File No: STD/1377

December 2010

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

MXDA/SM Adduct

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 Sustainability, Environment, Water, Population and Communities.

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 Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Itochu Australia Ltd. (ABN: 63 000 192 790)
Level 28, 570 Burke Street
Melbourne, VIC 3000

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 and structural formulae, molecular weight, composition, spectral data and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: particle size, flammability limits, acute dermal toxicity, acute inhalation toxicity, eye irritation and induction of germ cell damage

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Japan, USA, Germany, Korea, China (2003)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
MXDA/SM Adduct (>90% notified chemical)

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

3. COMPOSITION

DEGREE OF PURITY >99% (the notified chemical is a UVCB substance)

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: colourless to pale yellow liquid

Property	Value	Data Source/Justification
Freezing Point	<-20 °C	Measured
Boiling Point	>302 °C at 101.3 kPa	Measured
Density	1047 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.3 x 10^{-8} kPa at 25 °C	Measured
Water Solubility	2.05, 1.05 × 10^{-3}, 2.02× 10^{-2}, 3.61× 10^{-4} g/L at 20 °C*	Measured
Hydrolysis as a Function of pH	$t_{½}$ >1 year *	Measured
Partition Coefficient (n-octanol/water)	log Pow >6.20 at 20 °C	Measured
Surface Tension	49.8 mN/m at 20.5 °C	Measured
Adsorption/Desorption	log K_{oc} > 4.24	Calculated
Dissociation Constant	pKa = 7.06 – 9.71	Calculated
Flash Point	177 °C at 101.325 kPa	Measured
Autoignition Temperature	>400 °C	Measured

Explosive Properties	Predicted negative	Contains no functional groups that would imply explosive properties.

*Measured for four components of the notified chemical

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use. It is not compatible with strong oxidising agents or acids and heat should be avoided. Toxic and corrosive gases/vapours are released during the thermal decomposition of the chemical. The notified chemical will react in end-use when mixed with the other component of an epoxy 2-part coating.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified chemical is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However, the data above do not address all Dangerous Goods endpoints. Therefore, consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemical.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported at >90% concentration

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	<15	<25	<35	<45	<55

PORT OF ENTRY
Melbourne (sea and air).

IDENTITY OF MANUFACTURER/RECIPIENTS
Following its introduction into Australia, the notified chemical will be used at various sites across the country.

TRANSPORTATION AND PACKAGING
The notified chemical (>90%) will be supplied in 20 kg net iron pail cans, 200 kg net iron drums or 20 KL iso-containers. The chemical will be transported within Australia by road or air.

USE
The notified chemical will be used as a component of an epoxy resin hardener in 2-part coatings for the construction industry.

OPERATION DESCRIPTION
Typical processes are as follows:

Upon delivery of the notified chemical (at >90% concentration) to reformulations sites, it will be transferred to bulk storage tanks. The chemical will then be transferred to agitation tanks, where it will be blended with other components in a closed batch process. The resulting product (≤50% notified chemical) will then be filtered and transferred into containers for distribution to end-users using an open but dedicated line that will be designed to capture vapour and aerosol emissions and minimise spillage.

End-users in the construction industry will then mix the epoxy resin hardener (containing the notified chemical at ≤50% concentration) with epoxy resin in an open batch process via an electric agitator. The resin will then be applied to metal or concrete structures.

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 (days/year)*
Transport and storage	unspecified	unspecified	unspecified
Formulation workers (*ca*. 10 sites)	10/site	8	200
Construction workers (*ca.* 50 sites)	50/site	8	200

EXPOSURE DETAILS
Transport and storage workers are not likely to be exposed to the notified chemical (at >90% concentration) except in the event of an accident.

At reformulation sites, dermal or ocular exposure to the notified chemical and/or reformulated products (≤50% notified chemical) may occur whilst opening containers, during transfer processes and during cleaning of machinery. Inhalation exposure is not anticipated given the low vapour pressure of the notified chemical. Exposure should be mitigated by the use of exhaust ventilation and personal protective equipment (PPE: goggles, impervious gloves, vapour mask and protective clothing).

At construction sites the epoxy resin hardener products containing the notified chemical at ≤50% concentration will be handled by trained workers. Dermal or ocular exposure to the notified chemical may occur whilst opening containers, during mixing/transfer processes, during application and whilst cleaning equipment. Exposure should be mitigated by the use of exhaust ventilation and PPE.

Once the prepared epoxy resin is cured, the notified chemical is not expected to be bioavailable and further contact should not lead to exposure.

6.1.2. Public exposure
The notified chemical is intended for industrial use only, therefore the public may be exposed to the notified chemical (at >90% as imported or ≤50% in end-use products) only in the event of a transport accident. The public may come into contact with the metal or concrete structures to which the chemical has been applied. However, as the notified chemical will be cured, it will be unavailable for exposure.

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	LD50 between 500-2000 mg/kg bw; harmful
Rabbit, skin irritation (1)	corrosive
Rabbit, skin irritation (2)	corrosive
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOEL 5 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test.	non genotoxic

Toxicokinetics, metabolism and distribution.
The notified chemical is a UVCB substance and consists of several components. Based on the molecular weight (<500 Da), water solubility (3.61×10^{-4} - 2.05 g/L at 20 °C) and partition co-efficient (log Pow >6.20 at 20 °C) of the notified chemical, it is expected that some passive diffusion across the gastrointestinal (GI) tract and dermal absorption will occur. This is supported by the observations of mortalities and/or systemic toxicity effects that were noted in animal studies following oral and dermal exposure to the chemical. The notified chemical is a liquid with low vapour pressure, therefore absorption via the respiratory tract is not anticipated.

