File No: STD/1396

July 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

H-MI Ammonium Salt

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 inquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Hewlett Packard Australia Pty Ltd (ABN: 74 004 394 763)
33 Burwood Highway
Forest Hill
VIC 3131

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, analytical data, degree of purity, non-hazardous impurities, use details, import volume, site of manufacture/reformulation and identity of manufacturer/recipients.

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU, US, Korea, China

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
CC643Series Tri-color inkjet cartridge

OTHER NAME(S)
H-MI Ammonium Salt
MB-1
Magenta H-MI

MOLECULAR WEIGHT
Mn Value >500 Da

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

3. COMPOSITION ALL

DEGREE OF PURITY >90%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS None

ADDITIVES/ADJUVANTS None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Dark red solid

Property	Value	Data Source/Justification
Melting Point	Decomposed from approximately 243°C at 102.8 kPa	Measured
Boiling Point	Not determined	Decomposed prior to melting
Relative Density	1.41 at 21°C	Measured
Vapour Pressure	3.1 x 10^{-13} kPa at 25°C	Measured
Surface Tension	70.0 mN/m at 21.2±0.5°C	Measured
Water Solubility	≤ 300 g/L at 20°C	Measured
Hydrolysis as a Function of pH	$t_{1/2}$ > 1 year at 25°C	Measured
Partition Coefficient (n-octanol/water)	log Kow = -3.51 at 21°C	Measured
Adsorption/Desorption	log K_{oc} < 1.25 at 30°C	Measured
Dissociation Constant	Not determined	The notified chemical is a salt and is expected to be dissociated at environmental pH (4 -9).
Particle Size	Inhalable fraction (<100 μm): 34.8% Respirable fraction (≤10 μm): 0.43%	Measured
Flash Point	Not determined	The notified chemical is a solid.
Flammability (Solid)	Not highly flammable.	Measured
Autoignition Temperature	395°C	Measured
Oxidising properties	Unlikely to have oxidising properties	Based on the chemical structure of the notified chemical.
Explosive Properties	Not likely to be explosive	Based on the chemical structure 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 environmental conditions.

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 as a dye component (<10%) in inkjet printer inks.

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

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

PORT OF ENTRY
Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Recipients are located in Victoria.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a dye component in inkjet printer inks, primarily by air but may be

by sea as well. The ink containing the notified chemical will be contained within a sealed plastic inkjet cartridge, which is further wrapped within a foil pouch and held within a cardboard box.

USE
Dye component for inkjet printer inks.

OPERATION DESCRIPTION
The notified chemical will be imported as a dye component (<10% of notified chemical) in inkjet printer inks, sealed within a cartridge. There will not be any processing or reformulation of the notified chemical in Australia. The cartridges (inks) containing the notified chemical will be used mostly in consumer and small business printers in closed systems.

The ink cartridge will fit directly into the printing machine and the ink cartridge is designed not to allow release of ink containing the notified chemical except during printing operation. Printing will be mostly a closed process. The cartridge containing the ink will be installed and/or replaced by service technicians, office workers, and the general public.

The ink containing the notified chemical will be printed on typical media such as plain paper, glossy paper, photo paper, and various coated media. The inks containing these dyes are not intended for commercial printing or for the large format media that would accompany those applications.

Approximately 80% of the imported notified chemical is expected to be used in inkjet cartridges supplied to the public whilst the remaining 20% is expected to be used by office/commercial enterprises.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Transport and storage	Unknown	-	Each working day
Office workers (change of ink cartridge)	Unknown	~ 5 mins during handling	Each working day
Service and maintenance engineers	Unknown	~ 5-10 mins	During routine maintenance

EXPOSURE DETAILS
Exposure to the notified chemical during the importation, transport and storage of the printer cartridges is not expected, except in the unlikely event of an accident where the cartridge and its packaging may be breached.

Both office workers and service technicians may be exposed (dermal or ocular) to the notified chemical in inks (< 10% concentration) while changing printer cartridges, and service technicians may additionally be exposed during printer maintenance. Dermal exposure to small quantities of the notified chemical may occur if the print heads are touched while replacing the cartridges. In addition, dermal and possibly ocular exposure could occur when handling faulty or ruptured cartridges. Exposure during handling and cleaning of printer components is likely to be limited to the fingertips. Therefore, the exposure of these workers is expected to be minimal and infrequent.

Dermal exposure of workers may also occur when handling printed media before the ink is adequately dried, especially when printing on non-absorbent materials. Dermal exposure of office workers to the notified chemical from dried inks on printed paper is expected to be minimal, as the dye will be largely bound to the paper within the matrix of the dried ink.

6.1.2. Public exposure

The exposure of the public to the notified chemical in inkjet printer inks is expected to be identical to, or of a lesser extent than, that experienced by office workers using the same ink.

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 >2000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Human epidermis in vitro skin model	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOEL = 30 mg/kg bw/day NOAEL= 1000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity–in vitro-Chinees Hamster CHL/IU Cells	non genotoxic

Toxicokinetics, metabolism and distribution.

No data were available to assess toxicokinetics, metabolism and distribution of the notified chemical. Although dermal absorption may occur due to low log Kow, higher molecular weight (>500) may be a limiting factor in dermal absorption.

Acute toxicity.

As the acute oral LD50 was >2000 mg/kg bw in rats, the notified chemical was considered to be of low toxicity via the oral route.

