File No: LTD/1310

June 2007

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

FSM-004Y in PictureMate Photo Cartridge T5852

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

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

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

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

Director
NICNAS

TABLE OF CONTENTS

FULL PUBLIC REPORT 3
1. APPLICANT AND NOTIFICATION DETAILS 3
2. IDENTITY OF CHEMICAL 3
3. COMPOSITION 3
4. INTRODUCTION AND USE INFORMATION 4
5. PROCESS AND RELEASE INFORMATION 4
5.1. Distribution, transport and storage 4
5.2. Operation description 4
5.3. Occupational exposure 4
5.4. Release 5
5.5. Disposal 5
5.6. Public exposure 5
6. PHYSICAL AND CHEMICAL PROPERTIES 6
7. TOXICOLOGICAL INVESTIGATIONS 9
7.1. Acute toxicity – oral 9
7.2. Acute toxicity – dermal 9
7.3. Irritation – skin 10
7.4. Irritation – eye 11
7.5. Skin sensitisation – mouse local lymph node assay (LLNA) 11
7.6. Repeat dose toxicity 12
7.7. Genotoxicity – bacteria 14
7.8. Genotoxicity – *in vitro* 15
8. ENVIRONMENT 16
8.1. Environmental fate 16
8.1.1. Ready biodegradability 16
8.2. Ecotoxicological investigations 17
8.2.1. Acute toxicity to fish 17
8.2.2. Acute toxicity to aquatic invertebrates 17
8.2.3. Algal growth inhibition test 18
8.2.4. Inhibition of microbial activity 19
9. RISK ASSESSMENT 20
9.1. Environment 20
9.1.1. Environment – exposure assessment 20
9.1.2. Environment – effects assessment 20
9.1.3. Environment – risk characterisation 20
9.2. Human health 20
9.2.1. Occupational health and safety – exposure assessment 20
9.2.2. Public health – exposure assessment 21
9.2.3. Human health – effects assessment 21
9.2.4. Occupational health and safety – risk characterisation 23
9.2.5. Public health – risk characterisation 24
10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS 24
10.1. Hazard classification 24
10.2. Environmental risk assessment 24
10.3. Human health risk assessment 24
10.3.1. Occupational health and safety 24
10.3.2. Public health 24
11. MATERIAL SAFETY DATA SHEET 24
11.1. Material Safety Data Sheet 24
11.2. Label 24
12. RECOMMENDATIONS 25
12.1. Secondary notification 25
13. BIBLIOGRAPHY 26

FULL PUBLIC REPORT

FSM-004Y in PictureMate Photo Cartridge T5852

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Epson Australia Pty Ltd (ABN 91 002 625 783) of 3 Talavera Rd, North Ryde NSW 2113

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year)

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical names, CAS number, Molecular formula, Structural formula, Molecular weight, Spectral data, Methods of detection and determination, Purity, %wt of Non-Hazardous Impurities, and Import volume

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
UK (2006)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
FSM-004Y in PictureMate Photo Cartridge T5852

OTHER NAME(S)
Orange azo dye J-9

METHODS OF DETECTION AND DETERMINATION

METHODS *Identity (detection):* UV/Visible spectroscopy, Infrared spectroscopy, ^{1}H nuclear magnetic resonance (NMR) and electrospray ionisation liquid chromatography-mass spectrometry (ESI LC-MS).

Purity (determination/assay): HPLC

3. COMPOSITION

DEGREE OF PURITY
>80%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

ADDITIVES/ADJUVANTS
None

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be manufactured and formulated into inks overseas. It will be imported into Australia as a component of inkjet printer inks, contained within inkjet printer cartridges.

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

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

USE
The notified chemical will be used as a dye component of imported inkjet printer inks (<5% notified chemical).

The inks will be used by the public for routine but varied colour printing operations in home and small office scenarios. Sealed ink cartridges containing the notified chemical will be used as necessary to replace spent cartridges in inkjet printers.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
None known at this time. Potentially, the inkjet printer cartridges containing the notified chemical will be supplied to offices and retailers nationwide.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of ready-to-use sealed plastic inkjet cartridges of 5-100 mL volumes. The cartridges are individually wrapped in plastic and cardboard packaging, and these will be imported in bulk in cardboard cartons. The cartridges will be transported by road.

