File No: STD/1082

April 2004

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

AKDE-3

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

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at:

Library
National Occupational Health and Safety Commission
25 Constitution Avenue
CANBERRA ACT 2600
AUSTRALIA

To arrange an appointment contact the Librarian on TEL + 61 2 6279 1161 or + 61 2 6279 1163.

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

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

Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

AKDE-3

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Epson Australia Pty Ltd
3 Talavera Rd
NORTH RYDE NSW 2113

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data, purity, impurities, exact use and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: manufacturing process, hydrolysis, dissociation constant, particle size, flash point, explosive properties, oxidising properties, acute inhalation toxicity, dominant lethal test and Daphnia reproduction study.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
LVC permit no. 547, 2003.

NOTIFICATION IN OTHER COUNTRIES
EU (No. 02-06-1624-01, 2003).

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
ADKE-3.

MOLECULAR WEIGHT
High.

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	HPLC, UV/Vis, IR and MS

3. COMPOSITION

DEGREE OF PURITY
High.

ADDITIVES/ADJUVANTS
None.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
In cartridges for ink jet printers packed in cardboard boxes.

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

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

USE
Component of ink for use in ink jet printing onto paper.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Unknown.

IDENTITY OF MANUFACTURER/RECIPIENTS
Notifier.

TRANSPORTATION AND PACKAGING
In plastic ink jet cartridges in cardboard boxes packed in larger cardboard containers.

5.2. Operation Description

The notified chemical is imported from overseas as a component of printer ink contained in a sealed cartridge packaged in cardboard.

The cartridges will be transported and stored prior to national distribution where they will be used in office or home printing equipment. The cartridges will be installed/replaced either by office workers, service technicians or consumers.

5.3. Occupational exposure

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 sealed cartridge and its packaging may be breached. The cartridges (up to 100,000 per year) will be distributed a number of outlets, the cardboard cartons opened and individual boxes stacked on shelves. Possibly 20 – 50 workers up to 8 hours per day, 50 – 100 days per year may be involved in import, transport, storage and stacking shelves.

Office workers and service technicians may be exposed to the notified chemical when changing printer cartridges with service technicians also potentially exposed during printer maintenance. Approximately 1,000 office workers may change cartridges 2 – 3 times per year, with the change taking 10 minutes each time. Service technicians may visit a site once per year, the service taking 45 minutes.

Users of the printers may be exposed to the notified chemical during handling of printed paper, however, the notified chemical is bound to the paper matrix and not expected to be readily bioavailable except if the paper or other substrate is handled before the ink has dried.

5.4. Release

RELEASE OF CHEMICAL AT SITE
Environmental release of the notified chemical is unlikely during importation, storage and transportation, and spillage during a transport accident is the most likely reason for environmental release. Printer ink is imported in ready-to-use cartridges (containing ≤ 3% notified chemical).

Individual container capacity, container and packaging specifications would limit the extent of release.

RELEASE OF CHEMICAL FROM USE
Printer ink containing the notified chemical will be applied to paper products. Release of the printer ink to the environment is not expected under the normal use pattern. Each printer ink cartridge is designed to prevent leakage. However, if leakage does occur, the printer ink will be collected and sent to landfill for disposal.

Used cartridges will be sent to landfill for disposal (containing up to 10% of residual printer ink). Residues contained in the cartridges are expected to remain within these containers, although release could occur from deterioration of the cartridge while in the landfill waste.

5.5. Disposal

The total import volume of the notified chemical will ultimately be disposed of in either landfill or be incinerated with a fraction potentially sent to sewer from the waste paper recycling process. Some waste paper containing the printer ink may be disposed of directly to landfill with the notified chemical strongly bound to the paper. In addition to landfill, some of the printed paper will enter the paper recycling process. During such processes, waste paper is repulped using a variety of alkaline, dispersing and wetting agents, water emulsifiable organic solvents and bleaches. These agents enhance fibre separation, printer ink detachment from the fibres, pulp brightness and the whiteness of paper. These aqueous wastes are expected to go to sewer, but wastewaters may be treated on-site prior to disposal. Normally, very little of the notified chemical is expected to partition to the supernatant water, with most partitioned to solids. However, in this case, more may go into water due to the very high water solubility of the notified chemical. Sludge generated during the wastewater treatment process is typically dried and incinerated or sent to landfill for disposal.

5.6. Public exposure

Members of the public may be exposed to the notified chemical through handling of the printed paper. Assuming 1 g of ink produces 3000 A4 pages of text, each page contains 0.3 mg of dye. Once printed onto paper the notified chemical is bound and unavailable for release. Nevertheless, exposure is possible from handling printed pages prior to the ink being fully dried or if a non-absorbent substrate is placed in the printer. Exposure is also possible from residues in the printer although the cartridges are designed to minimise these residues.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa Purple powder.

