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January 2013

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

OS-1600 Crosslinking agent

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 Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This 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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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1416	Honeywell Ltd	OS-1600 Crosslinking Agent	Yes	≤ 10 tonnes per annum	Crosslinking agent for silicone sealant and adhesive formulations

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the table below.

Hazard classification	*Hazard statement*
Acute toxicity (Category 4)	H302 - Harmful if swallowed

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R22: Harmful if swallowed

The environmental hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute Category 3	H402: Harmful to aquatic life

Human health risk assessment
Provided the recommended control measures are in place, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

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

Environmental risk assessment
On the basis of the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - H302- Harmful if swallowed

- The following should be used for products/mixtures containing the notified chemical:
  - Conc. ≥ 25%: H302

CONTROL MEASURES
Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation:
  - Enclosed, automated processes, where possible
  - Ventilation system including local exhaust ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Coveralls, impervious gloves, goggles

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- 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
  - information on the inhalation toxicity of the notified chemical becomes available.

Or

(2)Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a crosslinking agent for silicone sealant and adhesive formulations, or is likely to change 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 (M)SDS of the notified chemical and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Honeywell Ltd (ABN: 74 000 646 882)
OMIT Level 3, 71 Queens Rd
MELBOURNE VIC 3004

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, spectral data, degree of purity, impurities, and import volume.

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Belgium (2008)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
OS-1600 Crosslinking agent (notified chemical)
OS-1600 (notified chemical)
OTTOSEAL S 18 (contains ≤ 5% notified chemical)
OTTOSEAL S 70 (contains ≤ 5% notified chemical)
OTTOSEAL S 110 (contains ≤ 5% notified chemical)

MOLECULAR WEIGHT
< 500 Da

3. COMPOSITION

DEGREE OF PURITY > 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless to yellowish liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -90 °C	Measured
Boiling Point	Decomposes without boiling at > 250 °C	Measured
Density	955 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.03 x 10^{-2} kPa at 20 °C	Measured
Water solubility	Not determined	Rapidly hydrolyses on contact with water
Hydrolysis as a Function of pH	$t_{½}$ < 4 min at 25 °C (pH 4, 7 and 9)	Measured
Partition Coefficient (n-octanol/water)	Not determined	Rapidly hydrolyses on contact with water
Adsorption/Desorption	Not determined	Rapidly hydrolyses on contact with water
Dissociation Constant	Not determined	Rapidly hydrolyses on contact with

		water
Flash Point	82 °C at 102.1 kPa	Measured
Flammability	Not measured	Does not contain any functional groups that imply flammability.
Autoignition Temperature	285 °C	Measured
Explosive Properties	Not explosive	Measured
Oxidising Properties	Not oxidising	Measured

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

Reactivity
Stable under recommended storage conditions. On contact with moisture the notified chemical readily hydrolyses to release the combustible liquid (flash point 69 °C) 2-pentanone oxime (CAS No. 623-40-5).

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia as part of high viscosity silicone sealant products at ≤ 5% concentration. It is proposed that the notified chemical may at some point in the future also be imported in neat form.

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

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

PORT OF ENTRY
Melbourne and Sydney.

IDENTITY OF MANUFACTURER/RECIPIENTS
The neat notified chemical will be manufactured in the USA.

The notified chemical will be added to the silicone sealant product by the formulator Herman Otto GmbH, Krankenhausstraße 14, 83413 Fridolfing, Germany.

TRANSPORTATION AND PACKAGING
The neat notified chemical will be imported from the USA by sea and air in 55 gallon (~208 L) steel drums and 950 kg IBC totes.

The finished silicone sealant products containing the notified chemical will be imported from Germany by air and sea in 310 mL cartridges and 400 or 580 mL aluminium foil bags.

Distribution within Australia will be by road.

USE
The notified chemical will be used as a crosslinking agent for silicone sealant and adhesive formulations. It causes silicone polymers to crosslink at room temperature in the presence of moisture, forming a rubber like-material.

OPERATION DESCRIPTION
The notified chemical will be imported into Australia as part of silicone sealant products (≤ 5%) which will be delivered to the end-user in the same form in which they are imported.

The notified chemical may at some point in the future be imported in neat form for formulation into silicone

sealant and adhesive products.

Formulation of silicone sealant and adhesive products
The notified chemical will be added to the mixing tank. Mixing will be highly automated and may occur via an open batch or closed batch continuous system, followed by automated packaging into containers of various sizes.

In the open batch process the reactor vessels and blades will be wiped of uncured sealant using mineral spirits. In the closed batch process, any cleaning of the reactor vessels will be done using brushes operated by machines to remove all residues.

Emptied drums will be collected weekly and transported to a reconditioning site. At this site drums are assessed for reconditioning potential. Drums which cannot be reconditioned will be rinsed, crushed and sent to landfill. Drums suitable for reconditioning will be rinsed with mineral spirits and the rinsate collected and distilled for recovery.