5.2. Operation description

No reformulation or repackaging of the notified chemical will occur in Australia. The products containing the notified chemical will be delivered to the end-user in the same form that they will be imported.

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 or replaced into the inkjet printer by office workers, service technicians or consumers.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Importation/Waterside workers	10	4 hrs per day	70 days per year
Storage and transport	100	6 hrs per day	240 days per year
Office workers, service technicians, consumers	10,000	<0.1 hrs per day	20 day per day

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. The cartridges will be distributed to a number of outlets, where the cardboard cartons will be opened and boxes containing individual cartridges will be stacked on shelves.

Both office workers and service technicians may be exposed to the notified chemical in ink while

changing printer cartridges, and service technicians may additionally be exposed during printer maintenance. Replacement of printer cartridges involves removal of the old printer cartridge from the printing machine and directly loading the new cartridge. 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.

Dermal exposure of workers may occur when handling printed media before the ink is adequately dried, especially when printing on non-absorbent materials. One kilogram of pure dye would be expected to print several million A4 paper sheets of coloured text or graphics. Under worst-case conditions, each piece of A4 paper could be assumed to incorporate 1 mg of notified chemical. After printed inks are dry, the notified chemical will be bound to the paper or other media, and is not expected to be readily available to cause exposure.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Printer ink will be imported in ready-to-use cartridges (containing <5% notified chemical). No release is expected as manufacturing and reformulation of the ink containing the notified chemical will not take place in Australia. 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. Individual container capacity, container and packaging specifications would limit the extent of release.

RELEASE OF CHEMICAL FROM USE

The ink cartridges are designed to prevent leakage and will not open during transport, use, installation or replacement. Therefore, release of ink containing the notified chemical to the environment is not expected under normal conditions of use. Installation and replacement will be contained with absorbent and disposed of in landfill.

Most of the notified chemical (>98%) will be bound to the printed paper, which will be disposed of to landfill, recycle or incinerated. Recycling of treated paper may result in the release of a proportion of the notified chemical to the aquatic compartment. Waste paper is repulped using a variety of chemical treatments, which result in fibre separation and ink detachment from the fibres. The waste is expected to go to trade waste sewers. Approximately 50% of the ink printed on paper will enter paper recycling of which a proportion of the ink is expected to be recovered during recycling. While most may partition to water, due to the low percentage of the notified chemical in these inks and the widespread use, release to the aquatic compartment from any given recycling plant will still be low based on worst case assumptions. Any chemical absorbed to sludge during recycling process will be disposed of to landfill.

5.5. Disposal

The total import volume of the notified chemical will ultimately be disposed as normal office/domestic waste that will end up in either landfill or be incinerated. Some waste paper printed with the ink may be disposed of directly to landfill with the notified chemical bound to the paper. Some will enter the paper recycling process. Used cartridges may be sent to recycling and disposal centres. The cartridges will be broken down into component parts for recycling. Residual ink (<2% of the notified chemical) left in the empty cartridges will be separated from the cartridges and incinerated during the recycling of the cartridges.

Any notified chemical that is incinerated is expected to thermally decompose to form predominantly simple organic compounds and various salts. Similarly, notified chemical that is disposed of to landfill should eventually degrade.

5.6. Public exposure

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

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Reddish brown powder, forming a blood red aqueous solution upon dissolution.