Melting Point/Freezing Point Decomposed prior to melting at 310°C

METHOD EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Method: differential scanning calorimetry.
TEST FACILITY Safepharm (2002a).

Density 1550 kg/m^3 at 20°C

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Measured with gas comparison pycnometer.
TEST FACILITY Safepharm (2002a).

Vapour Pressure < 4.2 x 10^{-8} kPa at 25°C.

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Measured using a vapour pressure balance between 100 and 185°C with linear regression used to calculate vapour pressure at 25°C. Very slightly volatile (Mensink et al., 1995)
TEST FACILITY Safepharm (2002b).

Water Solubility 212 g/L at 20 ±0.5 °C (range 207-215 g/L).

METHOD EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Shake-flask Method. Preliminary and definitive tests were performed. Samples containing 4.5027, 4.5098 and 4.4821 g test material was added to flasks with 15 mL double-distilled water. After shaking (30 °C) and standing (20 °C for >24 h), the contents were centrifuged (2500 rpm for 15 min), with supernatant analysed spectrophotometrically. Supernatant pH was 5.9-6.0. Readily soluble in water.
TEST FACILITY Safepharm (2002a)

Hydrolysis as a Function of pH Not determined.
Remarks The notifier has indicated that hydrolysis is not anticipated as there are no hydrolysable groups in the structure.

Partition Coefficient (n-octanol/water) log P_{ow} = < -2.96 at 20ºC.

METHOD EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks Shake-flask Method. Preliminary and definitive tests were conducted. Test material (0.2069 g) was added to 200 mL octanol-saturated water (adjusted to pH 7.0 using 1 M NaOH). Six partitions with octanol were performed at 22-22.5 °C. After shaking each (5 min) and centrifuging (2500 rpm for 10 min), aliquots of both phases were analysed spectrophotometrically. Very hydrophilic.
TEST FACILITY Safepharm (2002a)

Adsorption/Desorption log K_{oc} = < -0.519 at 20 °C.

METHOD Estimated using Quantitative Structure Activity Relationship (QSAR) based on EC Directive 93/67/EEC Risk Assessment of New Substances.
Remarks Estimated using the equation: $\log_{10}K_{oc}$ = 0.52 X $\text{Log}_{10}P_{ow}$ + 1.02 where: log P_{ow} = < -2.96. Likely to be highly mobile and partition to the aqueous phase.
TEST FACILITY Safepharm (2002a)

Dissociation Constant Not determined.
Remarks The notifier has indicated that the number of dissociable groups is too numerous to measure a dissociation constant with any degree of accuracy. The sulphonic acid groups are strongly acidic and are expected to remain ionised in the environmental pH range of 4-9.

Surface tension 67.2 mN/m at 23 ±0.5 °C.

METHOD EC Directive 92/69/EEC A.5 Surface Tension
Remarks ISO304 Ring Method. Test solution concentration 1070 mg/L. Not a surface-active substance.
TEST FACILITY Safepharm (2002a)

Particle Size
Remarks Not determined.

Flash Point
Remarks Not applicable for solid.

Flammability Limits Not highly flammable.

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks A standard pile of material did not burn when subjected to a Bunsen burner flame for 2 minutes.
TEST FACILITY Safepharm (2002b).

Autoignition Temperature 374ºC

METHOD	92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
TEST FACILITY	Safepharm (2002b).

Explosive Properties

Remarks	Not expected to be explosive based on structure.

Reactivity

Remarks	Expected to be stable under normal environmental conditions.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 > 2000 mg/kg bw	low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	severely irritating
Guinea pig, skin sensitisation - adjuvant test test.	no evidence of sensitisation.
Rat, oral repeat dose toxicity - 28 days.	NOEL = 140 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberrations	non genotoxic

7.1. Acute toxicity – oral

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain Rat/Sprague-Dawley.
Vehicle Distilled water.
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3/sex	2000	None.

LD50 > 2000 mg/kg bw
Signs of Toxicity None.
Effects in Organs None.
Remarks - Results Pink coloured urine noted in all animals one day after dosing.

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

TEST FACILITY Safepharm (2002c).

7.2. Acute toxicity - dermal

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 402 Acute Dermal Toxicity – Limit Test.
EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain Rat/Sprague-Dawley.
Vehicle Distilled water.
Type of dressing Semi-occlusive.
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	None

LD50 > 2000 mg/kg bw
Signs of Toxicity - Local None.
Signs of Toxicity - Systemic None.
Effects in Organs None.
Remarks - Results Pink staining precluded evaluation of erythema in all animals prior to day 5, and persisted in the females for up to 8 days.

CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Safepharm (2002d).

7.3. Irritation – skin

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None.
Observation Period	72 hours.
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.
RESULTS	
Remarks - Results	Faint pink/purple staining was noted at all treated skin sites throughout the study. Slight erythema was noted in one animal at 24 hours after patch removal.
CONCLUSION	The notified chemical is slightly irritating to skin.
TEST FACILITY	Safepharm (2002e).