Acute toxicity, Irritation and Sensitisation

The notified chemical was found to be harmful in an acute oral toxicity study in rats. No deaths were recorded following administration of the test substance at up to 500 mg/kg bw. However, at the next dosage level (2000 mg/kg bw), all male animals died within 3 hours of administration of the test substance and all females died within 4.5 hours of administration. Therefore, the LD50 was considered to be between 500 and 2000 mg/kg bw. No acute dermal or inhalation toxicity data are provided for the notified chemical.

In two studies, the notified chemical was found to be corrosive to rabbits. In the first study involving 3 animals, moderate to severe erythema, severe oedema and petechial hemorrhage were noted in all animals within 1-hour post-exposure. The test sites then turned to scabs, which none of the animals recovered from during the observation period. In the second study, the notified chemical was administered to 3 sites on a single animal, with exposure times of 3 minutes, 1 hour and 4 hours. In all cases, moderate to severe erythema/eschar and oedema scores were recorded at the 24, 48 and 72 hour observation time points.

The notified chemical was found to be a sensitiser in a local lymph node assay in mice. At 0.5 and 5% concentration of the test substance, the reported stimulation indices were 28.3 and 84.7 respectively. At 50% concentration of the test substance, 2/4 of the animals tested were found dead 3 days after application of the test substance and the remaining 2 were killed *in extremis*.

Due to the corrosive nature of the notified chemical, acute dermal, acute inhalation and eye irritancy studies have not been conducted. However, for corrosive substances, the risk of severe damage to the eyes is considered implicit.

Repeated Dose Toxicity.
A 28-day repeat dose oral toxicity study in rats established an NOEL of 5 mg/kg bw/day, based on the presence of adverse effects at higher dose levels. Following the observation of deaths and significant systemic effects in a preliminary 14-day toxicity study, the maximum dosage selected for the main study was 50 mg/kg bw/day. No mortalities were recorded in the main study. Toxicologically significant effects that were recorded at the high and/or mid-dose (15 mg/kg bw/day) levels included clinically observable signs, modified haemotology and blood chemistry parameters and microscopic changes in the liver, spleen, adrenals, heart, urinary bladder, small intestine, lungs, mesenteric lymph nodes, ovaries and skeletal muscle. All animals treated with 50 mg/kg bw/day notified chemical for 28 days had foamy alveolar macrophages throughout the lung parenchyma with no regression during the recovery period.

The deaths of treated mice in the local lymph node assay are suggestive of harmful systemic effects following dermal exposure to the notified chemical.

Mutagenicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study and was not clastogenic in an in vitro mammalian chromosome aberration test.

Health hazard classification
Based on the data provided, the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R22 Harmful if swallowed
R35 Causes severe burns
R43 May cause sensitisation by skin contact
R48/21/22 Danger of serious damage to health by prolonged exposure if swallowed and in contact with skin.

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
The notified chemical will be handled by workers at >90% concentration as imported, and at ≤50% in end-use products. At such concentrations, the primary risks associated with use will be due the corrosive nature of the chemical. While the notified chemical is considered to be harmful to human health via the oral route, ingestion is unlikely under the occupational settings described.

Provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to the health of workers from use of the notified chemical is not considered to be unacceptable.

6.3.2. Public health

The notified chemical is intended for use in industrial settings by trained workers. The public may be exposed to the metal and concrete structures to which the notified chemical has been applied. However, the notified chemical will be cured and will not be bioavailable. Therefore, when used in the proposed manner, the risk to public health from the notified chemical is not considered to be unacceptable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be manufactured overseas and imported into Australia. Once imported, the notified chemical will be blended with other components in a closed-batch process into epoxy resin hardener preparations. The notified chemical may be released to the environment due to accidental spills (<1% of annual import volume), or as residue (2% of annual import volume) remaining in transport containers and reformulation equipment. The MSDS of the product containing the notified chemical states that in the event of accidental release, spillages should be contained by bunding and the spill collected in containers for disposal according to State/Territory regulations. All drains should be closed to prevent release to the aquatic compartment.

RELEASE OF CHEMICAL FROM USE

End-use products containing the notified chemical will be used by workers in the construction industry. Any waste containing the notified chemical (including residues and contaminated packaging) arising from either the formulation or end use processes will be disposed of in accordance with State/Territory regulations. Once the epoxy resin is applied to metal or concrete articles and cured, no further potential for release or environmental exposure to the notified chemical can occur, as the notified chemical will be chemically bound into the epoxy resin during the curing process.

RELEASE OF CHEMICAL FROM DISPOSAL

Notified chemical in coatings is expected to share the fate of the substrate to which it has been applied. Notified chemical in coatings applied to metal articles will be either thermally decomposed during metal reclamation processes at the end of the article's useful life, or disposed of to landfill. Cured coating removed by physical means (e.g. sandpaper/scraping) and non-metal articles at the end of their useful life are expected to be disposed of to landfill.

7.1.2 Environmental fate

Environmental fate studies provided by the notifier indicate the notified chemical has the potential to bioconcentrate and is not ready biodegradable. However, the majority of the notified chemical is expected to be cured into an inert matrix as part of its normal use pattern as an epoxy resin hardener. The notified chemical is irreversibly bound into the matrix and, in this form, is not expected to be bioavailable or biodegradable. Notified chemical in solid waste disposed of to landfill, or in epoxy resin spilt to the ground during application, is not expected to be mobile and will slowly degrade *in situ*, primarily by abiotic processes. The notified chemical will eventually degrade in landfill, or by thermal decomposition during metal reclamation processes, to form water and oxides of carbon and nitrogen.

