheal administration of the test substance. Agglomeration of secretion was observed in the gastric mucosa of animals treated with 1,000 mg/kg bw/day. Acanthosis and hyperkeratosis of the forestomach epithelium of were also observed.

The absolute adrenal weight was statistically reduced in all treated males. When considered relative to terminal bodyweight, this effect was only significant at 50 and 1,000 mg/kg bw/day, although reduced adrenal weights were also observed at 250 mg/kg bw/day. The reduced significance at this dose may be due to a slightly reduced bodyweight in males treated with the highest two dose levels (not otherwise significant). This result was considered by the investigators to be of no toxicological significance, due to the lack of correlating histopathological findings and due to the lack of an apparent dose-response. However, the latter argument may be flawed, as an effect on adrenal weight may have occurred at all doses ≥50 mg/kg bw/day.

One female treated with 1,000 mg/kg bw/day showed an enlarged, discoloured and fluid-filled kidney upon necropsy that was found to be due to a malignant tubular carcinoma. This result was considered to have been spontaneous and of no toxicological significance

Remarks – Results
The microscopic gastric and tracheal changes seen at 250 and/or 1,000 mg/kg bw/day, together with associated incidental clinical findings, were considered due to the irritant nature of the test material, and were considered not to represent a true systemic effect. Exclusion of the findings associated with irritancy results in a NOAEL of 1,000 mg/kg bw/day.

The study investigators stated their No Observed Effect Level (NOEL) to have been established as 50 mg/kg bw/day. However, the justification for this NOEL value is not considered accurate, as the effects on adrenal weight observed in males at all doses are considered to be of relevance.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day.
The No Observed Effect Level (NOEL) could not be established from the results presented in this study.

TEST FACILITY SafePharm (2004h)

### B.7. Genotoxicity – bacteria

| | |
|---|---|
| TEST SUBSTANCE | Notified chemical (solid) |
| METHOD | OECD TG 471 Bacterial Reverse Mutation Test.<br>Plate incorporation procedure |
| Species/Strain | *S. typhimurium*: TA1535, TA1537, TA98, TA100, and TA102 |
| Metabolic Activation System | Phenobarbitone/β-naphthoflavone-induced rat liver S9 mix |
| Concentration Range in Main Test | a) With metabolic activation: 50 to 5,000 µg/plate.<br>b) Without metabolic activation: 50 to 5,000 µg/plate. |
| Vehicle | Acetone |
| Remarks – Method | No significant protocol deviations. |

RESULTS

| Metabolic Activation | | Test Substance Concentration (µg/plate) Resulting in: | | | |
|---|---|---|---|---|---|
| | | Cytotoxicity in Preliminary Test | Cytotoxicity in Main Test | Precipitation | Genotoxic Effect |
| *Present* | Test 1 | >5000 | >5000 | 5000 | Negative |
| | Test 2 | | >5000 | 5000 | Negative |
| *Absent* | Test 1 | >5000 | >5000 | 5000 | Negative |
| | Test 2 | | | 5000 | Negative |

Remarks – Results

A slight, shiny precipitate was observed under an inverted microscope at 5,000 µg/plate, but this did not prevent the scoring of revertant colonies.

A small, statistically significant increase (1.18-fold) in revertant colony frequency was observed in TA100 (without S9) at 150 µg/plate in the first experiment. This increase was considered not to be of biological relevance because of the lack of both dose-response relationship and reproducibility, and because of the small magnitude of the increase.

CONCLUSION

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

TEST FACILITY

SafePharm (2004i)

### B.8. Genotoxicity – *in vitro*

TEST SUBSTANCE

XP 339

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
Cell Type/Cell Line: Peripheral lymphocytes
Metabolic Activation System: Phenobarbitone/β-naphthoflavone-induced rat liver S9 mix
Vehicle: Dimethylsulfoxide (DMSO)
Remarks – Method: No significant protocol deviations.

| Metabolic Activation | | Test Substance Concentration (µg/mL) | Exposure Period | Harvest Time |
|---|---|---|---|---|
| *Present* | Test 1 | 0*, 156.25, 312.5, 625*, 1250*, 1875*, 2500* | 4 | 24 |
| | Test 2 | 0*, 78.13*, 156.25*, 312.5*, 625*, 1250, 2500 | 4 | 24 |
| *Absent* | Test 1 | 0*, 156.25*, 312.5*, 625* | 4 | 24 |
| | Test 2 | 0*, 156.25*, 312.5*, 625*, 1250, 1875, 2500 | 24 | 24 |

*Cultures selected for metaphase analysis.