7.5. Irritation - eye

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion. EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	1
Observation Period	21 days.
Remarks - Method	A single animal was tested and, based on the results for this animal, testing on additional animals was not conducted.
RESULTS	
Remarks - Results	No inflammation of the cornea or iris was observed. Moderate redness of the conjunctiva at 1 hour persisted to 24 hours and was slight by 48 hours. Moderate chemosis and discharge at 1 hour was slight at 24 hours. Dark red/purple staining of the cornea, iris and conjunctiva was noted up to and including day 7. Staining of the conjunctiva persisted to the study termination on day 21.
CONCLUSION	The notified chemical is severely irritating to the eye on the basis of conjunctival staining persisting to the end of the observation period.
TEST FACILITY	Safepharm (2002f).

7.6. Skin sensitisation

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 406 Skin Sensitisation – Maximisation test. EC Directive 96/54/EC B.6 Skin Sensitisation - Maximisation test.
Species/Strain	Guinea pig/Dunkin-Hartley.
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: unable to be evaluated due to staining topical: 10% (w/w); 25% and 50% concentrations could not be evaluated due to staining
MAIN STUDY	
Number of Animals	Test Group: 10 Control Group: 5
INDUCTION PHASE	Induction Concentration: intradermal: 10% (w/w) topical: 50% (w/w)
Signs of Irritation	Irritation at topical induction sites could not be evaluated because of staining.
CHALLENGE PHASE	
1st challenge	topical: 25% (w/w) topical: 50% (w/w)
Remarks - Method	Topical induction concentration was chosen as the maximum attainable.
RESULTS	
Remarks - Results	No erythema or oedema was noted at any of the test or control challenge sites. Staining at the challenge sites did not preclude evaluation of erythema or oedema.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Safepharm (2002g).

7.7. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical.
METHOD	EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral). Notification on Partial Revision of Testing Methods Relating to the New Chemicals Substances (Notification No. 700 of the Planning and Coordination Bureau, EA, No. 1039 of the Pharmaceutical Affairs Bureau, MHW & No. 1014 (1986) of the Basic Industries Bureau, MITI, December 5, 1986) 28-Day Repeated Dose Toxicity Study in Mammalian Species.
Species/Strain	Rat/Crj: CD(SD) IGS
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	Purified water.
Remarks - Method	Doses were selected based on results of a 14-day study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	6/sex	0	0
II (low dose)	"	25	0
III (mid dose)	"	140	0
IV (high dose)	"	800	1 male
V (control recovery)	"	0	0
VI (high dose recovery)	"	800	0

Mortality and Time to Death

One animal in the high dose group died on day 25 of renal dysfunction.

Clinical Observations

Dark red stool of animals low, mid and high dose groups; brownish urine and reddish salivation in the high dose animals.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Clinical chemistry: Increased creatinine, α2-globulin and γ-globulin were noted in high dose animals, decreased albumin and albumin/globulin ratio in high dose males and increased γ-glutamyltransferase in high dose females. Increased creatinine was observed in high dose females at the end of the recovery period.
Haematology: Decreased haemoglobin concentration and haematocrit were noted in high dose animals and increased white blood cells in high dose males. Decreased haemoglobin concentration and haematocrit were present at the end of the recovery period as was increased white blood cells and reticulocyte count.
Urinalysis: Brownish or reddish colour change, occult blood and increased urine cast in high dose animals and increased epithelial cells in high dose males. Reddish change of the urine and increased urine cast were observed at the end of the recovery period.

Effects in Organs

Organ weights: Increased relative liver weights, absolute and relative kidney and spleen weights in high dose animals. The increased kidney and spleen weights were maintained at the end of the recovery period. Increased relative liver weights were observed in high dose females at the end of the recovery period.
Macroscopic findings: Enlargement and reddish change of the kidneys, enlargement of the spleen and hepatic lymph node and reddish change of the wall of the large intestine were observed in high dose animals. Reddish change of the wall of the small intestine, enlargement of the liver and elevation of the limiting ridge of the forestomach occurred in high dose males.
Microscopic findings: Aggregation of histiocytic cells in the perivascular area of the lung and periportal area of the liver, infiltration of histiocytic cells in the heart, aggregation of histiocytic cells in the glomeruli, infiltration of histiocytic cells in the interstitium and reddish pigment deposition in the tubular epithelium of the kidney, infiltration of histiocytic cells in the surrounding tissue of the hepatic lymph node, hyperplasia of the squamous epithelium in the limiting ridge of the forestomach in high dose animals. All but hyperplasia of the squamous epithelium in the limiting ridge of the forestomach were maintained at the end of the recovery period.