Acute dermal and inhalation toxicity studies have not been submitted on the notified chemical. With respect to acute dermal toxicity study, absorption through the skin barrier of compounds with a molecular weight above 500 Da is expected to be low. As such, an acute dermal toxicity study was not considered necessary for the risk assessment. With respect to acute inhalation toxicity study, based on formulation, use scenario and packaging, inhalation exposure is not expected to be significant. Therefore, an acute inhalation toxicity study was not considered necessary for the risk assessment.

Irritation and Sensitisation:

Based on human epidermis in vitro skin model and in vivo skin irritation study in rabbit, the notified chemical was not irritating to the skin. The notified chemical was slightly irritating to the eyes of rabbit and was not a skin sensitiser in guinea pigs.

Repeated Dose Toxicity (sub acute, sub chronic, chronic).

In an oral repeat dose toxicity study in rats, the notified chemical was administered orally by gavage once daily (7 days/week) for 28 days at 0, 30, 300 or 1000 mg/kg bw/day. A recovery group of the high dose group was also observed for 14 days after the termination of the main study.

The only significant clinical observation noted was an increase in water consumption in non-recovery 1000 mg/kg bw/day males from week 3 onwards and recovery 1000 mg/kg bw/day males up to and including week 5. Females from this treatment group showed an increase in water consumption during weeks 3 and 4. This effect could have been due to the oral administration of an unpleasant tasting and/or irritant test material formulation. No such effect was detected in animals of either sex treated with 30 and 300 mg/kg bw/day or recovery 1000 mg/kg bw/day females.

There were no toxicologically significant changes in organ weight measurement and macroscopic examination of the tissues. Histopathological examination of the tissues showed that main changes were only noticed in stomach. These included agglomeration of secretion, mucous cell hypertrophy/hyperplasia, mucosal basophilia, and acanthosis/hyperkeratosis of the limiting ridge in animals of either sex treated with 1000 mg/kg/day or 300 mg/kg/day. These changes were considered to have generally regressed among recovery animals of either sex treated with 1000 mg/kg bw/day following an additional fourteen days without treatment, although two 1000 mg/kg bw/day males had residual changes.

The changes identified at 1000 mg/kg bw/day were isolated increased salivation, increased water consumption and histopathological changes in the stomach. These changes were considered adaptive and not to represent 'serious damage' to health. Histopathological changes noted in stomach at 1000 mg/kg bw/day were also observed in rats at 300 mg/kg bw/day but to a lesser degree. There were no toxicologically significant effects at 30 mg/kg bw/day.

The No Observed Adverse Effect Level (NOAEL) was established as 1000 mg/kg bw/day in this study, based on lack of adverse effect at this dose level. The No Observed Effect Level (NOEL) was established as 30 mg/kg bw/day in this study, based on lack of treatment-related effects at this dose level.

Mutagenicity:
The notified chemical was found to be negative in a bacterial reverse mutation test, and also showed no evidence of clastogenicity in a Mammalian Chromosome Aberration Test, using Chinese Hamster Lung (CHL/IU) Cells. Based on these results, the notified chemical is not expected to be genotoxic

Carcinogenicity:
No data were available to assess the potentials for carcinogenicity.

Toxicity for reproduction:
No data were available to assess the potentials for toxicity for reproduction.

Health hazard classification
Based on the submitted data, the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the submitted toxicology data, the primary concern for workers using the notified chemical is the possibility for slight eye irritation. However, the risk of eye exposure to office workers and service technicians is extremely low given that the inkjet printer inks, sealed within a cartridge packaging, and printing process is unlikely to lead to ocular exposure to the ink. In addition, the low concentration of the notified chemical within the ink (< 10%) further reduces the risk of potential eye irritation from exposure.

Office staff and service technicians may experience dermal exposure when replacing spent cartridges, clearing paper jams or during maintenance and servicing, but the notified chemical is neither a skin irritant nor a skin sensitiser and direct exposure to the notified chemical is unlikely as it binds to the paper when dried.

Overall the notified chemical is not considered to pose an unreasonable risk to workers, based on the expected minimal exposure.

6.3.2. Public Health
The exposure and hazard of the notified chemical to the members of the public during the use of in inkjet printer inks, sealed within a cartridge, are expected to be identical or similar to that experienced by office workers. Therefore, the notified chemical is not considered to pose an unreasonable risk to the public if the ink cartridges are used as intended.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical is a component of ink and will be imported into Australia in ready-to-use sealed printing cartridges for home or office inkjet printers. No manufacturing, reformulation or repackaging of the notified chemical will take place in Australia. Environmental release of the notified chemical is unlikely to occur during importation, storage and transportation as containers are designed to minimise release. In the event of an accidental spill the ink containing the notified chemical will be absorbed with inert material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be contained in ink cartridges and it is expected that <1% of the annual import volume of the notified chemical may be spilt. If leakage or spillage does occur, the ink will be physically contained with absorbent material and disposed of to landfill. The ink cartridges will be contained within the printer until the contents are consumed. The empty cartridges, estimated to contain <1% of the annual import volume of notified chemical, will be removed and disposed of to landfill or sent for recycling.

RELEASE OF CHEMICAL FROM DISPOSAL

Most of the notified chemical will be bound to printed paper and, once the ink has dried, will be contained in an inert matrix. It is assumed that 50% of the waste paper will end up in landfill and the rest will undergo paper recycling processes. During recycling processes, waste paper is repulped using a variety of chemical agents which, amongst other things, enhance detachment of ink from the fibres. The notified chemical may partition to the supernatant water, due to its high water solubility, which is released to the sewer. Notified chemical in the sludge generated during the recycling process will be sent to landfill for disposal.