RESULTS

| Metabolic Activation | | Test Substance Concentration (µg/mL) Resulting in: | | | |
|---|---|---|---|---|---|
| | | Cytotoxicity in PreliminaryTest | Cytotoxicity in Main Test | Precipitation | Genotoxic Effect |
| *Present* | Test 1 | ≥2500 | ≥625 | ≥1250 | Negative |
| | Test 2 | | ≥625 | ≥1250 | Negative |
| *Absent* | Test 1 | ≥625 | >2500 | ≥625 | Negative |
| | Test 2 | | >2500 | ≥625 | Negative |

Remarks – Results

The test substance was toxic to cultured cells, but did not induce chromosomal aberration frequency in two independent experiments. The dose range included a dose level that was either the maximum practical dose, or one that induced a ~50% inhibition of the mitotic index.

| | |
|---|---|
| | The positive controls induced the appropriate statistically significant increases in the frequency of cells with chromosome aberrations.<br><br>S9 was present at 2% in Test 1 and 1% in test 2. |
| CONCLUSION | The notified chemical was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test. |
| TEST FACILITY | SafePharm (2004j) |

# APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

**Note:** Several studies were performed using a related chemical, "XP 339", that is an acceptable, structurally related analogue of the notified chemical.

## C.1. Environmental Fate

### C.1.1. Ready biodegradability

| | |
|---|---|
| TEST SUBSTANCE | Notified chemical |
| METHOD | OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.<br>EC Directive 92/69/EEC C.4-D<br>US EPA Fate, Transport and Transformation Test Guidelines OPPTS 835.3110 Paragraph (q). |
| Inoculum | Activated sludge |
| Exposure Period | 28 d |
| Auxiliary Solvent | None |
| Analytical Monitoring | BOD |
| Remarks - Method | The test substance was dispersed in culture medium and subject to ultrasonication prior to the test. The test substance was tested in triplicates at nominal test concentration of 100 mg/L with inoculum for up to 28 days. The test system consisted of the inoculum control, reference substance aniline at 100 mg/L and the toxicity control containing the test substance, reference substance and inoculum. The consumption of oxygen was measured using respirometer and the evolved $CO_2$ was absorbed in ethanolamine. The amount of $O_2$ consumed was expressed as % of ThOD calculated from the molecular formulae. The pH and temperatures were measured during the test. |

RESULTS

| *Test substance* | | *Aniline* | |
|---|---|---|---|
| *Day* | *% degradation* | *Day* | *% degradation* |
| 4 | 10 | 4 | 19 |
| 14 | 76 | 14 | 71 |
| 21 | 84 | 21 | 75 |

| | |
|---|---|
| Remarks - Results | The pH and temperatures were within acceptable range. The test material attained 88% degradation after 28 days. The 10-day window criterion was satisfied. The reference substance attained 71% degradation after 14 days and 76% after 28 days and thus validating the test system. |
| CONCLUSION | The notified chemical is considered to be readily biodegradable. |
| TEST FACILITY | SafePharm (2004k) |

### C.1.2. Bioaccumulation

Given the rapid hydrolysis in contact with water and the ready biodegradation of the notified chemical, it has little potential to bioaccumulate.

## C.2. Ecotoxicological Investigations

### C.2.1. Acute toxicity to fish

| | |
|---|---|
| TEST SUBSTANCE | Notified chemical |
| METHOD | OECD TG 203 Fish, Acute Toxicity Test –semi static. |

| | |
|---|---|
| | EC Directive 92/69/EEC C.1 Acute Toxicity for Fish, semi-static. |
| Species | Rainbow trout (*Oncorhynchus mykiss*) |
| Exposure Period | 96 h |
| Auxiliary Solvent | None |
| Water Hardness | 100 mg $CaCO_3$/L |
| Analytical Monitoring | GC. |
| Remarks – Method | Following a range-finding test, 2 groups of 10 fish were exposed to a nominal test concentration of 100 mg/L and 10 fish to a control for a period of 96 h under semi-static conditions. The media were renewed daily. The test material was stirred in diluent for 24 h to allow hydrolysis of the test substance. The test material dispersion was filtered prior to the test in order to remove any undissolved test substance that may have exerted a physical effect on the test organisms. Concentrations of hydrolysis products were used to determine the stability and concentrations of the test solutions at 0 and 24 h. The mortalities and sub-lethal effects were determined at 3, 6, 24, 48, 72 and 96 h after the start of exposure. The temperature, pH and dissolved oxygen were recorded daily throughout the test. |