End-use
The finished silicone sealant and adhesive products containing the notified chemical at ≤ 5% concentration will be manually applied by professional applicators to joints using a cartridge gun or spatula.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

EXPOSURE DETAILS
Transport and storage
Transport and storage workers may come into contact with the notified chemical in the neat form or as a component of finished silicone sealant and adhesive products (≤ 5%) only in the event of accidental rupture of containers.

Formulation of products
Dermal and ocular exposure of workers to the neat notified chemical may occur during formulation when charging the mixing tanks and while performing maintenance and cleaning of equipment and drum reconditioning. Inhalation exposure is not expected due to the low vapour pressure of the notified chemical unless aerosols are formed. Exposure to the notified chemical will be of an average duration of ≤ 2 hours/day for 30 days a year. Exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems and through the use of personal protective equipment (PPE) such as coveralls, safety glasses and impervious gloves.

End-use
Dermal and ocular exposure to the notified chemical (at ≤ 5%) may occur when professional applicators apply the silicone sealant and adhesive products. In addition, there is potential for dermal and ocular exposure to the hydrolysis product of the notified chemical (2-pentanone oxime) released during curing. Inhalation exposure to the hydrolysis product is not expected given its low vapour pressure (3.53×10^{-2} at 25 °C) (MPBPVP v1.43; US EPA 2012). Exposure to the notified chemical and its hydrolysis product is expected to be minimised through the use of personal protective equipment (PPE) such as coveralls, safety glasses and impervious gloves including the use of respiratory protection in poorly ventilated areas.

Workers will likely make dermal contact with the silicone sealant and adhesive products after application. However, once dried and cured, the notified chemical will be reacted into the polymer matrix and will not be available for exposure.

6.1.2. Public Exposure
The finished silicone sealant and adhesive products containing the notified chemical will only be used by professional applicators and will not be sold to the public. The public may come into contact with the applied sealant and adhesive products. However, once the sealants and adhesives are cured the notified chemical will be reacted into the silicone matrix and will not be available for exposure.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical and its hydrolysis product (2-pentanone oxime) are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 1234 mg/kg bw; harmful
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation*	moderately irritating
Guinea pig, skin sensitisation –non-adjuvant test*	no evidence of sensitisation
Mouse, skin sensitisation – Local lymph node assay*	no evidence of sensitisation
Rat, combined repeat dose oral toxicity and reproduction/developmental toxicity study – 35-42 days*	NOAEL for repeat dose effects = 15 mg/kg bw/day NOAEL for reproductive and developmental effects = 150 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration	clastogenic
Genotoxicity – in vitro mammalian cell gene mutation	non genotoxic
Genotoxicity – in vivo mammalian erythrocyte micronucleus	non genotoxic

* Conducted on the hydrolysis product of the notified chemical (2-pentanone oxime).

Toxicokinetics, metabolism and distribution.

The notified chemical has a low molecular weight (< 500 Da) and rapidly hydrolyses in contact with moisture to release 2-pentanone oxime and form a siloxane polymer (half-life < 4 minute at 25°C and pH 4, 7 and 9). Due to this reaction, the notified chemical is expected to undergo hydrolysis if in contact with mucous membranes lining the respiratory system, eyes and to a lesser extent the skin. Thus effects observed in the toxicological studies are likely to be due to the hydrolysis product 2-pentanone oxime. Studies on the hydrolysis product have therefore been provided for certain endpoints instead of the notified chemical.

Acute toxicity.

The notified chemical was found to be harmful in an acute oral toxicity study conducted in rats. There were no mortalities at doses of 175 and 550 mg/kg bw but 5 animals out of 7 died at a dose of 2000 mg/kg bw. Based on this result, the LD_{50} was estimated by the study authors as 1234 mg/kg bw.

Acute dermal and inhalation toxicity data were not provided for the notified chemical. The notified chemical has a low molecular weight hence dermal absorption may occur. Given the notified chemical has also been shown to be harmful by the oral route, the potential for adverse acute effects from the notified chemical via the skin cannot be ruled out. The vapour pressure of the notified chemical is low ($\leq 1.03 \times 10^{-2}$ kPa at 20 °C) and therefore inhalation of the vapour of the notified chemical is not expected to occur under normal environmental conditions unless aerosols are formed.

Irritation and sensitisation.

The notified chemical was determined to be only slightly irritating to the skin of rabbits, with only very slight erythema noted.

Eye irritation or skin sensitisation data were not provided for the notified chemical. However, studies were provided for the hydrolysis product of the notified chemical (2-pentanone oxime).

2-Pentanone oxime was found to be moderately irritating to the eye of rabbits. Irritation effects were observed in the cornea, iris and conjunctivae that completely resolved in all test animals within 14 days. However, the severity of the effects is insufficient to warrant classification as a potential eye irritant according to the GHS and the Approved Criteria (NOHSC, 2004).

2-Pentanone oxime was found to be not a skin sensitiser in a Guinea pig non-adjuvant skin sensitisation test and when tested up to 100% concentration in a LLNA test.