7.1.2. Environmental Fate

The majority of the notified chemical will be bound to paper, of which half is assumed to be recycled. During the paper recycling process, waste paper is repulped using a variety of alkaline, dispersing and wetting agents, water emulsifiable organic solvents and bleaches. Some of the ink in the recycled paper may partition to sludge and will therefore be disposed of to landfill. However, due to the high water solubility of the notified chemical, a greater proportion can be expected to remain in the aqueous phase released to the sewer. The notified chemical is not readily or inherently biodegradable, however, its potential for bioaccumulation was found to be low in exposed aquatic organisms.

In landfill, notified chemical in sludge may leach due to its high water solubility. However, the notified chemical is likely to remain in the ink matrix bound to paper that is disposed of to landfill. The notified chemical is expected to slowly degrade through biotic and abiotic processes to form water, oxides of carbon, nitrogen and sulfur.

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

7.1.3. Predicted Environmental Concentration (PEC)

A predicted environmental concentration (PEC) worst case scenario has been calculated on the assumptions that 50% of the annual import of the notified chemical is released to the sewer as de-inking aqueous wastes from paper recycling over 260 days/year, with no removal of the notified chemical by sewage treatment plant (STP) processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	50%	
Annual quantity of chemical released to sewer	500	kg/year
Days per year where release occurs	260	days/year
Daily chemical release:	1.92	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.45	µg/L
PEC - Ocean:	0.05	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.454 µg/L may potentially result in a soil concentration of approximately 3.029 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 15.15 µg /kg and 30.29 µg /kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (96 h)	LC50 > 100 mg/L	Not harmful
Daphnia Toxicity (48 h)	EC50 > 100 mg/L	Not harmful
Algal Toxicity (72 h)	E_rC50 > 100 mg/L	Not harmful
Inhibition of Bacterial Respiration (3 h)	IC50 > 1000 mg/L	Does not inhibit microbial respiration

Under the Globally Harmonised System of Classification and Labelling of Chemicals (United Nations, 2009) the notified chemical is not classified for acute hazard. Based on the acute toxicity data and biodegradation studies, the notified chemical is not classified for long-term hazard.

7.2.1. Predicted No-Effect Concentration

The minimum ecotoxicity endpoint for fish, daphnia and algae was identical (100 mg/L). The predicted no-effect concentration (PNEC) was therefore calculated with this endpoint, and an assessment factor of 100, as the endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 fish, EC50 daphnia and algae	100	mg/L
Assessment Factor	100	
PNEC:	1000	µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	*Q*
Q - River:	0.45	1000	1×10^{-3}
Q - Ocean:	0.05	1000	1×10^{-4}

The concentration of the notified chemical in surface waters is expected to be very low based on the reported use pattern and the maximum import volume. It is not expected to bioaccumulate, based on its high water solubility and low partition coefficient. As the risk quotients are well below 1, the notified chemical is not expected to pose an unreasonable risk to the aquatic environment.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

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

Human health risk assessment

Under the conditions of the occupational settings described, 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 PEC/PNEC ratio and the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  - Avoid contact with eyes;
  - Printers should be located in well-ventilated areas.

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

- Service personnel should wear cotton or disposable gloves and ensure adequate ventilation is present when removing spent inkjet printer inks cartridges containing the notified chemical and during routine maintenance and repairs.

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

- If products and mixtures containing the notified chemical/polymer 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(2) of the Act; if
- the function or use of the chemical has changed from a dye component for inkjet printer inks contained within sealed cartridges, or is likely to change significantly;
- the amount of chemical being introduced has increased from one tonne/annum, 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.

No additional secondary notification conditions are stipulated.

Material Safety Data Sheet
The MSDS of the product containing 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 Decomposed from approximately 243ºC at 102.8 kPa

Method EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks The test material has been determined to decompose from approximately 243ºC at 102.8 kPa. Therefore, no value for melting temperature could be determined by using differential scanning calorimetry.
Test Facility Harlan Laboratories Ltd (2009a)

Relative Density 1.41 at 21.0±0.5ºC

Method EC Directive 92/69/EEC A.3 Relative Density.
Remarks Determined using a pycnometer at 21ºC
Test Facility Harlan Laboratories Ltd (2009a)

Vapour Pressure 3.1×10^{-13} kPa at 25ºC

Method EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Determined using a vapour pressure balance
Test Facility Harlan Laboratories Ltd (2009b)

Water Solubility ≤ 300 g/L at 20°C

Method OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method. It was not possible to prepare samples at 5 times saturation level, as recommended in the guideline, due to the formation of highly viscous samples. Hence water solubility was estimated based on visual inspection.
Test Facility Harlan Laboratories Ltd (2009a)

Hydrolysis as a Function of pH $t_{1/2}$ > 1 year at 25°C, pH 4-9

Method OECD TG 111 Hydrolysis as a Function of pH.
EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH.

pH	*T (°C)*	*$t_{½}$*
4	25	>1 year
7	25	>1 year
9	25	>1 year

Remarks Less than 10% hydrolysis was observed after 5 days at 50°C at pH 4, 7, and 9. Therefore, the test material is considered stable with a half life greater than 1 year at 25°C.
Test Facility Harlan Laboratories Ltd (2009a)

Partition Coefficient (n-octanol/water) log Kow = -3.51.at 21°C

Method EC No 440/2008, Method A8, Partition Coefficient
Remarks Shake flask method. The test material concentration was determined by HPLC.
Test Facility Harlan Laboratories Ltd (2009a)

Adsorption/Desorption log K_{oc} < 1.25 at 30°C

Method OECD TG 121: Estimation of the Adsorption Coefficient (Koc) on Soil and Sewage Sludge using High Performance Liquid Chromatography
Remarks HPLC Method. The adsorption coefficient was determined by extrapolation from a calibration curve constructed from known standards (log K_{oc} range 1.25-5.63) in accordance with the guidelines above. Testing was conducted at pH 7.