Hyperplasia of the lymphoid cells in the Peyer's patches of the rectum and mesenteric lymph node, increased mitoses of hepatocytes, vacuolisation of the tubular epithelium of the kidney, oedema in the submucosal layer of the glandular stomach and caecum in high dose males. In recovery males, enlargement and hyperplasia of the lymphoid cells in the hepatic lymph node, hyperplasia of the lymphoid cells in the axillar and mesenteric lymph nodes, infiltration of the histiocytic cells in the submucosal layer of the rectum and infiltration of the histiocytic cells in the surrounding tissue of the axillar and renal lymph nodes were observed.

Basophilic tubules in the kidney and oedema in the submucosal layer of the rectum in high dose females. Hyperplasia of the squamous epithelium in the limiting ridge of the forestomach and hyperplasia of the lymphoid cells in the renal lymph node was observed at the end of the recovery period.

Remarks – Results

The anaemia observed at the end of the dosing period was considered to be reversible because of the increased reticulocyte count. At the end of the recovery period the severity of reddish change and enlargement of the tissues and organs were decreased and histiocytic and lymphoid cells were also decreased. Increases in histiocytic and lymphoid cells and increases in α2-globulin and γ-globulin were considered to indicate

systemic inflammation.

The test substance was judged to demonstrate immunological effects with reversibility.

CONCLUSION
The No Observed Effect Level (NOEL) was established as 140 mg/kg bw/day in this study, based on effects on haematological parameters, blood chemistry parameters and specific organs including the kidneys, lymphatic system, digestive system, liver, lungs and heart at the higher dose.

TEST FACILITY Chemicals Evaluation and Research Institute (2002a).

7.8. Genotoxicity - bacteria

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
Standards for Toxicity Investigations (Ministry of Labour, Notification No. 77, September 1, 1988 and Notification No. 67, June 2, 1997), and Procedures of Mutagenicity Test Using Microorganisms and Evaluation of Test Results (Ministry of Labour, Official Notification, February 8, 1999) Notification on Partial Revision of Testing Methods Relating to the New Chemicals Substances (Notification No. 700 of the Planning and Coordination Bureau, EA, No. 1039 of the Pharmaceutical Affairs Bureau, MHW & No. 1014 (1986) of the Basic Industries Bureau, MITI, December 5, 1986)
Pre incubation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100. *E. coli*: WP2 *uvrA*.
Metabolic Activation System	Rat liver S9 fraction following phenobarbital and 5,6-benzoflavone administration.
Concentration Range in Main Test	a) With metabolic activation: 156 - 5000 µg/plate. b) Without metabolic activation: 156 - 5000 µg/plate.
Vehicle	Distilled water.
Remarks - Method	Two independent tests were performed in triplicate.

RESULTS

Remarks - Results	No induced mutants were observed in any strain at any dose level. Negative and positive controls gave the expected responses. No signs of toxicity were observed.

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

TEST FACILITY Chemicals Evaluation and Research Institute (2002b).

7.9. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.
Standards for Toxicity Investigations (Ministry of Labour, Notification No. 77, September 1, 1988 and Notification No. 67, June 2, 1997), and Procedures of Mutagenicity Test Using Microorganisms and Evaluation of Test Results (Ministry of Labour, Official Notification, February 8, 1999) Notification on Partial Revision of Testing Methods Relating to the New Chemicals Substances (Notification No. 700 of the Planning and Coordination Bureau, EA, No. 1039 of the Pharmaceutical Affairs

	Bureau, MHW & No. 1014 (1986) of the Basic Industries Bureau, MITI, December 5, 1986 and Notification No. 287 of the Planning and Coordination Bureau, EA, No. 127 of the Environmental Health Bureau, MHW & No. 2 (1986) of the Basic Industries Bureau, MITI, October 31, 1997)
Cell Type/Cell Line	Chinese Hamster Lung fibroblasts (CHL/IU).
Metabolic Activation System	Rat liver S9 fraction following Phenobarbital and 5,6-benzoflavone administration.
Vehicle	Distilled water.
Remarks - Method	Test concentrations were based on a preliminary cell growth inhibition test.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	1250, 2500, 5000	6 hours	24 hours
Test 2	313, 625, 1250	24 hours	24 hours
Present			
Test 1	1250, 2500, 5000	6 hours	24 hours

*Cultures selected for metaphase analysis.

RESULTS

Remarks - Results	Positive and negative controls gave the expected responses. The notified chemical did not increase the percentage of cells will chromosomal aberrations and growth rates were not markedly affected at the highest concentrations. The notified chemical did not precipitate in the cultures.

CONCLUSION	The notified chemical was not clastogenic to Chinese Hamster Lung cells treated in vitro under the conditions of the test.
TEST FACILITY	Chemicals Evaluation and Research Institute (2002c).