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

7.1.3 Predicted Environmental Concentration (PEC)

A PEC was not calculated as there is no release expected to the aquatic compartment.

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	LL50 (96 h) = 4.0 mg/L	Toxic
Daphnia Toxicity - Acute	EL50 (48 h) = 3.4 mg/L	Toxic
Daphnia Toxicity - Chronic	NOEC (reproduction) = 0.12 mg/L	Toxic with long lasting effects
Algal Toxicity	E_rL_{50} (72 h) = 0.15 mg/L	Very toxic
Inhibition of Bacterial Respiration	IC50 (3 h) = 70 mg/L	Harmful

Under the Globally Harmonised System of Classification and Labelling of Chemicals (United Nations, 2009) the notified chemical is classified as acutely very toxic to algae, toxic to fish and aquatic invertebrates and harmful to bacteria. The notified chemical exhibits long lasting toxic effects to aquatic invertebrates.

7.2.1 Predicted No-Effect Concentration

Since no aquatic exposure is expected, a PNEC was not calculated.

7.3. Environmental risk assessment

The notified chemical has the potential to bioconcentrate, is not ready biodegradable and is acutely very toxic to algae and toxic to all other aquatic trophic levels. However, during use, no deliberate release of the notified chemical to the aquatic compartment is expected. The notified chemical will be used in the construction industry by professional tradespeople. The majority of the imported volume of notified chemical is expected to be cured into an epoxy resin and therefore will not be bioavailable or bioaccumulate. The notified chemical is therefore not expected to pose a risk to the environment based on its proposed use pattern.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the data provided, the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)], with the following risk phrases:

R22 Harmful if swallowed
R35 Causes severe burns
R43 May cause sensitisation by skin contact
R48/21/22 Danger of serious damage to health by prolonged exposure if swallowed and in contact with skin

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, 2009) 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***
Corrosive	1	Danger: Causes severe burns and eye damage
Acute toxicity	4	Warning: Harmful if swallowed
Sensitization	1	Warning: May cause an allergic skin reaction
Target organ toxicity	2	Warning: May cause damage to organs through prolonged or repeated exposure
Environment	Acute 1	Very toxic to aquatic life
	Chronic 2	Toxic to aquatic life with long lasting effects

Human health risk assessment

Under the conditions of the occupational settings described, the notified chemical is not considered to pose an 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 reported use pattern, the notified chemical is not expected to pose a risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following health hazard classification for the notified chemical:
  - Xn: R22 Harmful if swallowed
  - C: R35 Causes severe burns
  - Xi: R43 May cause sensitisation by skin contact
  - Xn: R48/21/22 Danger of serious damage to health by prolonged exposure if swallowed

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc. ≥25%: C; R35; R22; R48/21/22; R43;
  - ≥10% Conc. <25%: C; R35; R48/21/22; R43;
  - ≥5% Conc. <10%: C; R34; R43;
  - ≥1% Conc. <5%: Xi; R36/38; R43;

- The notified chemical should be classified as follows under the ADG Code:
  - Class 8 (Corrosive)

Health Surveillance

- As the notified chemical is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced (>90%) and when handling the end-use products (≤50%):
  - Automated processes, where possible

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced (>90%) and when handling the end-use products (≤50%):
  - Avoid contact with skin and eyes
  - Avoid spills and splashing during use
  - Prevent leaks and spills
  - A shower and eyewash station should be available

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced (>90%) and when handling the end-use products (≤50%):
  - Coveralls
  - Gloves
  - Full face mask

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

- Only workers with sufficient training in handling hazardous substances should handle the notified chemical or products containing it.

- 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.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
  - the use pattern or recommended disposal changes such that release to fresh water (river or lake) is proposed or expected

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of an epoxy resin hardener for the construction industry, or is likely to change significantly;
  - the amount of chemical being introduced has increased from 55 tonnes, or is likely to increase, significantly;
  - the chemical has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

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

Melting Point/Freezing Point <-20 °C

Method EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Determined by cooling a tube containing the sample in a dry ice/acetone bath
Test Facility SafePharm (2002a)

Boiling Point >302 °C at 101.3 kPa

Method EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Determined by differential scanning calorimetry (DSC).
The test material lost a volatile fraction from *ca*. 302 °C. The degree of response from the endotherms and resulting residues remaining on completion of the tests (*ca*. 400 °C) indicated incomplete boiling.
Test Facility SafePharm (2002a)

Density 1047 kg/m^3 at 20 °C

Method EC Directive 92/69/EEC A.3 Relative Density.
Remarks Determined using a pycnometer.
Test Facility SafePharm (2002a)

Vapour Pressure 1.3 x 10^{-8} kPa at 25 °C

Method EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Determined using a vapour pressure balance
Test Facility SafePharm (2002b)

Water Solubility 2.05, 1.05 × 10^{-3}, 2.02× 10^{-2}, 3.61× 10^{-4} g/L at 20 °C

Method EC Directive 92/69/EEC A.6 Water Solubility
Remarks Flask Method. The water solubility was calculated for each of the 4 components of the test substance.
Test Facility SafePharm (2002a)

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)*	*t½*
4	25	> 1 year
7	25	> 1 year
9	25	> 1 year

Remarks All components of the notified chemical had $t_{½}$ > 1 year
Test Facility SafePharm (2002a)