Test Facility Harlan Laboratories Ltd (2009a)

Particle Size

Method OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.

Range (μm)	*Mass (%)*
<100	34.8
<10.0	≤0.43
<5.5	≤0.16

Remarks Two few particles were of a size less than 10.0 μm to allow accurate assessment of mass median aerodynamic diameter.
Test Facility Harlan Laboratories Ltd (2009a)

Flammability (Solids) Not highly flammable.

Method EC Directive 92/69/EEC A.10 Flammability (Solids).
Test Facility Harlan Laboratories Ltd (2009b)

Autoignition temperature 395°C

Method EC Directive 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Test Facility Harlan Laboratories Ltd (2009b)

Surface Tension 70.0 mN/m at 21.2±0.5°C

Method EC Directive 92/69/EEC A.5 Surface Tension.
Remarks Concentration: 1.05 g/L
Test Facility Harlan Laboratories Ltd (2009a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical (>90%)

METHOD: OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure.
EC Directive 92/69/EEC B.1 bis Acute toxicity (oral) fixed dose method.

Species/Strain: Rat/ Wistar
Vehicle: Arachis oil BP
Remarks - Method: No deviations from the protocol.
Following a sighting test at dose levels of 300 and 2000 mg/kg bw, a further group of four fasted females were given a single oral (gavage) dose of test substance at a dose level of 2000 mg/kg bw.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1 F	300	0
2	1 F	2000	0
3	4 F	2000	0

LD50: > 2000 mg/kg bw
Signs of Toxicity: No signs of systemic toxicity were noted during the observation period. Faeces stained red was noted one and two days after dosing.
Effects in Organs: No abnormalities were noted at necropsy.
Remarks - Results: The animals showed expected gains in bodyweight over the observation period.

CONCLUSION: The notified chemical is of low toxicity via the oral route.

TEST FACILITY: Harlan Laboratories Ltd (2009c)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical (>90%)

METHOD: Evaluation of Skin Irritation Potential using the EPISKIN™ Reconstituted Human Epidermis Model. The principle of the assay is based on the measurement of cytotoxicity in reconstituted human epidermal cultures following topical exposure to the test material.

Vehicle: None
Remarks - Method: Phosphate Buffered Saline (PBS) was used as the negative control and Sodium Dodecyl Sulphate (SDS) as the positive control.
Triplicate tissues were treated with the test material for an exposure period of 15 minutes and after which, each tissue was rinsed before incubating for approximately 42 hours. At the end of 42 hours incubation period, the maintenance medium from beneath each tissue was collected for possible inflammatory mediator determination.
For MTT loading, the tissues were transferred to the MTT filled wells and incubated for 3 hours before being transferred to micro tubes containing acidified isopropanol for extraction of formazan crystals out of the MTT loaded tissues. At the end of the formazan extraction, each tube was mixed thoroughly and duplicate 200 µl samples were transferred to the appropriate wells of a 96-well plate for the measurement of optical density at 540 nm. Data are presented in the form of % viability (MTT reduction in the test material treated tissue relative to negative control tissues).

RESULTS

Substance	OD_{540} of tissues	Mean OD_{540} of triplicate tissues	± SD of OD_{540}	Relative individual tissue viability %	Relative mean % viability	± SD of % viability
Negative Control	0.758 0.753 0.798	0.770	0.025	98.4 97.8 103.6	100*	3.19
Negative Control	0.045 0.033 0.097	0.058	0.034	5.8 4.3 12.6	7.6	4.42
Test substance	0.803 0.782 0.785	0.790	0.011	104.3 101.6 101.9	102.6	1.48

*The mean viability of the negative control tissues is set as 100%.

Remarks - Results

The relative mean viability of the test substance treated tissues was 102.6% after a 15-minute exposure.
Following the 15-minute exposure the test substance treated tissues appeared blue which was considered indicative of viable tissue.
The relative mean tissues viability for the positive control treated tissues was ≤ 40% relative to the negative control treated tissues and the Standard Deviation (SD) value of the % viability was ≤ 20%. The positive control acceptance criterion was therefore satisfied.
The mean OD_{540} for the negative control treated tissues was ≥ 0.6 and the SD value of the % viability was ≤ 20%. The negative control acceptance criterion was therefore satisfied.

CONCLUSION

The notified chemical is non-irritating to the skin.

TEST FACILITY

Harlan Laboratories Ltd (2009d)

B.3. Irritation – skin

TEST SUBSTANCE

Notified chemical (>90%)

METHOD

OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive No. 440/2008 B.4 Acute Toxicity (Skin Irritation)

Species/Strain: Rabbit/New Zealand White
Number of Animals: 2 M
Vehicle: Moistened with distilled water
Observation Period: 72 hours
Type of Dressing: Semi-occlusive.
Remarks - Method: No deviations from the protocol.
Only two rabbits were used for the study.

RESULTS

Lesion	*Mean Score* Animal No.*		*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2			
Erythema/Eschar	0 (STA)	0 (STA)	0 (STA)	0 (STA)	0 (STA)
Oedema	0	0	0	0	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.
STA = red-coloured staining of the skin.

Remarks - Results

No evidence of skin irritation was noted during the study. Red-coloured-staining was noted at the treatment sites of both animals throughout the study.

All animals showed expected gains in bodyweight during the study.