Repeated Dose Toxicity and Reproduction/Developmental Toxicity
No repeated dose toxicity data were provided for the notified chemical.

In a 28-day combined repeated dose toxicity and reproduction/developmental toxicity study in rats, the hydrolysis product of the notified chemical (2-pentanone oxime) was administered by oral gavage at doses of 15, 50 or 150 mg/kg bw/day. There were no mortalities and no treatment related changes were observed by physical examination and there were no clinical signs of adverse effects on the number of implantations, litter size and offspring bodyweight.

The study showed that the test substance affects red blood cells and spleen weight and appearance at doses of 50 mg/kg bw/day and above. Haemosiderosis was observed at doses of 15 mg/kg bw/day and above as well as congestion and extramedullary haemopoiesis at higher dose levels, however the effects observed at 15 mg/kg bw/day were not considered adverse since the red blood cell count parameters were not affected. After the two-week off-dose recovery period complete recovery was seen in many parameters but was not complete for spleen weight, macroscopic and microscopic appearance. The No Observed (Adverse) Effect Level (NO(A)EL) was established as 15 mg/kg bw/day based on adverse effects to the spleen and blood chemistry and 150 mg/kg bw/day for reproductive and developmental toxicity based on no adverse effects at the maximum dose tested.

Mutagenicity/Genotoxicity.
The notified chemical was negative in a bacterial reverse mutation and an *in vitro* gene mutation study, but was positive in an *in vitro* chromosome aberration study in the presence of metabolic activation. However, it was not genotoxic *in vivo* in a mouse micronucleus test.

Health hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Acute toxicity (Category 4)	H302 - Harmful if swallowed

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase:

R22: Harmful if swallowed

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified chemical is harmful by the oral route and slightly irritating to the skin. Based on studies conducted on the hydrolysis product, the notified chemical is expected to be moderately irritating to the eyes. The notified chemical may be absorbed and has the potential to cause systemic toxicity (NOAEL 15 mg/kg bw/day). Toxicity by the inhalation route is not known. However, based on the low vapour pressure, inhalation exposure is not expected unless aerosols are formed.

During curing of the silicone sealants and adhesives, the notified chemical hydrolyses to release 2-pentanone oxime. The toxicity profile of 2-pentanone oxime is expected to be similar to that of the notified chemical. Inhalation exposure under normal environmental conditions is not expected given its low vapour pressure.

Reformulation
Based on the low NOAEL for the hydrolysis product (which is considered to reflect the systemic toxicity potential of the notified chemical), reformulation workers may be at risk of chronic toxicity effects when handling the neat notified chemical, following repeated exposure over the long term. However, provided that adequate PPE is used and engineering controls are in place to limit exposure, the risk to the health of reformulation workers is not considered to be unreasonable.

End-use
Professional applicators apply the silicone sealant and adhesive products containing the notified chemical at concentrations up to 5%. Given the low concentration in the end-use products, the risk of irritation and chronic toxicity effects is low. The expected use of PPE should further reduce these risks. Therefore, the risk to the

health of professional applicators from use of the notified chemical under the occupational settings described is not considered to be unreasonable.

6.3.2. Public Health

The public is not expected to be exposed to the notified chemical; hence, the risk to public health is not considered unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical is imported into Australia as a component in finished products (silicone sealant formulations). Accidental spills and leaks during transport are expected to be physically contained and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

No environmental release of the notified chemical is expected from the use of sealant products because of its propensity to rapidly hydrolyse. Curing of the notified chemical commences upon diffusion of air humidity into the product. The notified chemical reacts with the silicone polymer within the product to form an inert three-dimensional polymeric network and a hydrolysis product (2-pentanone oxime). This reaction consumes the entire notified chemical and is irreversible. After curing of the silicone sealant the notified chemical is bound within a polymeric matrix and therefore cannot be released into the environment. Surplus product that is left over during application of the sealant product also cures and these remains are expected be disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

Spent cartridges are expected to be disposed of to landfill. Packages that are not cleaned are expected to be disposed of according to Local, State and Territory regulations. The sealant will remain within jointed surfaces until the articles to which it is bound are disposed of to landfill or thermally decomposed if metal articles are recycled. In all cases the residual notified chemical is expected to have fully cured prior to disposal.

7.1.2. Environmental Fate

The notified chemical is not readily biodegradable. However it rapidly hydrolyses in the presence of water and hydroxyl compounds. The sealant is not expected to contain any notified chemical after curing. For the details of the environmental fate studies please refer to Appendix C.

Aquatic exposure to the notified chemical is not expected when it is used as proposed in sealant products. A small amount of sealant products may be washed to the sewerage system following spills or cleaning of residues from application equipment. In water, the notified chemical will degrade rapidly because of its hydrolytic instability and is therefore not expected to bioaccumulate. In landfill and during metal reclamation, the cured polymer matrix containing the notified chemical is expected to degrade to water and oxides of carbon, nitrogen and silicon.