Partition Coefficient (n-octanol/water) log Pow > 6.20 at 20 °C

Method EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks HPLC Method. The mobile phase was adjusted to pH 11.0 to ensure the test substance was in its non-ionised form. Computer estimations, by the test facility, indicated possible overestimation of the partition coefficient for a number of components probably due to surface activity of some components with the analytical column.
Test Facility SafePharm (2002a)

Surface Tension 49.8 mN/m at 20.5 ºC

Method	EC Directive 92/69/EEC A.5 Surface Tension.
Remarks	Concentration: 90% saturation solution contained 2.28, 1.06 x 10^{-3}, 1.97 x 10^{-2} and 1.80 x 10^{-4} g/L of four components of the test substance. The test material is considered to be a surface active material.
Test Facility	SafePharm (2002a)

Adsorption/Desorption log K_{oc} >4.24

Method	Calculated
Remarks	The adsorption/desorption coefficient was calculated based on the log Pow of the test substance.
Test Facility	SafePharm (2002a)

Dissociation Constant pKa = 7.06 – 9.71

Method	Calculated
Remarks	Calculated with the pKalc program. The minimum and maximum calculated pKa values for the 4 components of the test substance are reported.
Test Facility	Exponent (2010)

Flash Point 177 ºC at 101.325 kPa

Method	EC Directive 92/69/EEC A.9 Flash Point.
Remarks	Determined using a closed cup equilibrium method
Test Facility	SafePharm (2002b)

Autoignition Temperature >400 ºC

Method	EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	Determined by heating aliquots of the test material in a flask and observing any ignition
Test Facility	SafePharm (2002b)

Explosive Properties

Method	Observation of functional groups that would infer explosive properties
Remarks	Predicted negative
Test Facility	SafePharm (2002b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD
- Species/Strain: Rat/Crj: CD(SD)IGS, SPF
- Vehicle: Olive oil
- Remarks - Method: No significant protocol deviations. Dosage refers to notified chemical. Control animals were treated with the vehicle.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	6M/6F	25	0/12
II	6M/6F	50	0/12
III	6M/6F	200	0/12
IV	6M/6F	500	0/12
V	6M/6F	2000	12/12

- LD50: Between 500 and 2000 mg/kg bw
- Signs of Toxicity: For groups I-III, no abnormalities were noted.

  For group IV (500 mg/kg bw), body descent, squatting, abnormal gait, diarrhoea and loss of fur were noted for some or all of the animals. All signs vanished by 3-days post-administration. Reduced body weight gain was seen by day 2 in both males and females.

  For group V (2000 mg/kg bw), all males died within 40 minutes to 3-hours post-administration and all females died within 40 minutes to 4.5 hours. Clinical signs for these animals included body descent, prostration, tremor, jumping, struggling and abnormal gait.
- Effects in Organs: No effects were noted for groups I-IV. The animals in group V (2000 mg/kg bw) showed mucosal bleeding in the grandular stomach, intestinal tract and anterior stomach, white anterior stomach mucous membrane and intestinal tract mucosal colliquation.

CONCLUSION: The notified chemical is harmful via the oral route.

TEST FACILITY: MGCC (2002a)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD
- Species/Strain: Rabbit/Japanese white KbL:JW(SPF)
- Number of Animals: 3 male
- Vehicle: None
- Observation Period: 17 days
- Type of Dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviations.

RESULTS
- Remarks - Results: Moderate to severe erythema, severe oedema and petechial hemorrhage were noted in all animals within 1-hour post-exposure. At 24 hours, the application sites had turned grey due to necrosis and gradually turned to a scab (day 7 or later). None of the animals recovered from the scabs within

the observation period of 17 days.

CONCLUSION The notified chemical is corrosive to the skin.

TEST FACILITY MGCC (2002b)

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 female
Vehicle None
Observation Period 72 hours
Type of Dressing Semi-occlusive.
Remarks - Method As it was suspected that the test substance may produce severe irritancy/corrosive effects, initially a single rabbit was treated. Three test patches were applied successively to separate skin sites on the animal. The first patch was removed after 3-minutes, the second patch then added and removed after 1 hour, and then the third added and removed after 4 hours. Based on the results in one animal, additional animals were not treated.

RESULTS

Lesion	*Mean Score**			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Exposure Time	3 min	1 hr	4 hr			
Erythema/Eschar	3.33	3.33	3.67	4	-	4
Oedema	4	4	3.67	4	-	4

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

Remarks - Results A green and brown colouration appeared at each site 24 hours and 48 hours, respectively, after patch removal. These zones were reported to have been surrounded by an erythemateous zone. In addition, the skin suppleness decreased and the beginnings of necrosis noted from 48 hours.

Additional monitoring to day 8 was not conducted as severe irritation to corrosion was apparent at 72 hours.

CONCLUSION The notified chemical is corrosive to the skin.

TEST FACILITY CERB (2004)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE Notified chemical

METHOD Similar to OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/ CBA/Ca (CBA/CaCruBR) Female
Vehicle Acetone/olive oil (4:1)
Remarks - Method An initial pre-screen test was not conducted. Concurrent tests involving a positive control were not run, but had been conducted previously in the test laboratory.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*

Test Substance		
0 (vehicle control)	494.5	-
0.5	14001.3	28.3
5	41879.2	84.7
50	-	-

Remarks - Results

2/4 animals treated with 50% test substance were found dead three days after application of the test substance. The remaining 2 were killed *in extremis*, with noted signs of toxicity including hunched posture, lethargy, pilo-erection, decreased respiratory rate, laboured respiration, hypothermia and splayed gait.