RESULTS

| *Concentration mg/L* | *Number of Fish* | *Mortality* | | | | |
|---|---|---|---|---|---|---|
| *Nominal* | | *3h* | *24h* | *48h* | *72h* | *96h* |
| 0 | 10 | 0 | 0 | 0 | 0 | 0 |
| 100 | 10 | 0 | 0 | 0 | 0 | 0 |
| 100 | 10 | 0 | 0 | 0 | 0 | 0 |

| | |
|---|---|
| $LC_{50}$ | >100 mg/L at 96 hours. |
| NOEC | 100 mg/L at 96 hours. |
| Remarks – Results | The temperature, pH and dissolved oxygen were within acceptable range. Analysis of one hydrolysis product's concentration for fresh and 24 h old samples indicated 73-77% and 67-79% of the theoretical concentration, respectively. Analysis of another hydrolysis product's concentration for fresh and 24 h old samples indicated 69-96% and 62-83% of the theoretical concentration, respectively. The hydrolysis products were stable in the test medium for the duration of the period of media renewal. The test solutions were observed to be clear, colourless solution throughout the test. Neither mortalities nor sub-lethal effects were observed in the test solution or the control during the 96 h exposure. Given that toxicity cannot be attributed to any one, or more, of the hydrolysis products, the results are based on nominal concentrations of the test substance alone. |
| CONCLUSION | The test substance is considered to be non-toxic to fish. |
| TEST FACILITY | SafePharm (2005a) |

**C.2.2. Acute toxicity to aquatic invertebrates**

| | |
|---|---|
| TEST SUBSTANCE | Notified chemical |
| METHOD | EC Directive 92/69/EEC C.2 Acute Toxicity for *Daphnia* - static.<br>OECD TG 202 *Daphnia sp*, Acute immobilisation test and reproduction test |
| Species | *Daphnia magna* |
| Exposure Period | 48 hours |
| Auxiliary Solvent | None |
| Water Hardness | 250 mg $CaCO_3$/L |
| Analytical Monitoring | GC. |

Remarks – Method

Following a range-finding test, 10 daphnids in duplicate were exposed to nominal test concentrations of 1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56 and 100 mg/L and a control group for a period of 48 h under static conditions. The test material was stirred in diluent for 24 h to allow hydrolysis of the test substance. The test material dispersion was filtered prior to the test in order to remove any undissolved test substance that may have exerted a physical effect on the test organisms. Concentrations of hydrolysis products were used to determine the stability and concentrations of the test solutions at each time point. Any immobilisation of daphnids was recorded at 24 and 48 h after the start of exposure. The temperature, pH and dissolved oxygen were recorded throughout the test. The $EC_{50}$ and confidence limits at 24 and 48 h were calculated by probit analysis method.

RESULTS

| *Concentration (mg/L)* | | *Number of* D. magna | *Number Immobilised* | |
|---|---|---|---|---|
| *Nominal* | *Actual** | | *24 h* | *48 h* |
| 0 (control) | 0 | 20 | 0 | 0 |
| 1.0 | 64-77% | 20 | 0 | 0 |
| 1.8 | 64-77% | 20 | 0 | 0 |
| 3.2 | 64-77% | 20 | 0 | 0 |
| 5.6 | 64-77% | 20 | 0 | 0 |
| 10 | 64-77% | 20 | 0 | 0 |
| 18 | 64-77% | 20 | 0 | 0 |
| 32 | 64-77% | 20 | 15 | 45 |
| 56 | 64-77% | 20 | 55 | 90 |
| 100 | 64-77% | 20 | 75 | 100 |

*The actual values were based on the measured concentrations of a single hydrolysis product as a % of the theoretical values.

EC50 35 mg/L (CI: 30-41 mg/L) at 48 hours

NOEC 18 mg/L at 48 hours

Remarks – Results

The temperature, pH and dissolved oxygen were within acceptable range. The measured concentrations of each hydrolysis product at each time point were shown to be in excess of 77% of the theoretical concentration. The hydrolysis products were stable in the test medium for the duration of the exposure period. The test solutions were observed to be clear, colourless solution throughout the test. 15% immobilisation was observed at a nominal test concentration of 32 mg/L and complete immobilisation occurred at 100 mg/L. Given that toxicity cannot be attributed to any one, or more, of the hydrolysis products, the results are based on nominal concentrations of the test substance alone.