When the notified chemical contacts water or humid air, a hydrolysis product is expected to form. Based on its physicochemical properties the hydrolysis product will mainly partition to the air compartment during the application and curing process where it is expected to degrade with a calculated half-life of < 48 hours (AOPWIN v1.92; US EPA 2012). Hence, the hydrolysis product will not have a significant environmental exposure.

7.1.3. Predicted Environmental Concentration (PEC)

A predicted environmental concentration was not determined because the notified chemical is not expected to persist in water due to its hydrolytic instability. Very limited aquatic exposure to the notified chemical and the hydrolysis product is expected when the notified chemical is used as proposed in sealant products. The notified chemical will be cured in a polymer matrix and will not be available to the environment.

7.2. Environmental Effects Assessment

The notified chemical rapidly hydrolyses in the presence of water and humidity in the air to form its hydrolysis product, 2-pentanone oxime. The ecotoxicity results for the hydrolysis product are acceptable in lieu of toxicity of the notified chemical as the notified chemical is expected to rapidly hydrolyse in environmental waters. The results from ecotoxicological investigations conducted on 2-pentanone oxime are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LC50 > 100 mg/L*	Not harmful to fish
Daphnia Toxicity	EC50 ≥ 100 mg/L*	Not harmful to aquatic invertebrates
Algal Toxicity	E_rC50 = 88 mg/L*	Harmful to algae
	NOEC = 32 mg/L*	

*Toxicity for the hydrolysis product of the notified chemical, 2-pentanone oxime

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) 2-pentanone oxime is considered to be harmful to algae on an acute basis. It is not considered harmful to fish or aquatic invertebrates. As the notified chemical rapidly hydrolyses to form 2-pentanone oxime, the notified chemical is formally classified under the GHS with respect to the GHS classification. Therefore, the notified chemical is formally classified under the GHS as Acute Category 3: Harmful to Aquatic Life.

7.2.1. Predicted No-Effect Concentration

Since there is expected to be very little exposure of the notified chemical or hydrolysis products to the water compartment, the PNEC was not calculated.

7.3. Environmental Risk Assessment

All spills and dried cleaning waste of the notified chemical are expected to be disposed to landfill. The majority of the notified chemical will be consumed during the polymerisation process and immobilised within a cured polymer matrix. It will not be available to the environment. 2-Pentanone oxime will mainly partition to the air compartment during the application and curing process where it is expected to degrade due to photochemical reactions. Since there is expected to be very limited exposure to aquatic organisms, the notified chemical and the hydrolysis product are therefore not expected to pose an unreasonable risk to the environment based on its assessed use pattern.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -90 °C

Method OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC. A.1 Melting/Freezing Temperature.
Remarks Determined by differential scanning calorimetry (DSC). The sample was cooled to -90 °C and heated to 300 °C at a rate of 20 °C/min. During cooling as well as during heating no effects were observed which were indicative of crystallisation or melting.
Test Facility NOTOX (2008a)

Boiling Point Decomposes at > 250 °C at 101.3 kPa

Method OECD TG 103 Boiling Point.
EC Directive 92/69/EEC. A.2 Boiling Temperature.
Remarks Determined by differential scanning calorimetry (DSC). The sample was heated from 25 °C to 400 °C at a rate of 20 °C/min. From ~250 °C the signal became exothermic indicative of decomposition. A black coloured deposit remained at the end of the experiment.
Test Facility NOTOX (2008a)

Density 955 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC. A.3 Relative density.
Remarks Pycnometer method.
Test Facility NOTOX (2008a)

Vapour Pressure 1.03 x 10^{-2} kPa at 20 °C

Method OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC. A.4 Vapour pressure.
Remarks Isothermal thermogravimetric effusion method.
Test Facility NOTOX (2008a)

Hydrolysis as a Function of pH $t_{½}$ < 4 minutes at 25 °C (pH 4, 7 and 9)

Method OECD TG 111 Hydrolysis as a Function of pH.

pH	*T (°C)*	*$t_{½}$ (minutes)*
4	25	< 4
7	25	< 4
9	25	< 4

Remarks Rapid hydrolysis was expected therefore a screening test was performed instead of the method outlined in the test guidelines. During the test, the test substance and solutions containing the test substance were kept under nitrogen and exposure to light was limited. Test substance was mixed with the buffer solutions (pH 4, 7 and 9) in separate glass vessels. Vessels were inverted 10 times and the phases were allowed to separate. A sample was taken for analysis from the organic phase at 4 minutes and 1 hour after preparation. Gas chromatography (GC) was used for quantitative analysis of the test solutions. The test substance was considered hydrolytically unstable after 4 minutes and no further testing was required.

Test Facility NOTOX (2008a)

Flash Point 82 °C at 101.3 kPa

Method EC Directive 92/69/EEC. A.9 Flash Point.
Remarks Pensky-Martens closed cup method.