No signs of systemic toxicity were noted in animals treated with the vehicle or 0.5% test substance. Signs of toxicity noted for animals treated with 5% test substance were hunched posture, pilo-erection and lethargy. In addition, animals treated with 5% substance showed body weight loss over the 5 day period.

A stimulation index of >3 was observed for the test substance.

CONCLUSION

There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY

SafePharm (2002c)

B.5. Repeat dose toxicity

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).

Species/Strain: Rat/Sprague-Dawley Crl:CD® (SD) IGS BR

Route of Administration: Oral – gavage

Exposure Information: Total exposure days: 28 days
Dose regimen: 7 days per week
Post-exposure observation period: 14 days

Vehicle: Arachis oil BP

Remarks - Method: No significant protocol deviations. Dosage levels were selected following the effects observed in a preliminary 14-day range-finder study in the rat (50, 250 and 750 mg/kg bw/day).

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M/5F	0	0
low dose	5M/5F	5	0
mid dose	5M/5F	15	0
high dose	5M/5F	50	0
control recovery	5M/5F	0	0
high dose recovery	5M/5F	50	0

Clinical Observations

No significant findings are reported for low and mid-dose treatment groups.

Increased salivation prior to and up to 10 minutes after dosing was noted for the high dose group from day 6 onwards. From the third week of treatment, hunched posture, pilo-erection, tiptoe gait, waddling gait, increased lachrymation, respiratory pattern changes and staining of the fur were noted. In general, the clinical signs regressed following cessation of treatment. However, hunched posture was still evident in a portion of the animals at the end of the observation period. An adverse effect on bodyweight gain and dietary intake was

also noted for animals of both sexes in the high dose groups.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No significant findings are reported for low and mid-dose treatment groups.

For animals of both sexes in the high dose group, elevated plasma aspartate aminotransferase, alanine aminotransferase and cholesterol were noted, with the values reportedly being outside the normal ranges for rats of the strain and age used. Males also showed reductions in plasma glucose, albumin and total protein concentration. Elevated aspartate aminotransferase levels were evident in animals following the recovery period. The animals also showed an increased platelet count relative to control animals and males showed an increased erythrocyte count. An increased incidence of haemoglobin in the urine was also noted for both males and females at this dose level compared to control animals and an increased urine volume of reduced specific gravity noted for males.

Effects in Organs

No treatment-related macroscopic findings were noted. Statistically significant increases in relative kidney and liver weight (and increased relative adrenal weight in males) were noted for animals in the high dose group. The elevated kidney weight was evident in females post-recovery. The following treatment-related observations were noted:

LIVER: For both males and females in the high dose group, foamy vacuolation of hepatocytes, generalised hepatocyte enlargement, and vacuolar distension of scattered cells. In addition, single cell hepatocyte necrosis was observed for females, and a lower incidence of glycogen-type vacuolation was seen for males. All conditions were observed to have regressed following recovery.

SPLEEN: For both males and females in the high dose group, lymphoid hyperplasia and vacuolar distension of scattered cells with associated apoptosis was noted. All conditions were observed to have regressed following recovery.

ADRENALS: For both males and females in the high dose group, higher grades of severity of vacuolation of cortical cells were noted. This condition was observed to have regressed following recovery.

HEART: For both males and females in the high dose group, a greater incidence of myocarditis was noted (and may also have been evident for the mid-dose group). There was no toxicologically significant difference in the incidence or severity of myocarditis between control and the high dose treated animals following recovery.

URINARY BLADDER: Treatment-related hyperplasia of the transitional epithelium was noted for three females in the high dose group. A similar effect was noted for 2 females in the low dose group, but this is reported to not be as a consequence of treatment. This effect was not observed in recovery animals.

SMALL INTESTINE: For both males and females in the high dose group, vacuolation of lamina propria cells in the duodenum, jejunum, and ileum was noted. A similar effect in the ileum only was noted in a few animals in the mid dose group. This condition was observed to have regressed to an extent following recovery.

LUNGS: For both males and females in the high dose group, foamy alveolar macrophages throughout the lung parenchyma were noted. There was no evidence of regression of the condition following recovery.

MESENTERIC LYMPH NODES: For both males and females in the high dose group, foamy histiocytes were noted. Residual lesions characterised by accumulations of macrophages with amorphous eosinophilic cytoplasm were noted for the high dose recovery animals.

OVARIES: For females in the high dose group, foamy vacuolation of corpora luteal cells was noted. Partial regression of the condition was observed post-recovery.

SKELETAL MUSCLE: For both males and females in the high dose group, muscle fibre degeneration and necrosis and proliferation of sarcolemmal nuclei were noted. The latter effect was also noted for animals in the mid-dose group, but to a lesser extent. Significant regression of the conditions was apparent post-recovery.

CONCLUSION

The only effect observed in the low dose group was hyperplasia of the transitional epithelium of the urinary bladder in two females. The study authors reported that this effect was not treatment-related, although significant effects at the high dose were considered to be treatment related. Therefore, the No Observed Effect Level (NOEL) was established as 5 mg/kg bw/day in this study, based on the presence of toxicologically significant effects at the higher dosage levels.