CONCLUSION The notified chemical is non-irritating to the skin.

TEST FACILITY Harlan Laboratories Ltd (2009e)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical (>90%)

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive No. 440/2008 B.5 Acute Toxicity (Eye Irritation).

Species/Strain	Rabbit/New Zealand White
Number of Animals	2 M
Observation Period	7 days
Remarks - Method	No deviations from the protocol. Only two rabbits were used for the study.

RESULTS

Lesion	*Mean Score* Animal No.*		*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2			
Conjunctiva: redness	0.33	1.67	2	< 7 days	0
Conjunctiva: chemosis	0	0.67	1	< 72 hrs	0
Conjunctiva: discharge	0	0.33	1	< 48 hrs	0
Corneal opacity	0	0.33	1	< 72 hrs	0
Iridial inflammation	0	0	0	0	0

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

Remarks - Results Red colour staining of the fur was noted around the treated eye throughout the study.
All animal showed expected gain in bodyweight during the study.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Harlan Laboratories Ltd (2009f)

B.5. Repeat dose toxicity

TEST SUBSTANCE Notified chemical (>90%)

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).
USA EPA Health Effects Test Guidelines, OPPTS 870.3050 Repeated Dose 28-Day Oral Toxicity Study in Rodents, July 2000.
The Japanese Ministry of Economy Trade and Industry (METI), Ministry of Health, Labour and Welfare (MHLW) and Ministry of the Environment (MOE) Guidelines of 21 November 2003 for a twenty-eight day repeat dose oral toxicity study.

Species/Strain	Rat/Wistar Han:HsdRccHan:WIST
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	Distilled water
Remarks - Method	No significant deviation from test protocol. A 14-day preliminary repeated-dose oral toxicity study was carried out in three male and 3 female rats at three doses of 250, 500 or 1,000 mg/kg bw/day. A reduction in body weight gain was detected in animals of

either sex treated with 1000 mg/kg bw/day. No such effects were detected in animals of either sex treated with 250 or 500 mg/kg bw/day. Therefore, high dose level at 1,000 mg/kg bw and two lower doses at 300 and 30 mg/kg bw/day were set for the main study. Recovery groups were prepared in the 1,000 mg/kg bw/day and vehicle control groups and they were sacrificed after 14-day treatment-free recovery period. Functional observations including behavioural assessment, functional performance tests, sensory reactivity assessments, were also performed during on some occasion during the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
Control	5/sex	0	0
Low dose	5/sex	30	0
Mid dose	5/sex	300	0
High dose	5/sex	1000	0
Control recovery	5/sex	0	0
High dose recovery	5/sex	1000	0

Mortality and Time to Death

There were no deaths during the study.

Clinical Observations

An isolated episode of increased salivation was observed in one animal of either sex treated with 1000 mg/kg bw/day. No such effect was noted in animals of either sex treated with 30 or 300 mg/kg bw/day. No treatment-related effect on food consumption and body weight changes was detected for treated animals, in comparison to control animals.

An increase in water consumption was seen in non-recovery 1000 mg/kg bw/day males from week 3 onwards and recovery 1000 mg/kg bw/day males up to and including week 5. Females from this treatment group showed an increase in water consumption during weeks 3 and 4. No such effect was detected in animals of either sex treated with 30 and 300 mg/kg bw/day or recovery 1000 mg/kg bw/day females.

There were no treatment-related changes in the behavioural parameters and in sensory reactivity assessments. Also, there were no adverse changes in the functional performance parameters measured.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

There were no toxicologically significant changes in the blood chemical parameters and haematological parameters measured. Similarly, no adverse effect on urinalysis was detected for treatment animals, in comparison to controls.

Effects in Organs

There were no toxicologically significant changes in organ weight measurement. Macroscopic examination of the tissues also did not reveal any toxicologically significant findings.

With respect to histopathology, main changes were only noticed in stomach. These included agglomeration of secretion, mucous cell hypertrophy/hyperplasia, mucosal basophilia, and acanthosis/hyperkeratosis of the limiting ridge in animals of either sex treated with 1000 mg/kg/day or 300 mg/kg/day. One female treated with 30 mg/kg/day also demonstrated changes but these conditions are seen occasionally and spontaneously among control animals such that effects in one animal, even in the absence of such effects among concurrent controls, cannot be reliably regarded as an effect of treatment.

These changes were considered to have generally regressed among recovery animals of either sex treated with 1000 mg/kg bw/day following an additional fourteen days without treatment, although two 1000 mg/kg bw/day males had residual changes. One recovery control animal demonstrated all conditions.

Remarks – Results

The oral administration of the notified chemical to rats resulted in treatment-related effects at 300 and 1000 mg/kg bw/day. The changes identified at 1000 mg/kg bw/day were isolated increased salivation, increased water consumption and histopathological changes in the stomach. These changes were considered adaptive and not to represent 'serious damage' to health. Main histopathological changes noted in stomach at 1000 mg/kg

bw/day were also observed in rats at 300 mg/kg/day. There were no treatment-related effects at 30 mg/kg bw/day.

CONCLUSION
The NOAEL was established as 1000 mg/kg bw/day in this study, based on lack of adverse effect at this dose level. The NOEL was established as 30 mg/kg bw/day in this study, based on lack of treatment-related effects at this dose level.