Test Facility NOTOX (2008b)

Auto-ignition Temperature 285 °C

Method EC Directive 92/69/EEC. A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks The lowest temperature at which ignition occurred was 289 °C. This was rounded off to the nearest 5 °C.
Test Facility NOTOX (2008a)

Explosive Properties Not explosive

Method EC Directive 92/69/EEC. A.14 Explosive Properties.
Remarks The test substance was found to be not explosive under the thermal sensitivity and mechanical sensitivity by shock tests.
Test Facility NOTOX (2008a)

Oxidizing Properties Not oxidising

Method EC Directive 92/69/EEC. A.21 Oxidizing Properties (Liquids).
Remarks The mean pressure rise time for the reference mixture (1:1 w/w mixture of 65% w/w aqueous nitric acid and cellulose) was 7.7 seconds, while that for the test substance mixtures (1:1 w/w mixture of the test substance and cellulose) was 23.2 seconds. Since the time for the test substance mixture was much greater than that for the reference mixture, the test substance was considered to be a non-oxidiser.
Test Facility Huntingdon (2012a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 425 Acute Oral Toxicity: Up-and-Down Procedure.
Species/Strain	Rat/ Wistar strain Crl:WI (outbred, SPF-Quality), female
Vehicle	Test substance administered as supplied
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	1F	175	0/5
II	5F	550	0/5
III	7F	2000	5/7

LD50	1234 mg/kg bw
Signs of Toxicity	At 175 mg/kg: Hunched posture. At 550 mg/kg: Lethargy, hunched posture, uncoordinated movements, flat posture, slow breathing, shallow respiration, piloerection, and hypothermia. All signs of toxicity were resolved by Day 4. There were no mortalities. At 2000 mg/kg: Lethargy, hunched posture, uncoordinated movements, flat posture, slow breathing, shallow respiration, piloerection, watery discharge eye, ptosis and salivation. Five out of 7 animals died on Day 1. For the remaining two surviving animals, clinical signs of toxicity were resolved by Day 5.
Effects in Organs	There were no macroscopic abnormalities. However, the weight of the spleen for one animal dosed at 550 mg/kg was below the historical data range. Haematology for this animal showed a slight increase in red blood cells, haemoglobin and haematocrit.
Remarks - Results	The oral LD50 value of the test substance was estimated to be 1234 mg/kg bw.
CONCLUSION	The notified chemical is harmful via the oral route.
TEST FACILITY	NOTOX (2008c)

B.2. Irritation – skin

Test Substance	Notified chemical
Method	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	Until irritation no longer observed i.e. 9 days
Type of Dressing	Semi-occlusive.
Remarks - Method	Observations were made at 1, 24, 48 and 72 hours and on Days 5, 6, 7, 8 and 9 after patch removal.

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	1.0	1.0	1.0	1.0	< 9 days	0
Oedema	0.0	0.0	0.0	0.0	-	0

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

Remarks - Results: Very slight erythema was observed for all animals throughout the first 5 days persisting in two animals on Day 7 and in one on Day 8. All signs of irritation were resolved by Day 9.

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

Test Facility: Huntingdon (2012b)

B.3. Irritation – eye

TEST SUBSTANCE: 2-Pentanone oxime

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.

Species/Strain: Rabbit/New Zealand White
Number of Animals: 3
Observation Period: 14 days
Remarks - Method: Observations were made 24, 48, and 72 hours, and 7 and 14 days after exposure.

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	0.7	2.3	2.0	3	< 14 days	0
Conjunctiva: chemosis	0.3	1.3	1.3	4	< 7 days	0
Conjunctiva: discharge	0.3	1.3	1.3	4	< 7 days	0
Corneal opacity	0.0	1.0	1.0	1	< 7 days	0
Iridial inflammation	0.0	0.7	0.7	1	< 72 h	0

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

Remarks - Results: Instillation of the test substance resulted in effects in the cornea, iris and conjunctivae. The corneal injury consisted of opacity (maximum grade 1) and epithelial damage (maximum 50% of the corneal area) in two of three animals. The corneal injury had resolved within 7 days. Iridial irritation grade 1 was observed and had resolved within 24 hrs in one animal and within 72 hrs in the remaining animals. The irritation of the conjunctivae consisted of redness, chemosis and discharge. The irritation had completely resolved within 72 hrs in one animal and within 14 days in the remaining animals.

No evidence of ocular corrosion, no staining of (peri) ocular tissues, and no test substance remnants were seen. No symptoms of systemic toxicity were observed in the animals during the test period and no mortality occurred.

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

TEST FACILITY NOTOX (2007)

B.4. Skin sensitisation

TEST SUBSTANCE 2-Pentanone oxime

METHOD OECD TG 406 Skin Sensitisation – Buehler Method

Species/Strain Guinea pig/Hartley Albino
PRELIMINARY STUDY Maximum Non-irritating Concentration:
topical: 25%
MAIN STUDY
Number of Animals Test Group: 20 Control Group: 10
INDUCTION PHASE Induction Concentration:
topical: 100%
Signs of Irritation Slight erythema present in some animals in the induced group

CHALLENGE PHASE
1st challenge topical: 25%
Remarks - Method No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	25%	0/20	1/20	-	-
Control Group	25%	0/10	0/10	-	-

Remarks - Results In the test group, very faint erythema (score 0.5) was observed in one animal 24 hours after patch removal and very faint and faint erythema (score 1.0) was observed in two animals 48 hours after patch removal. No skin reactions were observed in the remaining animals.