TEST FACILITY SafePharm (2002d)

B.6. 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

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	Phenobarbitone/β-naphthoflavone-induced rat liver (S9 homogenate)
Concentration Range in Main Test	a) With metabolic activation: 5, 15, 50, 150, 500 and 1500 µg/plate b) Without metabolic activation: 1.5, 5, 15, 50, 150 and 500 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	A preliminary toxicity test (0-5000 µg/plate) was performed to determine the toxicity of the test material (TA100 and WP2uvrA) only. A range-finding study was then conducted using 7 concentrations of the test substance, assayed in triplicate against each tester strain (with metabolic activation: 1.5-1500 µg/plate; without metabolic activation: 0.5-500 µg/plate). The main study (Test 2) was conducted on a separate day to the range-finding study (Test 1) using fresh cultures of the bacterial strains and fresh test material formulations. Vehicle and positive controls were used in parallel with the test material. Positive controls: i) without S9: N-ethyl-N'-nitro-N-nitrosoguanidine (TA100, TA1535, WP2uvrA), 9-aminoacridine (TA1537) and 4-nitroquinoline-1-oxide (TA98); ii) with S9: 2-aminoanthracene (TA100, TA1535, TA1537, WP2uvrA) and benzo(a)pyrene (TA98).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥150	≥150	NA	Negative
Test 2		≥150	NA	Negative
Present				
Test 1	≥500	≥500	NA	Negative
Test 2		≥500	NA	Negative

Remarks - Results	In the preliminary toxicity study, the test material was toxic to both strains tested at and above 500 and 150 µg/plate, with and without metabolic activation, respectively. In the mutation studies, the test substance caused a visible reduction in the growth of the bacterial background lawn to all strains, from 150 µg/plate without metabolic activation and from 500 µg/plate with activation. Thus, the material was tested up to the toxic limit.

No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains up to and including the maximum dose, either with or without metabolic activation.

The positive controls gave satisfactory responses, confirming the validity of the test system.

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

TEST FACILITY SafePharm (2002e)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain Chinese hamster
Cell Type/Cell Line Chinese hamster lung (CHL)
Metabolic Activation System Phenobarbitone/β-naphthoflavone-induced rat liver (S9 homogenate)
Vehicle Dimethyl sulphoxide
Remarks - Method A preliminary toxicity study (0.5 to 5000 µg/mL) was performed to define the dose levels for the main test. A precipitate was observed at concentrations ≥1500 µg/mL.

Vehicle and positive controls (cyclophosphamide and mitomycin C) were used in parallel with the test material.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	3.75*, 7.5*, 15*, 30, 45, 60	6 h	24 h
Test 2a	0.31, 0.63, 1.25*, 2.5*, 3.75*, 5	24 h	24 h
Test 2b	0.25*, 0.5*, 1.0*, 1.5, 2.0, 2.5	48 h	48 h
Present			
Test 1	15, 30*, 45*, 60*, 90, 120	6 h	24 h
Test 2	7.5, 15, 30*, 45*, 60, 75*	6 h	24 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥50	≥30	>60	Negative
Test 2a	≥5	≥2.5	>5	Negative
Test 2b	≥2.5	≥0.25	>2.5	Negative
Present				
Test 1	≥150	≥90	>120	Negative
Test 2		≥75	>75	Negative

Remarks - Results For the main experiments, precipitates were not observed at the end of the observation period. Therefore, the maximum doses selected for metaphase analysis were based on the toxicity of the test substance.

For Test 1 with metabolic activation, a small but statistically significant increase in the frequency of cells with aberrations is noted. Similarly, statistically significant increases are noted in Test 2 for the 48 hour exposure group without metabolic activation and for the exposure group

	with activation. In all cases, the increases were deemed by the study authors to be of no toxicological significance as they were within the historical control levels. The positive and vehicle controls gave satisfactory responses, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to Chinese hamster lung cells treated in vitro under the conditions of the test.
TEST FACILITY	SafePharm (2002f)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE: Notified chemical

METHOD
- Inoculum: Standard activated sludge purchased from Chemicals Safety Center of Chemicals Inspection & Testing Institute, Japan
- Exposure Period: 28 days
- Auxiliary Solvent: None reported
- Analytical Monitoring: GC and TOC
- Remarks - Method: No significant protocol deviations were reported.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation**	*Day*	*% Degradation*
7	0	7	59
14	-0.3	14	73
21	-1.3	21	79
28	-2.0	28	83

*Mean of 3 replicates

- Remarks - Results: Quantitative analysis by GC showed that none of the 4 components of the test substance degraded to any significant extent (0-1% degradation). The negative degradation rates reported for the test substance were consistent with the quantitative GC analysis considering experimental error.

CONCLUSION: The notified chemical is not readily biodegradable

TEST FACILITY: Institute of Ecotoxicology (2002a)

C.1.2. Bioaccumulation

TEST SUBSTANCE: Notified chemical

METHOD
- Species: Common carp (*Cyprinus carpio*)
- Exposure Period: Exposure: 28 days Depuration: 14 days
- Auxiliary Solvent: Methanol
- Concentration Range: Nominal: 0.02 – 0.20 mg/L; Actual: 0.018 – 0.186 mg/L (average over 28 days)
- Analytical Monitoring: HPLC
- Remarks - Method: The test was conducted at two different concentrations (0.186 mg/L and 0.018 mg/L) under semi-static conditions. Fifty five fish were used in each test treatment and 8 fish were used in the control test. All the tests were controlled at 24.7 ± 0.4°C and a pH range of 6.9 – 7.1.

RESULTS
- Bioconcentration Factor: The BCF was calculated for each component of the notified chemical. At 0.186 mg/L the BCFs of the 4 components of the notified chemical were 11-49, 181-1024, 547-1450 and 1568-2901. At 0.018 mg/L the BCFs of the 4 components of the notified chemical were 18-143, 123-926, 403-954 and 859-2281.
- CT50: Not determined
- Remarks - Results: All validity criteria for the test guideline were satisfied. Since the BCF of some components of the notified chemical were > 500 the notified

chemical is considered to have the potential for bioconcentration.