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 301 C Ready Biodegradability: Modified MITI Test (I) and the Method for Testing the Biodegradability of Chemical Substances by Microorganisms stipulated in the Testing Methods for New Chemical Substances (July 13, 1974, Revised October 8, 1998, No.5, Planning and Co-ordination Bureau, Environment Agency; No. 615, Pharmaceutical Affairs Bureau, Ministry of Health and Welfare, and No. 392, Basic Industries Bureau, Ministry of International Trade and Industry, Japan.

Inoculum	Activated sludge (30 mg/L) giving a test concentration of 100 mg/L.
Exposure Period	28 days.
Auxiliary Solvent	None
Analytical Monitoring	Performed weekly during the tests.
Remarks - Method	Biodegradation was measured 3 ways: BOD, DOC and HPLC analysis of test substance. BOD was measured by means of a closed system oxygen consumption measuring apparatus. Dissolved organic carbon (DOC) was determined by analysis of TOC. Test temperature: 25±1°C. The test substance dissolved in the test solution with no observed insoluble components.

RESULTS

Test substance		*Aniline (acceptable minimum range 40-65%)*	
Day	*% degradation*	*Day*	*% degradation*
7	0	7	61
14	0	14	74
21	0	21	76
28	0-4	28	76

Remarks - Results: Biodegradation was 0-4% over the test duration.

CONCLUSION: Not readily biodegradable.

TEST FACILITY: Chemicals Evaluation and Research Institute (2002e)

8.1.2. Bioaccumulation

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 305 Bioconcentration: Flow-through Fish Test and Methods for Testing the Degree of Accumulation of Chemical Substances in Fish Body stipulated in the Testing Methods for New Chemical Substances (July 13, 1974, Revised October 8, 1998, No.5, Planning and Co-ordination Bureau, Environment Agency; No. 615, Pharmaceutical Affairs Bureau, Ministry of Health and Welfare, and No. 392, Basic Industries Bureau, Ministry of International Trade and Industry, Japan.

Species	Carp *Cyprinus carpio* (length 6.0-7.3 cm; yearlings)
Exposure Period	Exposure: 28 days Depuration: Not determined
Auxiliary Solvent	None
Concentration Range	
Nominal	Level 1: 1.03 mg/L Level 2: 0.103 mg/L
Analytical Monitoring	Analysis of test water samples by HPLC confirmed the stability of the

test substance for the duration of the tests.

Remarks - Method: Continuous flow conditions. Dilution water: hardness: 83 mg/L, pH: 7.9, TOC 0.3 mg/L. Temperature: ~24.5 °C. Dissolved oxygen: 8.0-8.1 mg/L. pH 8.0-8.1 (acceptable). Photoperiod: 14 hours light: 10 hours dark. Analysis of whole fish was performed 5 times at each level over the duration of exposure. Lipid content of fish was determined by gravimetric analysis after chloroform-methanol extraction.

RESULTS

Bioconcentration Factor: Level 1: BCF ≤ 0.32
Level 2: BCF ≤ 3.1

Remarks - Results: Reasons for the slightly higher BCF at lower exposure concentration were not discussed. No abnormalities in behaviour or appearance were observed in exposed fish. Lipid content: Initial: 4.31%, After termination of exposure: 2.60% (>25% reduction considered within the range of an individual difference).

CONCLUSION: Very slightly bioconcentrating potential (Mensink et al., 1995)

TEST FACILITY: Chemicals Evaluation and Research Institute (2002d)

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

8.2.1.1 Acute toxicity to rainbow trout

TEST SUBSTANCE: Notified chemical.

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

Species: Rainbow Trout *Oncorhynchus mykiss* (juveniles; 4.5 cm mean length; 1.01 g mean weight).

Exposure Period: 96 hours

Auxiliary Solvent: None

Water Hardness: 176 mg $CaCO_3$/L

Analytical Monitoring: Chemical analysis at 0, 24 and 96 hours. Temperature: 14 °C. Dissolved oxygen ≥ 9.4 mgO_2/L (acceptable).

Remarks – Method: Range-finding and definitive tests were conducted. Test material (2000 mg) was dissolved in dechlorinated tap water, adjusted to 20 L and stirred for 1 minute. The only test concentration was 100 mg/L. Photoperiod: 16 h light: 8 h dark with transition periods. Fish were acclimated 7 days prior to testing, and no mortality was recorded prior to the tests. Loading rate 0.51 g bw/L. Analytical testing showed that the test material was stable during the tests (104-110% of nominal). Standards and test solutions were tested by spectrophotometer.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	0	20	0	0	0	0	0
100 mg/L	105	20	0	0	0	0	0

LC50: >100 mg/L at 96 hours.

NOEC (or LOEC): 100 mg/L at 96 hours.

Remarks – Results: No mortality or sublethal effects were observed at the highest test concentration.