No signs of irritation were observed in the control group.

Body weight changes were normal.

CONCLUSION There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.

TEST FACILITY MB Research Laboratories (2009)

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

TEST SUBSTANCE	2-Pentanone oxime
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay EC Directive 67/548/EEC Skin Sensitisation (Local Lymph Node Assay) EPA OPPTS 870.2600 (2003) "Skin Sensitization"
Species/Strain	Mouse/CBA strain, inbred, SPF-Quality
Vehicle	Acetone/Olive Oil (4:1 v/v)
Remarks - Method	No significant protocol deviations. α-Hexylcinnamaldehyde (HCA) was used as the positive control.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0% (vehicle control)	240	1.0
25%	357	1.5
50%	260	1.1
100%	320	1.3
Positive Control (HCA)		
0% (vehicle control)	359	1.0
5%	628	1.7
10%	1018	2.8
25%	1302	3.6

Remarks - Results	No irritation of the ears was observed in any of the animals examined. All nodes of the experimental and control groups were considered normal in size, except for one extremely enlarged node with 50% of the test substance. Slight body weight loss was noted in some animals but was not considered toxicologically significant. A stimulation index of less than 3 was observed for all concentrations of the test substance.
CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the test substance.
TEST FACILITY	NOTOX (2009)

B.6. Repeat dose toxicity

TEST SUBSTANCE	2-Pentanone oxime
METHOD	OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test.
Species/Strain	Rat/ Crl:CD(SD)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: Males: At least 5 weeks commencing 2 weeks before pairing Females: Two weeks before pairing then throughout pairing and gestation until Day 6 of lactation Recovery group: 6 weeks Dose regimen: 7 days per week

	Post-exposure observation period: 14 days
Vehicle	Corn oil
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M/10F	0	0
low dose	10M/10F	15	0
mid dose	10M/10F	50	0
high dose	5M/10F	150	0
control recovery	5M/5F	0	0
high dose recovery	5M/5F	150	0

Mortality and Time to Death

There were no test substance related mortalities during this study. One female rat from the vehicle control group was found to have a punctured oesophagus and was euthanized. This was not considered treatment related.

Clinical Observations

No treatment related changes were observed by physical examination, sensory reactivity assessment or motor skills. There were no adverse bodyweight or food consumption effects in either males or females before or after mating, during lactation or during recovery. Parameters included to investigate the reproductive and developmental toxic potential of the test substance showed that there were no clinical signs of adverse effects on the number of implantations, litter size and offspring bodyweight.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Anaemia was detected by haematology and blood chemistry examination. Red blood cell (RBC) counts were reduced and reticulocytes increased in the 50 and 150 mg/kg bw/day treatment groups. High platelet levels were also observed in all animals at the 150 mg/kg bw/day treatment group. Blood chemistry showed high bilirubin for all animals at 50 and 150 mg/kg bw/day. Total protein was low for males in the 50 and 150 mg/kg bw/day groups with albumin also being low at 150 mg/kg bw/day. After the 14-day recovery period many of the haematology parameters noted to be abnormal had recovered.

Effects in Organs

Spleen

Anaemia was detected by organ weight assessment, macroscopic and microscopic examination. Adjusted mean spleen weight was high in all animals in the 150 mg/kg bw/day treatment group as well as three males in the 50 mg/kg bw/day treatment group. Dark colouration of the spleen was noted for all animals treated at 150 mg/kg bw/day and the majority of animals treated at 50 mg/kg bw/day as well as one male treated at 15 mg/kg bw/day. Histopathalogical examination of the spleen showed haemosiderosis and congestion in all animals in the 50 and 150 mg/kg bw/day treatments. An increase in extramedullary haemopoiesis was observed in males and females treated at 150 mg/kg bw/day. Mean adjusted spleen weights were higher than control groups for all animals receiving 50 or 150 mg/kg bw/day treatment.

After 14 days recovery the spleen weights were still higher than control animals for the 150 mg/kg bw/day group though this was deemed not to be statistically significant for the females. Additionally, an increase in haemosiderosis and reduction in congestion were observed in the spleens of all animals which had been previously treated with 150 mg/kg bw/day as well as complete recovery from extramedullary haemopoiesis.
Haemosiderosis was also observed in some animals treated at 15 mg/kg bw/day but was considered non-adverse since no RBC parameters were affected.

Kidneys
Dark colouration of the kidneys was observed in females treated at 50 or 150 mg/kg bw/day. After the 14-day recovery period the kidney weights of test substance treated males were higher than controls. Pigmentation was observed in the cortical tubules of the kidneys of some males and one female treated at 150 mg/kg bw/day. As there was no evidence of kidney damage by clinical pathology or histopathology these changes were not considered to be adverse.