An elimination study was performed after the 28 day exposure period. After 14 days all the components of the notified chemical were < 16% of the steady state values.

CONCLUSION The notified chemical has the potential for bioconcentration.

TEST FACILITY Institute of Ecotoxicology (2002b)

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	Juvenile Rainbow Trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None reported
Water Hardness	Approx. 100 mg $CaCO_3$/L
Analytical Monitoring	HPLC (total area of 4 peaks)
Remarks – Method	Following a range finding test, a definitive test was performed as follows. WAFs were prepared by adding amounts of the test substance to dechlorinated tap water which was stirred for 23 hours and allowed to stand for an hour. The aqueous phase was removed by mid-depth siphoning. Microscopic inspection showed no micro-dispersions or undissolved test substance to be present. The fish, introduced to the WAF and maintained at 12.6 – 14.1°C under semi-static conditions for 4 days (pH 7.4–8.1, 7.7–10.0 mg O_2/L), were observed for mortality and sub-lethal effects.

RESULTS

Concentration mg/L		*Number of Fish*	*Cumulative Mortality*				
Nominal	*Actual**		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	< LOQ (0.013)	10	0	0	0	0	0
1	0.956	10	0	0	0	0	0
1.8	0.928	10	0	0	0	0	0
3.2	1.65	10	0	0	0	0	1
5.6	4.44	10	0	0	0	2	10
10	Not reported	10	0	0	0	10	10

*Measured after 96 h (old medium)

LL50	4.0 mg/L (95% CI 3.6 – 4.5 mg/L) at 96 hours (based on loading rates)
NOEL	1.8 mg/L at 96 hours (based on loading rates)
Remarks – Results	All validity criteria for the test were satisfied. The temperature deviated below the minimum recommend by the test guideline (13°C) however there were no mortalities or sub-lethal effects observed in the control hence this was considered not to have affected the outcome of the test. The endpoints were calculated by the trimmed Spearman-Karber method. Since the test substance is a mixture of components and the dissolved fraction is a mixture of components, the results were based on the nominal loading rates.

CONCLUSION The notified chemical is toxic to fish.

TEST FACILITY SafePharm (2003a)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test - Static EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia - Static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None reported
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	A range finding test was performed. In the definitive test WAFs were prepared by adding amounts of the test substance to dechlorinated tap water which was stirred for 23 hours and allowed to stand for an hour. The aqueous phase was removed by mid-depth siphoning. Microscopic inspection showed no micro-dispersions or undissolved test substance to be present. The daphnia were observed for immobilisation over two days (test conditions: artificial light dark cycle of 16 to 8 hours, 20.2–20.9°C, pH 7.9–8.4, 8.2–8.4mg O_2/L).

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual**		*24 h*	*48 h*
0	< LOQ (0.0013)	20	0	0
0.10	0.0814	20	0	0
0.18	0.124	20	0	0
0.32	0.203	20	0	0
0.56	0.263	20	0	0
1.0	0.482	20	0	0
1.8	0.861	20	0	0
3.2	2.07	20	5	9
5.6	3.09	20	15	19
10	5.14	20	20	20

*Measured after 48 hours

EL50	3.4 mg/L (95% CI of 2.9 – 3.9 mg/L) at 48 hours (based on loading rates)
NOEL	1.8 mg/L at 48 hours (based on loading rates)
Remarks - Results	All validity criteria for the test guideline were satisfied. The initial measured concentrations of the lowest and highest test substance concentration were 0.0809 and 7.43 mg/L, respectively. After 48 h the concentrations had decreased to 0.0814 and 5.14 mg/L. There was no change in the chromatographic profile over 48 hours and a separate study analysis showed that the test substance was stable over 48 hours and it did not adsorb to glassware. Since the test substance is a mixture of components and the dissolved fraction is a mixture of components, the results were based on the nominal loading rates.
CONCLUSION	The notified chemical is toxic to aquatic invertebrates.
TEST FACILITY	SafePharm (2003b)

C.2.3. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction

	test. – Semi static
Species	*Daphnia magna*
Exposure Period	21 days
Auxiliary Solvent	Dimethylformamide
Water Hardness	250 – 272 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	The test substance was dissolved in an auxiliary solvent (dimethylformamide) to make up a stock solution. Three consecutive dilutions were performed on the stock solution to produce 5 test solutions with nominal concentrations 0.014 – 1.4 mg/L. Daphnia were exposed to the test solutions for a period of 21 days, under semi-static conditions (test conditions: artificial light dark cycle of 16 to 8 hours, 19.7-21.6°C, pH 8.0–8.2, 8.4–9.0 mg O_2/L). The time weighted mean concentrations varied from 32% - 114% of respective nominal concentrations. The variation in results for analytical determination is considered to be due to low concentrations employed, making it difficult to differentiate from base line noise. The EC50 (reproduction, 21 days) value calculated by the geometric mean method.