CONCLUSION	Practically non-toxic to rainbow trout.
TEST FACILITY	Safepharm (2002h)

8.2.1.2 Acute toxicity to Orange-red killifish

TEST SUBSTANCE	Notified chemical.
METHOD	Japanese Industrial Standard (JIS K0102-1998-71). Testing Methods for Industrial Waste Water, Acute Toxicity Test with Fish. Semi-static (24 h renewal).
Species	Orange-red killifish *Oryzias latipes* (mean length 3.2 cm; n=mean weight 0.32 g).
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	83.5 mg $CaCO_3$/L
Analytical Monitoring	Chemical analysis at 0, 24 and 96 hours. Temperature: 24.3-24.7 °C. Dissolved oxygen 6.6-8.1 mgO_2/L. pH 6.2-6.6 (acceptable). Analysis of test water samples by HPLC confirmed the stability of the test substance for the duration of the tests.
Remarks – Method	Dilution water consisted of local groundwater (tested).

RESULTS

Concentration mg/L	*Number of Fish*	*Mortality*				
Nominal		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	10	0	0	0	0	0
1030 mg/L	10	0	0	0	0	0

LC50	>1030 mg/L at 96 hours.
NOEC (or LOEC)	1030 mg/L at 96 hours.
Remarks – Results	No mortality or sublethal effects were observed at the highest test concentration.
CONCLUSION	Practically non-toxic to orange-red killifish.
TEST FACILITY	Chemicals Evaluation and Research Institute (2002d)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test and Reproduction Test – Static referenced as EC Directive 92/69/EEC C.2 Acute Toxicity for *Daphnia* - Static.
Species	Waterfleas *Daphnia magna* (1st instar)
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	Analytical monitoring at 0 and 48 hours showed that the test substance was stable during the tests. Test pH 7.9-8.0. Temperature 21.0°C. Dissolved oxygen 8.1-8.4 mg/L (acceptable).
Remarks - Method	Range-finding and definitive tests were performed. 100 mg of test material was dissolved in reconstituted water to give 1 L (100 mg/L). Photoperiod: 16 h light: 8 h dark with transition periods. Standards and test solutions were tested by spectrophotometer.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	0	40 (4 replicates of 10)	0	0
100	Not determined	40 (4 replicates of 10)	0	0

LC50	>100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks - Results	No immobilisation or sublethal effects were observed during the tests.

CONCLUSION Practically non-toxic to *Daphnia magna*

TEST FACILITY Safepharm (2002i)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 201 Alga, Growth Inhibition Test referenced as EC Directive 92/69/EEC C.3 Algal Inhibition Test, further refined for coloured test substances.

Species	Green algae *Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	
Nominal	0, 3.2, 10, 32, 100 and 320 mg/L
Auxiliary Solvent	None
Analytical Monitoring	
Remarks - Method	Constant illumination and stirring. Temperature 24±1 °C. Duplicate experiments (A and B) were performed to differentiate growth effects between toxicity and reduced light causes. Experiment A: Algae were exposed to test material in a flask enclosed from above by a petri dish containing culture medium only. Inhibition was due to a combination of toxicity and reduction in light intensity. In Experiment B, algae were not exposed to the test material in the flasks, but the flasks were enclosed by petri dishes containing the culture media and the test material. Therefore, inhibition of algal growth was due to a reduction in light intensity alone. The difference between Experiments A and B inhibition values is presumed to be due to the toxic effect of the test material on algal cells. Mean cell density in Expt. A was 1.26 x 10^4 cells/mL (initial) and 3.70 x 10^5 cells/mL (72 hours). Mean cell density in Expt. B was 1.23 x 10^4 cells/mL (initial) and 4.74 x 10^5 cells/mL (72 hours). Standards and test solutions were tested by spectrophotometer.

RESULTS

Experiment A: Growth ErC50 mg/L at 72 h	*Experiment B: Growth ErC50 mg/L at 72 h*	*Difference: Growth ErC50 mg/L at 72 h*
>320	>320	0

Remarks - Results	Inhibition of algal growth was due to a reduction in light intensity and not a toxic effect of the test substance. Algal biomass 72 h E_bC50 values from experiment A and B results were 280 mg/L and 42 mg/L, respectively, indicating that the biomass changes observed were predominantly due to reduced light rather than toxicity.

CONCLUSION The test material did not inhibit algal growth under the conditions tested.

TEST FACILITY Safepharm (2002j)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test referenced as EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test and USEPA Draft Ecological Effects Test Guidelines OPPTS 850.6800.
Inoculum	Activated sewage sludge (aeration stage), Severn Trent Water Plc Sewerage Treatment Plant (predominantly domestic sewage).
Exposure Period	3 hours
Concentration Range Nominal	1000 mg/L
Remarks – Method	Range-finding and definitive tests were performed. Testing of a reference material (3,5-dichlorophenol) verified the suitability of the test inoculum. The test substance was dissolved in water to generate a stock solution (SS; 2000 mg/L). An aliquot of SS was dispersed with synthetic sewage (16 mL), activated sludge (200 mL) and water to a final volume of 500 mL, giving the required concentration of 1000 mg/L. Three replicate vessels were tested. pH 8.0 (acceptable). Temperature 21°C. Vessels were aerated during the tests, and O_2 consumption rates were monitored. At a concentration of 1000 mg/L, no undissolved test material was observed.
RESULTS	
IC50	> 1000 mg/L
NOEC	1000 mg/L
CONCLUSION	The test substance did not inhibit activated sludge microorganisms.
TEST FACILITY	Safepharm (2002k)

9. RISK ASSESSMENT

9.1.1. Environment – exposure assessment

The environmental safety controls and use pattern for the notified chemical would indicate a limited potential for its release into the environment.