Liver
Minimal extramedullary haemopoiesis was observed in the liver of males and females treated at 50 and 150 mg/kg bw/day. This was considered to be a secondary response to changes in the spleen.

Heart
Slightly high adjusted mean heart weights were observed in females receiving 150 mg/kg bw/day.

Remarks – Results
The data show that the test substance affects red blood cells and spleen weight and appearance at doses of 50 mg/kg bw/day and above. Haemosiderosis was observed at doses of 15 mg/kg bw/day and above as well as congestion and extramedullary haemopoiesis at higher dose levels, however the effects observed at 15 mg/kg bw/day were not considered adverse. After the two-week off-dose recovery period complete recovery was seen in many parameters but was not complete for spleen weight, macroscopic and microscopic appearance. No adverse effects were seen on the reproductive/ developmental screening parameters at any dose level.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 15 mg/kg bw/day for general systemic toxicity based on adverse effects to the spleen and blood chemistry and 150 mg/kg bw/day for reproductive and developmental toxicity based on no adverse effects at the maximum dose tested.

TEST FACILITY Huntingdon (2012d)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure (Test 1) and Pre incubation procedure (Test 2)

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	Liver preparations (S9 mix) from rats treated with phenobarbital and 5,6-benzoflavone
Concentration Range in Main Test	a) With metabolic activation: 5-5000 µg/plate b) Without metabolic activation: 5-5000 µg/plate
Vehicle	DMSO
Remarks - Method	Aliquots of 0.1 ml of either test substance, positive, or negative control solution was used at seven concentrations up to 5000µg/plate. The negative control was DMSO and positive controls were sodium azide, 9-aminoacridine, 2-nitrofluorene, and 4-nitroquinoline-1-oxide in the absence of S9 mix and 2-aminoanthracene and benzo[a]pyrene in the presence of S9 mix.

RESULTS

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

Test 2	> 5000	> 5000	> 5000	negative
Present				
Test 1	> 5000	> 5000	> 5000	negative
Test 2	> 5000	> 5000	> 5000	negative

Remarks - Results

The test substance was tested up to the maximum recommended dose level of 5000 µg/plate. No toxicologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation.

All the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

CONCLUSION

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

TEST FACILITY

Huntingdon (2009)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 473 In vitro Mammalian Chromosome Aberration Test.

Cell Type/Cell Line: Human lymphocytes
Metabolic Activation System: Phenobarbital/5,6-benzoflavone, rat liver S9
Vehicle: DMSO
Remarks - Method: The positive controls used in the study were Mitocycin C (without metabolic activation) and Cyclophosphamide (with metabolic activation).

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	250, 500*, 1000, 2000, 2250*, 2500, 2750, 3000*, 3250, 3435.5	3	21
Present			
Test 1	250*, 500, 1000, 2000, 2250, 2500, 2750, 3000, 3250*, 3435.5*	3	21

*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	≥ 3435.50			
Test 1		≥ 3000	≥ 1000	negative
Present	≥ 3435.50			
Test 1		> 3435.50	≥ 500	positive

Remarks - Results

In the absence of metabolic activation, the test substance caused a reduction in the mitotic index to 50% of the vehicle control at 3000 µg/mL. In the presence of metabolic activation, the test substance caused a reduction in the mitotic index to 76% of the vehicle control at 3435.50 µg/mL.

In the absence of metabolic activation, there were no statistically significant increases in chromosomal aberrations at any concentration. In the presence of metabolic activation, there were statistically significant increases in chromosomal aberrations at a test substance concentration of

3250 and 3435.5 µg/mL. No statistically significant increases were observed at the lowest tested concentration of 250 µg/mL.

No statistically significant increases in the proportion of polyploid cells were observed during metaphase analysis.

The positive controls caused statistically significant increases in the proportion of aberrant cells, demonstrating the sensitivity of the test system and the efficacy of the S9 mix.

CONCLUSION The notified chemical was clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY Huntingdon (2012e)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 476 In vitro Mammalian Cell Gene Mutation Test.
EC Directive 2000/32/EC B.17 Mutagenicity - In vitro Mammalian Cell Gene Mutation Test.

Species/Strain	Mouse
Cell Type/Cell Line	Mouse/ L5178Y lymphoma cells
Metabolic Activation System	Phenobarbital/5,6-benzoflavone, rat liver S9
Vehicle	DMSO
Remarks - Method	Methyl methanesulphonate (without metabolic activation) and benzo[a]pyrene (with metabolic activation) were used concurrently as the positive controls.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection time*
Absent				
Test 1	200*, 1500, 2000, 2500*, 3000*, 3435.5*	3 h	48 h	10-14 days
Test 2	200*, 400, 800*, 1000, 1250*, 1500, 1750*, 2000	24 h	48 h	10-14 days
Present				
Test 1	200*, 1500, 2000, 2500*, 3000, 3435.5*	3 h	48 h	10-14 days

* Cultures assessed for determination of mutant phenotype

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 3435.5	≥ 2500	> 3435.5	negative
Test 2	≥ 1717.75	≥ 1250	> 2000	negative
Present				
Test 1	≥ 3435.5	≥ 3435.5	> 3435.5	negative

Remarks - Results The test substance did not induce any statistically significant increases in the mutant frequency at any tested concentration in each exposure group with and without metabolic activation.