CONCLUSION

The test substance is considered to be harmful to *Daphnia magna*

TEST FACILITY

SafePharm (2004m)

### 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 Green alga (*Scenedesmus subspicatus*)

Exposure Period 72 hours

Concentration Range Nominal: 1.0-320 mg/L

Auxiliary Solvent None

Water Hardness None

Analytical Monitoring None

Remarks - Method

Following a range-finding test, algae were exposed to nominal test

concentrations of 1.0, 3, 10, 32, 100 and 320 mg/L and a control group in triplicates for a period of 72 h under constant illumination and shaking. The test material was stirred in diluent for 24 h to allow hydrolysis of the test substance. The test material dispersion was filtered prior to the test in order to remove any undissolved test substance that may have exerted a physical effect on the test organisms. Concentrations of the hydrolysis products were used to determine the stability and concentrations of the test solutions at 0 and 72 h. Samples of the algal populations were removed daily and cell densities were determined for each control and treatment groups. The temperature and pH were recorded throughout the test. Statistical analyses were performed by one-way analysis of variance incorporating Bartlett's test for homogeneity of variance and Dunnett's multiple comparison procedure.

RESULTS

| *Biomass* | | *Growth* | |
|---|---|---|---|
| *$EbC_{50}$ mg/L at 72 h* | *NOEC mg/L* | *$ErC_{50}$ mg/L at 72 h* | *NOEC mg/L* |
| 7.3 | 1.0 | >320 mg/L | 1.0 |

Remarks - Results

The temperature and pH were within acceptable range. At 0 h all test cultures and control were clear colourless solutions. After 72 h the control and 1.0 mg/L test cultures were green dispersions, the 3.2 mg/L were pale green dispersions and the 10, 32 and 100 mg/L test cultures were extremely pale green dispersions. The 320 mg/L test cultures remained as clear colourless solutions throughout the test period. At 72 h there were decline in the measured concentrations of hydrolysis products. This appears to be due to adsorption to algal cells. The hydrolysis products were considered stable in the test medium for the duration of the exposure period. It was not possible to calculate confidence limits for $EC_{50}$ values as the data generated did not fit the models. Given that toxicity cannot be attributed to any one, or more, of the hydrolysis products, the results are based on nominal concentrations of the test substance alone.

CONCLUSION

The test substance is considered to be non-toxic to alga based on the $ErC_{50}$ of >320 mg/L.

TEST FACILITY

SafePharm (2005b)

**C.2.4. Inhibition of microbial activity**

TEST SUBSTANCE

XP 339

METHOD

OECD TG 209 Activated Sludge, Respiration Inhibition Test.
EC Directive 87/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
US EPA Draft Ecological effects test guidelines OPPTS 850.6800

Inoculum

A mixture of activated sewage sludge and synthetic sludge which acts as a respiratory substrate.

Exposure Period

3 hours

Concentration Range

Nominal: 1000 mg/L

Remarks – Method

Based on the range-finding tests' results, test organisms were exposed to a nominal concentrations of 1000 mg/L in triplicates and a control group in duplicates. A reference material, 3,5-dichlorophenol at concentrations of 3.2, 10 and 32 mg/L was used to validate the test. The test organisms were exposed to the test solutions for a contact time of 30 minutes and 3 h. The test material was stirred for 96 h at 21°C in sterile diluent to allow hydrolysis to occur. The test material dispersion was filtered prior to the

| | |
|---|---|
| | test in order to remove any undissolved test substance that may have exerted a physical effect on the test organisms. The pH was recorded for the test substance, control and reference substance throughout the test. The $EC_{50}$ for the test substance was determined by inspection of the inhibition of respiration rate data. |
| RESULTS | |
| $IC_{50}$ | >1000 mg/L at 3 h |
| NOEC | 1000 mg/L |
| Remarks – Results | The validation criteria for the control and reference substance were met. At the nominal concentration of 1000 mg/L, no undissolved test material was visible. |
| CONCLUSION | The test substance is considered to be non-toxic to sewage microorganisms. |
| TEST FACILITY | SafePharm (2004n) |

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