The notified chemical is readily soluble in water; however, aquatic release of the formulation containing the notified chemical is considered unlikely and after drying the notified chemical is likely to be stable within an inert matrix on printed paper products.

Emptied ink cartridges containing a residue of notified chemical will be sent to landfill for disposal. In a landfill, the notified chemical is expected to be immobile, and eventually it will degrade through biotic and abiotic processes, and consequently, should not pose a significant exposure hazard to the environment.

A proportion of the paper products containing the notified chemical may form litter; however, the expected small quantity and stable form is unlikely to pose an unacceptable risk to the environment.

Wastewaters from paper recycling facilities are expected to contain small quantities so the notified chemical, with most adsorbed to solids and settled as sludges within on-site WWTPs. Incineration of waste paper and sludges will destroy the compound with the generation of water vapour and oxides of carbon and nitrogen. Raw wastewaters are typically treated prior to discharge to sewer. While it is not possible to quantify a WWTP effluent discharge concentration, a model has been developed with the following assumptions: 50% of printed paper is recycled; 50% of the notified chemical on the paper is discharged to the on-site WWTP; 50% of this is in the supernatant effluent discharged to sewer; no degradation of the notified chemical occurs in the WWTP; and the discharge from the WWTP contributes 1% of the total Australian annual wastewater flow of 1.46×10^{12} L/annum. Given these assumptions, the predicted environmental concentration (PEC) of the notified chemical would be < 0.017 mg/L.

9.1.2. Environment – effects assessment

The notified chemical is practically non-toxic to aquatic organisms and is unlikely to bioaccumulate. It is also unlikely to adversely affect sewage sludge micro-organisms if it is discharged to sewer. However, the notified chemical is not readily biodegradable or hydrolysable and may persist in the aquatic environment until eventually degraded through biotic and abiotic processes. By dividing the lowest toxicity data of > 100 mg/L by a safety factor of 100, a predicted no effect concentration (PNEC) for aquatic organisms of > 1 mg/L has been derived. The notified chemical has low acute and chronic toxicity to mammalian species via oral (ie. NOEL > 100 mg/kg/day) or dermal (LD50 > 5000 mg/kg bw) exposure routes and is unlikely to pose an adverse risk to wildlife species which are unlikely to be exposed to the notified chemical based on the proposed use pattern.

9.1.3. Environment – risk characterisation

A PEC/PNEC ratio of < 0.017 for aquatic ecosystems via sewer discharge indicating a low environmental risk. This conclusion is in agreement with a preliminary risk assessment undertaken in accordance with the principles of EU Directive 93/67/EEC, provided by the notifier, which also found that the most likely cause of environmental release of the notified chemical was via discharge of effluent from waste paper recycling; however, with aquatic PECs of 6.78×10^{-6} mg/L (continental) and 2.09×10^{-5} mg/L (regional) a low environmental risk was predicted.

The notified chemical will interact with other components to form a stable chemical matrix and, once dry, is expected to be immobile and pose little risk to the environment. The notified chemical is not likely to present a hazard to the environment when it is stored, transported, used, recycled and disposed of in the proposed manner.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

The notified chemical will be imported in pre-packed sealed cartridges. During transport and storage, workers are unlikely to be exposed to the notified chemical except when cartridges are accidentally breached.

There is low potential for worker exposure to the notified chemical when replacing spent cartridges as the ink formulations are in a liquid form and therefore are unlikely to generate residual dusts. Service technicians may occasionally experience skin contact with the notified chemical during maintenance, however, the notified chemical is at a low concentration (< 5%) in the ink formulations. Exposure to the notified chemical on printed paper is low as the dye is bound to the paper matrix.

9.2.2. Public health – exposure assessment

Public exposure through importation, transportation or storage is assessed as negligible. There is little potential for exposure during cartridge changes. Ink containing the notified chemical on the printed page is bound to the paper and is not biologically available. Public exposure is assessed as low.