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

CONCLUSION The notified chemical was not genotoxic to mouse lymphoma cells treated in vitro under the conditions of the test.

TEST FACILITY Huntingdon (2012f)

B.10. Genotoxicity – in vivo

TEST SUBSTANCE Notified chemical

METHOD OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
EC Directive 2000/32/EC B.12 Mutagenicity - Mammalian Erythrocyte Micronucleus Test.

Species/Strain Rat/Crl:CD(SD)
Route of Administration Oral – gavage
Vehicle Corn oil
Remarks - Method No significant protocol deviations.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	6M	0	48
II (low dose)	6M	125	48
III (mid dose)	6M	250	48
IV (high dose)	8M	500	48
V (positive control, CP)	5M	20	24

CP=cyclophosphamide.

RESULTS

Doses Producing Toxicity There were no mortalities during the period of the study.

In preliminary toxicity tests males and females dosed at 1000 mg/kg bw/day showed severe clinical signs of toxicity and were euthanised after 1-2.5 hours. Animals dosed at 500 mg/kg bw/day showed clinical signs of toxicity including unsteady gait, piloerection, underactive behaviours and hunched posture. All animals at this dose survived until scheduled termination on Day 3.

In the main test no clinical signs were observed for the vehicle control, positive control or at 125 mg/kg bw/day test substance. At 250 mg/kg bw/day underactive behaviours, piloerection and unsteady gait were observed. At 500 mg/kg bw/day underactive behaviours, piloerection, unsteady gait, hindlimbs splayed, rales/noisy breathing and hunched posture were observed. Bodyweight loss of 15% was observed in one male dosed at 500 mg/kg bw/day as well as a small weight loss in another male in the same group.

Genotoxic Effects The test substance did not cause any statistically significant increases in the number of micronucleated polychromatic erythrocytes or normachromatic erythrocytes. No statistically significant decrease in the proportion of polychromatic erythrocytes was observed, demonstrating that the test substance was not cytotoxic to the bone marrow.

There was a statistically significant increase in the number of micronucleated cells in the positive control group, as compared to the vehicle control group, thus validating the conduct of assay.

CONCLUSION The notified chemical was not clastogenic under the conditions of this *in vivo* micronucleus test.

TEST FACILITY Huntingdon (2012g)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	CO_2 production
Remarks - Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	0	7	53
14	0	14	69
28	1	28	73

Remarks - Results	All relevant test validity criteria were met. The notified chemical rapidly hydrolyses in the presence of water and hydroxyl compounds. However, the hydrolysis products did not readily biodegrade. A toxicity control showed that the test substance was not inhibitory to microbial activity.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	NOTOX (2008d)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	2-Pentanone oxime
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Static.
Species	*Oncorhynchus mykiss*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	46.3 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks – Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	< 5	10	0	0	0	0	0
100	102	10	0	0	0	0	0

LC50	> 100 mg/L at 96 hours.
NOEC	100 mg/L at 96 hours.
Remarks – Results	All relevant test validity criteria were met.

CONCLUSION	The hydrolysis product of the notified chemcial, 2-Pentanone oxime, and by inference the notified chemical, is not harmful to fish.
TEST FACILITY	Brixham (2011)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	2-pentanone oxime
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test - Static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	251.3 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	< 0.30	4 × 5	0	1
100	99	4 × 5	0	0

EC50	> 100 mg/L at 24 hours ≥ 100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks - Results	All relevant test validity criteria were met. *D. magna* showed symptoms of toxicity apart from immobility in the presence of the test substance. At 48 hours, a proportion of the *D. magna* were floating on the meniscus of the water. However, they were fully mobile. A total of six *D. magna* were affected.
CONCLUSION	The hydrolysis product of the notified chemcial, 2-Pentanone oxime, and by inference the notified chemical, is not harmful to aquatic invertebrates.
TEST FACILITY	Brixham (2009a)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	2-pentanone oxime
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 0, 5.6, 10, 18, 32, 56, 100 mg/L Actual: < 0.3, < 0.3, 10, 18, 31, 56, 92 mg/L
Auxiliary Solvent	None
Water Hardness	Not determined
Analytical Monitoring	HPLC
Remarks - Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Biomass		*Growth*	
E_yC50	*NOEC*	*E_rC50*	*NOEC*

mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
50	32	88	32

Remarks - Results	All relevant test validity criteria were met.
CONCLUSION	The hydrolysis product of the notified chemcial, 2-Pentanone oxime, and by inference the notified chemical, is harmful to algae.
TEST FACILITY	Brixham (2009b)

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