TEST FACILITY	Harlan Laboratories Ltd (2009g)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical (>90%)
METHOD	Standards to be observed by Mutagenicity Testing Institutions (Notification No. 76, September I, 1988 & Notification No. 13, March 29, 2000, Ministry of Labour, Japan Amendment of the Reporting Form of the Results of the Mutagenicity Tests using Microorganisms" (Notification No. 653, September 29, 1997, Labour Standards Bureau, Ministry of Labour, Japan) Guidelines for Toxicity Testings of New Chemical Substances (Notification No. 1121002 of Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, No.2 of the Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry, & No. 031121002 of Environmental Policy Bureau, Ministry of the Environment, Japan, November 21,2003). Pre-incubation method
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 mix was prepared from the livers of phenobarbital/β-naphthoflavone induced male Sprague-Dawley rats.
Concentration Range in Main Test	a) With metabolic activation: 0, 313, 625, 1250, 2500 and 5000 µg/plate b) Without metabolic activation: 0, 313, 625, 1250, 2500 and 5000 µg/plate
Vehicle	Water
Remarks - Method	No deviations from the protocol. Negative control plates were treated with only water for injection that was used to prepare the solution of the notified chemical. Positive controls included AF-2, sodium azide, ICR-191, 2-Aminoanthracene, and benzo[a]pyrene. The dose range for the main test was determined from the dose-finding study using the dose levels: 1.2, 4.9, 20, 78, 313, 1250, and 5000 µg/plate. In the dose-finding test, the growth inhibition by the notified chemical was not observed in any strains either with or without metabolic activation. And the precipitate of the test substance on the plates was not observed either with or without metabolic activation.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	>5000	>5000	>5000	Negative
Test 2	Not performed	Not performed	Not performed	-
Absent				
Test 1	>5000	>5000	>5000	Negative
Test 2	Not performed	Not performed	Not performed	-

Remarks - Results: In the dose-finding test and main test, neither an increase in the number of revertant colonies (more than twice as many as that of the negative control) nor a dose-related response was observed at any doses in any strains, with or without metabolic activation.
The revenant colonies of the positive controls showed an increase of more than twice that of the negative controls and they were within limit of controls (means ± 3SD) in background data, indicating that this study was performed correctly.

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

TEST FACILITY: BML, INC (2008)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE: Notified chemical (>90%)

METHOD: OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
EC Directive 2000/32/EC B.10 Mutagenicity - In vitro Mammalian.

Cell Type/Cell Line: Chinese Hamster Lung (CHL/IU) cells
Metabolic Activation System: S9 mix was prepared from the livers of phenobarbital/β-naphthoflavone induced male Han Wistar rats.
Vehicle: Eagle's Minimal Essential Medium (MEM)
Remarks - Method: No deviations from the protocol.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*,156.25*,312.5*,625*, 1250*,2500*,5000*,MMC 0.1*	6 hrs	24 hrs
Test 2	0*,39.06,78.13*,156.25*,312.5*, 625*,1250,MMC 0.05*	24 hrs	24 hrs
Present			
Test 1	0*,156.25,312.5,625*, 1250*,2500*,5000*,CP 5*	6 hrs	24 hrs

*Cultures selected for metaphase analysis.
MMC = Mitomycin C, CP = Cyclophosphamide

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5000	> 5000	> 5000*	Negative
Test 2	≥ 1250	≥ 1250	> 1250*	Negative
Present				
Test 1	> 5000	> 5000	> 5000*	Negative

* No precipitate of the test material was observed at the end of the exposure period in either group. However, a red colouration was observed at all dose levels, increasing with dose.

Remarks - Results	The vehicle control had frequencies of cells with chromosome aberrations within the range expected for CHL cell line. All of the positive control materials induced highly significant increases in the frequency of cells with aberrations, indicating the satisfactory performance of the test and of the activity of the metabolizing system. The test substance did not induce any statistically significant increases in the frequency of cells with aberrations in the presence or absence of metabolic activation in any exposure group.
CONCLUSION	The notified chemical was not clastogenic to CHL cells treated in vitro under the conditions of the test.
TEST FACILITY	Harlan Laboratories Ltd (2009h)

B.8. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified chemical (>90%)
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay Method B42 Skin Sensitisation (Local Lymph Node Assay) of Commission Regulation (EC) No. 440/2008 United States Environmental Protection Agency Health Effects Test Guidelines OPPTS 870.2600 Skin Sensitisation March 2003
Species/Strain	Mouse/ CBA/Ca
Vehicle	Ethanol/distilled water 7:3
Remarks - Method	A preliminary screening test was performed in one mouse at a concentration of 25% w/w. As no clinical sign of toxicity was noted, this concentration was selected as the highest dose in the main test. In the main test, three groups, each of five animals, were treated with 50 µL (25 µL per ear) of the test material as a solution in ethanol/distilled water 7:3 at concentrations of 25%, 10% or 5% w/w. A further group of five animals was treated with ethanol/distilled water 7:3 alone.

RESULTS

Concentration (% w/v)	*Proliferative response (DPM/animal)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (*vehicle control*)	645.53	-
5	729.19	1.13
10	659.91	1.02
25	717.51	1.11
Positive Control (α-Hexylcinnamaldehyde)		
15%	-	9.49
Positive Control (2,4-Dinitrobenzenesulfonic acid, sodium salt)		
10%	-	13.71

Remarks - Results	There were no deaths. No signs of systemic toxicity were noted in the test and control animals during the test. Red coloured saining of the ears and fur was noted post dose on Days 1 to 3 in all test animals. A stimulation index of 9.49 and 13.71 were observed for positive controls α-Hexylcinnamaldehyde and 2,4-Dinitrobenzenesulfonic acid, sodium salt, respectively.

CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Harlan Laboratories Ltd (2009i)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability (study 1)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Activated sewage sludge
Exposure Period	28 days
Auxiliary Solvent	None reported
Analytical Monitoring	TOC analyser
Remarks - Method	The test was conducted for 28 days in accordance with the above guidelines. In an initial test conducted with the test substance at 10 mg C/L, inhibition of the sewage sludge microorganisms was observed and hence the definitive test was carried out at 5 mg C/L. The test substance was added to a liquid medium inoculated with sewage microorganisms and aerated with CO_2-free air at approximately 21°C. CO_2 production was analysed. A reference (sodium benzoate), and toxicity control were run in parallel.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
0	0	0	0
8	7	8	80
14	0	14	96
28	9	28	102
29	21	29	100

Remarks - Results	All validity criteria were satisfied. The reference compound reached the 60% pass level by day 14 indicating the suitability of the inoculum. The toxicity control attained 42% degradation after 14 days indicating the notified chemical is not toxic to the inoculum. The test substance was found to be biodegradable (21%) under the conditions of the test. However, as biodegradation did not reach the pass level of > 60% CO_2 production within the 10 day window, it cannot be classed as readily biodegradable.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Harlan Laboratories Ltd (2009j)

C.1.2. Ready biodegradability (study 2)

TEST SUBSTANCE	Notified chemical (purity > 90%)
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test
Inoculum	Activated sludge from domestic sewage plant
Exposure Period	28 days
Auxiliary Solvent	None reported
Analytical Monitoring	BOD
Remarks - Method	No significant deviations from the test guidelines were reported

RESULTS

Test substance	*Aniline*

Day	*% Degradation*	*Day*	*% Degradation*
1	2.3	1	0
7	1.0	7	84.4
14	2.0	14	91.2
28	2.7	28	94.4

Remarks - Results: All validity criteria were satisfied. The reference compound (aniline) reached the 60% pass level by day 14 indicating the suitability of the inoculum. The toxicity control attained 49.1% degradation after 14 days indicating the notified chemical is not toxic to the inoculum.

CONCLUSION: The notified chemical is not readily biodegradable

TEST FACILITY: Supervision and Test Center for Pesticide Safety Evaluation and Quality Control (2010a)

C.1.3. Inherent biodegradability

TEST SUBSTANCE: Notified chemical (purity > 90%)

METHOD: OECD TG 302 C Inherent Biodegradability: Modified MITI Test (II)

Inoculum: Samples from 10 sites including sewage treatment plants, rivers and lakes
Exposure Period: 28 days
Auxiliary Solvent: None reported
Analytical Monitoring: BOD
Remarks - Method: No significant deviations were reported.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
1	7.7	1	2.9
7	8.1	7	80.2
14	10.3	14	86.9
28	16.5	28	88.1

Remarks - Results: Degradation of the reference compound (aniline) exceeded 75% after 7 days thus verifying the activity of the inoculum and validating the test.

CONCLUSION: The notified chemical is not inherently biodegradable

TEST FACILITY: Supervision and Test Center for Pesticide Safety Evaluation and Quality Control (2010b)

C.1.4. Bioaccumulation

TEST SUBSTANCE: Notified chemical (purity > 90%)

METHOD: OECD TG 305 Bioconcentration: Flow-through Fish Test.
EC Directive 98/73/EC C.13 Bioconcentration: Flow-Through Fish Test.

Species: Carp (*Cyprinus carpio*)
Exposure Period: Exposure: 28 days Depuration: Not done
Auxiliary Solvent: None reported
Concentration Range: Nominal: 0.19 and 1.9 mg/L
Actual: 0.177 and 1.74 mg/L (mean of 6 measurements over 28 days)
Analytical Monitoring: HPLC
Remarks - Method: An acute toxicity test was conducted under semi static conditions with orange-red killifish (*Oryzias latipes*).

The bioconcentration test was conducted at two concentrations (Level 1 = 1.9 mg/L and Level 2 = 0.19 mg/L and) under semi-static conditions, with renewal of test water every 24 h. Fourteen fish were used at each test concentration and 12 fish were used in the control test. All the tests were controlled at 24.2 – 24.5°C and a pH range of 7.9 – 8.1.

RESULTS

Bioconcentration Factor	BCF ≤ 6.2 and 60 at the nominal concentrations of 1.19 and 0.19 mg/L, respectively.
CT50	Not determined
Remarks - Results	The LC50 (96 h) for the acute toxicity test was > 200 mg/L.
	All validity criteria for the bioconcentration test were satisfied.
	No depuration was conducted after the exposure of the fish to the test chemical. This is considered acceptable given the detected concentrations of the notified chemical in all test fish were not more than the minimum determination limit in the fish. Since all the BCFs were below the minimum calculable values, it was evaluated that a steady-state was reached after 28 days and the notified chemical is not considered to be bioconcentrating.

CONCLUSION The notified chemical is not considered to be bioconcentrating

TEST FACILITY Kurume Laboratory (2009)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish (study 1)

TEST SUBSTANCE Notified chemical (purity > 90%)

METHOD OECD TG 203 Fish, Acute Toxicity Test – Semi static
EC Directive 92/69/EEC C.1 Acute Toxicity for Fish – Semi static

Species	Rainbow trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None reported
Water Hardness	140 mg $CaCO_3$/L
Analytical Monitoring	UV/Vis
Remarks – Method	Following a range finding test, a limit test was conducted at 100 mg/L under semi static conditions for a period of 96 h according to the guidelines above. The controls were kept in dilution water. Test conditions were: 14°C, pH 7.5 – 7.8, 96 – 129% ASV O_2, 12 hours dark and 12 hours light period.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual (at 96 h)*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	< LOQ	7	0	0	0	0	0
100	100	7	0	0	0	0	0

LOQ = 2.4 mg/L

LC50	> 100 mg/L at 96 hours
NOEC	100 mg/L at 96 hours
Remarks – Results	All validity criteria for the test were satisfied and no significant deviations were reported. Some air saturated oxygen values were reported to be above 100% and were attributed to microscopic air bubbles in the media. This was not considered to have affected the outcome of the test since no mortalities were observed.