9.2.3. Human health - effects assessment

The notified chemical was of low acute oral and dermal toxicity in rats (LD50 > 2000 mg/kg bw), was a slight skin irritant and a severe eye irritant in rabbits (on the basis of persistent discolouration), was not a skin sensitiser in guinea pigs, was not mutagenic in bacteria and did not induce chromosomal aberrations in mammalian cells in vitro. The NOAEL in a 28-day oral repeat dose study in rats was 140 mg/kg/day bw as a result of systemic inflammation.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is likely to be a severe eye irritant and could be harmful following repeated or prolonged exposure. However, the ink to be imported contains the notified chemical at < 5% and would not be expected to exhibit these effects. In addition, the potential for exposure is low even during printer maintenance as current printer cartridges typically are designed to release ink only onto paper or transparencies.

9.2.5. Public health – risk characterisation

Members of the public are not likely to make contact with the notified chemical during cartridge changes unless the cartridge is ruptured or otherwise tampered with. Additionally the notified chemical is present at low concentrations in a formulation which is not classified as hazardous. Ink containing the notified chemical when deposited on the printed pages is bound to the paper and is not bioavailable. Therefore, the risk to public health from exposure to the notified chemical is considered low. The public could potentially contact the ink before it is completely dry on the paper substrate but deliberate or inadvertent smudging of printed documents is not a common practice.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*. The classification and labelling details are:

R41: Risk of serious damage to eyes

and

As a comparison only, the classification of notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes. No environmental classification is derived as the notified chemical is practically non-toxic to aquatic organisms.

Eye irritant (category 1)

10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its PEC/PNEC ratio and reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is Negligible Concern to public health when used as described.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for a product containing the chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS

Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - R41 Risk of serious damage to eyes

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - ≥ 10%: R41
  - 5% ≤ concentration ≤ 10%: R36

CONTROL MEASURES

Occupational Health and Safety

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

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

Disposal

- The notified chemical should be disposed of by incineration or to landfill in accordance with State/Territory waste disposal regulations. Paper products impregnated with ink containing the notified chemical may be incinerated, recycled or landfilled.

Emergency procedures

- Spills/release of the notified chemical should be handled by mechanically collecting spilled material (eg. sweeping dried material). Avoid raising dust. Do not allow material to contaminate ground, groundwater or waterways. Prevent product from entering drains or stormwater system.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(2) of the Act:
- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

13. BIBLIOGRAPHY

Chemical Evaluation and Research Institute (2002a) Twenty-Eight-Day Repeated Dose Oral Toxicity Study of M-119 in Rats. Study Code: B11-0682. Chemical Evaluation and Research Institute, Japan (unpublished report submitted by notifier).

Chemical Evaluation and Research Institute (2002b) Mutagenicity Test of M-119 Using Microorganisms. Study Code: K01-2678. Chemical Evaluation and Research Institute, Japan (unpublished report submitted by notifier).

Chemical Evaluation and Research Institute (2002c) Chromosomal Aberration Test of M-119 Using Cultured Mammalian Cells. Study Code: K06-0916. Chemical Evaluation and Research Institute, Japan (unpublished report submitted by notifier).

Chemical Evaluation and Research Institute (2002d). Final Report: Bioconcentration Study of M-119 in Carp. Chemicals Evaluation and Research Institute, Japan (unpublished report submitted by notifier).

Chemical Evaluation and Research Institute (2002e). Final Report: Biodegradation Study of M-119 by Microorganisms. Chemicals Evaluation and Research Institute, Japan (unpublished report submitted by notifier).

Mensink, B. J. W. G., Montforts, M., Wijkhuizen-Maslankiewicz, L., Tibosch, H. and Linders, J. B. H. J (1995) Manual for Summarising and Evaluating the Environmental Aspects of Pesticides. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. Report No. 679101022.

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edn [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

Safepharm (2002a) M-119: Determination of General Physico-chemical Properties. Project No. 1307/110. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002b) M-119: Determination of Hazardous Physico-chemical Properties. Project No. 1307/111. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002c) M-119: Acute Oral Toxicity in the Rat - Acute Toxic Class Method. Project No. 1307/112. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002d) M-119: Acute Dermal Toxicity (Limit Test) in the Rat. Project No. 1307/113. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002e) M-119: Acute Dermal Irritation in the Rabbit. Project No. 1307/114. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002f) M-119: Acute Eye Irritation in the Rabbit. Project No. 1307/115. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002g) M-119: Skin Sensitisation in the Guinea Pig – Magnusson and Kligman Maximisation Method. Project No. 1307/116. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002h) M-119: Acute Toxicity to Rainbow Trout (*Onchorhynchus mykiss*). Project No. 1307/117. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002i) M-119: Acute Toxicity to *Daphnia magna*. Project No. 1307/118. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002j) M-119: Inhibition of Algal Growth caused by Coloured Test Substances. Project No. 1307/119. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (2002k) M-119: Assessment of the Inhibitory Effect on the Respiration of Activated Sewage Sludge. Project No. 1307/121. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

United Nations (2003) Globally Harmonised System of Classification and Labelling of Chemicals (GHS). United Nations Economic Commission for Europe (UN/ECE), New York and Geneva.