RESULTS

Day 21			
Concentration (mg/L)		*Mean Percent Adult Survival*	*Mean Number of Living Offspring Produced per female – cumulative*
Nominal	*Actual**		
Control	0	100	72
Solvent Control	0	100	74
0.014	0.0045	100	74
0.044	0.027	100	75
0.14	0.12	100	71
0.44	0.46	40	3
1.4	1.6	0	0

*Time weighted mean of measured test concentrations

EC50 (reproduction)	0.23 mg /L (based on time-weighted mean measured test concentrations)
LOEC (reproduction)	0.46 mg /L (based on time-weighted mean measured test concentrations)
NOEC (reproduction)	0.12 mg / L (based on time-weighted mean measured test concentrations)
Remarks - Results	Immobilisation occurred predominantly in the highest test concentration with 100% mortality on day 4. Significant immobilisation also occurred throughout the test in the 0.44 mg/L group with 10% and 60% mortality by days 12 and 21 respectively. There was a significant effect on colour of the daphnids in that 100% of the surviving daphnids of days 2 and 3 at concentration 1.4 mg/L were markedly paler in colour than solvent control animals. There was a significant effect on size and colour in the 0.44 mg/L concentration group where 100% of the surviving daphnids were markedly smaller and paler than control species. After 21 days, there were no statistically significant differences between solvent control and the 0.014, 0.044 and 0.14 mg/L test groups in terms of the number of live young produced per adult. The 0.44 and 1.4 mg/L groups were not included in the statistical analysis due to significant mortalities in P_1 generation, and all animals being dead by end of test respectively.

After 21 days, there were no statistically significant differences between solvent control and the 0.014, 0.044 and 0.14 mg/L test groups in terms of the length of each surviving adult. The 0.44 and 1.4 mg/L groups were not included in the statistical analysis due to significant mortalities in P_1 generation, and all animals being dead by end of test respectively.

F_1 generation daphnids for 0.014,0.044, 0.14 and 0.44 mg/L daphnids were found to be in similar condition to control F_1 daphnids. All daphnids died before reproduction could begin in the 1.4 mg/L group. Number of unhatched eggs and dead young were low in all control and treatment groups surviving to maturation.

CONCLUSION The notified chemical is toxic to aquatic life with long lasting effects

TEST FACILITY SafePharm (2006)

C.2.4. 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	*Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 0.01 – 0.16 mg/L (WAFs) Actual: <LOQ (0.00087 mg/L) – 0.0085 mg/L
Auxiliary Solvent	Diethyl ether
Water Hardness	Not reported
Analytical Monitoring	HPLC
Remarks - Method	A range finding test was performed. In the definitive test WAFs were prepared by the preparation of a stock solution (320 mg test substance in 10 mL diethyl ether). A series of dilutions were made from this solvent stock solution to give further solvent stock solutions. An aliquot (100 µL) of each of the stock solutions was dispensed on a glass slide and the solvent was allowed to evaporate. The glass slides were then suspended in 20 L of culture medium to give test loading rates of 0.010, 0.020, 0.040, 0.080 and 0.16 mg/L loading rate WAFs. These were stirred for 23 hours and allowed to stand for an hour. The aqueous phase was removed by mid-depth siphoning. Microscopic inspection showed no micro-dispersions or undissolved test substance to be present. Algae with a density of 0.873×10^4 – 1.14×10^4 cells per mL were exposed to a WAF of the test material at loading rates of 0.01 – 0.16 mg/L (3 replicates). The test mixtures were irradiated 24 h/day at pH 7.9–8.4 and 24 ± 1°C for a period of 72 hours.

RESULTS

Biomass		*Growth*	
E_bL_{50} mg/L at 72 h	*NOEL mg/L*	*E_rL_{50} mg/L at 72 h*	*NOEL mg/L*
0.12 (95% CI 0.11 – 0.14) (Based on loading rates)		0.15 (Based on loading rates)	0.04

Remarks - Results The concentration of test substance in test solutions at the start of the test ranged from < LOQ to 0.125 mg/L. Analysis at 72 hours showed a marked decline in the concentration of test substance with all but one measurement being < LOQ. The 72 h chromatograms showed no

	significant change over the test period. The test substance was assumed to be adsorbing to algal cells. Since the test substance is a mixture of components and the dissolved fraction is a mixture of components, the results were based on the nominal loading rates. The results should be treated with caution since there was adsorption of the test substance to algal cells. Statistical analysis of the area under the growth curve data was carried out for the solvent control an all loading rates using one way analysis of variance incorporating Bartlett's test for homogeneity of variance and Dunnett's multiple comparison treatment for comparing several treatments with a control.
CONCLUSION	The notified chemical is very toxic to algae.
TEST FACILITY	SafePharm (2003c)

C.2.5. 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	Activated sewage sludge from a municipal sewage treatment plant
Exposure Period	3 hours
Concentration Range	Nominal: 10 - 1000 mg/L Actual: Not reported
Remarks – Method	After a range-finding test was conducted, tests were conducted by exposing activated sewage sludge to 10, 32, 100, 320 and 1000 mg/L dispersions of the test substance and synthetic sewage for a period of 3 h at 21°C and pH 8.0 - 8.1. The test substance was dissolved in water with the aid of ultrasonication. Reference material (3,5–dichlorophenol) at concentrations of 3.2, 10, and 32 mg/L was used in order to confirm the suitability of the inoculum. The test water had a total hardness of approximately 100 mg $CaCO_3$/L.
RESULTS	
IC50	70 mg/L
NOEC	10 mg/L
Remarks – Results	All validity criteria for the test guideline were satisfied. In some instances, the initial and final dissolved oxygen concentrations were below those recommended in the test guidelines. However, this was not considered to have adversely affected the test results given that the O_2 consumption rate was determined over the linear portion of the O_2 consumption trace.
CONCLUSION	The notified chemical is harmful to microbial respiration
TEST FACILITY	SafePharm (2002g)

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