CONCLUSION	The notified chemical is not harmful to fish
TEST FACILITY	Harlan Laboratories Ltd (2009k)

C.2.2. Acute toxicity to fish (study 2)

TEST SUBSTANCE	Notified chemical (purity >90%)
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi static EC Directive 92/69/EEC C.1 Acute Toxicity for Fish – Semi static
Species	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 hours
Auxiliary Solvent	None reported
Water Hardness	126 mg $CaCO_3$/L
Analytical Monitoring	UV/Vis
Remarks – Method	Following a range finding test, a limit test was conducted at 100 mg/L under semi static conditions for a period of 96 h according to the guidelines above. The controls were kept in dilution water. Test conditions were: 23 ± 2°C, pH 7.5 – 7.8, ≥ 80% ASV O_2, 12 hours dark and 12 hours light period.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual**		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	< LOQ	10	0	0	0	0	0
100	100.9	10	0	0	0	0	0

LOQ = 2.4 mg/L. *Mean of fresh and expired solutions at 24, 72 and 96 h.

LC50	> 100 mg/L at 96 hours
NOEC	100 mg/L at 96 hours
Remarks – Results	All validity criteria for the test were satisfied and no significant deviations were reported. No mortalities or toxic signs were observed.
CONCLUSION	The notified chemical is not harmful to fish
TEST FACILITY	Supervision and Test Center for Pesticide Safety Evaluation and Quality Control (2010c)

C.2.3. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical (purity >90%)
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation 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	UV/Vis
Remarks - Method	Following a range-finding test, a limit test was conducted in accordance with the guidelines above. No significant deviations to protocol were reported. Test conditions were: 19-20°C, pH 7.8–8.0, 8.6–9.0 mg O_2/L. A positive control was run with potassium dichromate.

RESULTS

Concentration mg/L		*Number of D. magna*	*Cumulative Number Immobilised*	
Nominal	*Actual at 48 h*		*24 h*	*48 h*

Control	< LOQ	20	0	1
100	99.2	20	1	1

LOQ = 2.4 mg/L

EC50	> 100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks - Results	The results from the positive control was EC50 = 0.78 mg/L at 48 hours, which was in the normal range for the reference material. All validity criteria for the test were satisfied.

CONCLUSION The notified chemical is not harmful to aquatic invertebrates

TEST FACILITY Harlan Laboratories Ltd (2009l)

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	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 100 mg/L Actual: 110 mg/L (at 72 h)
Auxiliary Solvent	None reported
Water Hardness	0.15 mmol Ca^{2+} and Mg^{2+}
Analytical Monitoring	UV/Vis
Remarks - Method	Following a range finding test, a limit test at 100 mg/L was conducted in accordance with the guidelines above. A positive control with potassium dichromate was run under similar exposure conditions to the limit test. Due to the coloured nature of test solutions, the method was modified to have increased light intensity and decreased test volume. This is recommended (EC, 2006) to minimise the effects of light adsorption by the test material at the wavelengths required for photosynthetic growth. Test conditions were: 24 ± 1°C, pH 7.3 – 7.7, constant illumination at 10,000 lux and shaking. NOECs were estimated by Student's t-test incorporating Bartlett's test for homogeneity of variance. EC50s were estimated by inspection of the growth rate and area under the curve data.

RESULTS

Biomass		*Growth*	
E_bC50	*NOEC*	*E_rC50*	*NOEC*
mg/L at 72 h	*mg/L*	*mg/L at 72 h*	*mg/L*
> 100	100	> 100	100

Remarks - Results	All validity criteria were satisfied. Results from the positive control were within normal range for the reference material. Spectrophotometer measurements taken at the wavelength required for photosynthesis (460 and 665 nm) showed that the most significant absorption of the test solutions occurred at 460 nm at both 20 and 200 mg/L. Modifications to the guidelines above to increase the light intensity and decrease the sample volume overcame this absorption effect, resulting in no significant effect on algal cells. The reported toxicity endpoints were based on nominal concentrations since the measured concentrations were within ±20% of nominal values.

CONCLUSION The notified chemical is not harmful to algae

TEST FACILITY	Harlan Laboratories (2009m)

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
Exposure Period	3 hours
Concentration Range	Nominal: 10, 32, 100, 320 and 1000 mg/L Actual: Not reported
Remarks – Method	After a range finding test, the definitive test was conducted according to the guidelines above at test substance concentrations of 10 - 1000 mg/L dispersed in dechlorinated tap water with the addition of a synthetic sewage as a respiratory substrate. A blank control and reference (3,5-dichlorophenol) control were run in parallel. The rate of respiration was determined after 3 h contact time and compared to the results from the control and reference material. Test conditions: approximately 21°C, pH 7.5 – 8.1.
RESULTS	
IC50 (3 h)	> 1000 mg/L
NOEC (3 h)	640 mg/L
Remarks – Results	All validity criteria for the test were satisfied and no significant deviations were reported.
CONCLUSION	The notified chemical does not inhibit the respiration of waste-water microorganisms
TEST FACILITY	Harlan Laboratories Ltd (2009n)

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