Melting Point/Freezing Point >315ºC at 100.7 kPa

METHOD Differential scanning calorimetry according to EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks The substance decomposed without melting, starting at ~315°C.
TEST FACILITY SafePharm (2005a)

Boiling Point Not determined

Remarks The notified chemical decomposed prior to melting.
TEST FACILITY SafePharm (2005a)

Density 1,520 kg/m^3 at 21.4 ± 0.5ºC

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks The relative density of the notified chemical was determined by gas comparison pycnometry.
TEST FACILITY SafePharm (2005a)

Vapour Pressure <2.8 x 10^{-5} kPa at 25ºC

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Value shown is the highest extrapolated estimate, based on readings at 250ºC using a vapour pressure balance.
TEST FACILITY SafePharm (2006a)

Water Solubility 16.0-18.1% (w/w) at 20.0 ± 0.5ºC

METHOD The method used was based on EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method. Samples of the notified chemical could not be prepared at five times the saturation level, as recommended in the test guideline, as the saturation point was unable to be determined. No analysis could be performed due to the high solubility producing unfilterable mixtures. Therefore, the water solubility was estimated based on visual inspection.
TEST FACILITY SafePharm (2005a)

Hydrolysis as a Function of pH Hydrolytically stable

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

pH	*T (°C)*	*$t_{½}$ <hours or days>*
4	25	>365
7	25	>365
9	25	>365

Remarks The preliminary test showed less than 10% hydrolysis (by HPLC) after 5 days at 50ºC in buffers of pH 4, 7 and 9, which is estimated to be equivalent to a half-life of >1 year at 25ºC at any pH.
TEST FACILITY SafePharm (2005a)

Partition Coefficient (n-octanol/water) log P_{ow} at 22°C < -3.47

METHOD EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks Analytical Method: HPLC. No significant deviations from the test protocol (Shake Flask Method) were reported.

It is evident from the information obtained in the hydrolysis test and data relating to the pH of the test material in water that negligible hydrolysis of the sample solutions occurred during the course of the test.
TEST FACILITY SafePharm (2005a)

Adsorption/Desorption log K_{oc} <1.25 at 40°C

METHOD OECD TG 106 Adsorption - Desorption Using a Batch Equilibrium Method.
Remarks Test was performed using the HPLC screening method at pH 7. The notified chemical eluted before the standard solution of acetanilide, indicating it is highly mobile in soil or sediment.

The low adsorption properties of the notified chemical containing acidic functional groups that were determined by the HPLC estimation method were consistent with the extremely high water solubility and low partition coefficient characteristics observed in other tests. While the K_{oc} value is believed to accurately represent the affinity of the test material for the organic carbon content of soils and sewage sludge, the method guideline specifically requires the analysis of substances in an ionised form if present within the environmentally relevant pH range of 5.5 to 7.5. In addition, the mobility of the notified chemical in soil and sewage sludge may also be influenced by additional interactions other than partitioning not addressed by the test method, due to the anionic nature of the test material.

The alternative use of computer-based estimation programs and/or Quantitative Structure Activity Relationships (QSARs) for materials of this nature are considered invalid as estimates are typically derived from the partition coefficient value. Therefore, once more the possible secondary interaction originating from the anionic charges present on the test material are not addressed.
TEST FACILITY SafePharm (2005a)

Dissociation Constant Not determined

METHOD OECD TG 112 Dissociation Constants in Water.
Remarks No determination of dissociation constant was possible by Methods described in TG 112 of the OECD Guidelines for Testing Chemicals, 12 May 1981, as the predicted values were outside the range of the prescribed test methods. Estimates were obtained using specialist software (ACD/I-Lab Web Service (ACD/pKa 8.03). the results of these predictions are as follows:

Functional Group	Predicted pKa
Loss of protons above pKa	13.4 to 17.9
Loss of protons above pKa	-1.3 to 0.28
Gain of protons below pKa	-1.4 to -2.4

As the salts are of very strong acids, the notified chemical will remain dissociated throughout the environmental pH range of 4-9.
TEST FACILITY SafePharm (2005a)

Particle Size

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

Range (μm)	*Method used*	*Mass (%)*
<100 μm	100 μm sieve	22.2
<10.2 μm	Cascade impactor	9.94
<5.4 μm	Cascade impactor	2.29

Remarks Too few particles were of a size <10.2 μm to allow for accurate measurement of the mass median aerodynamic diameter (MMAD).
TEST FACILITY SafePharm (2005a)

Flash Point Not determined.

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks Not applicable as the notified chemical is a solid with low vapour pressure.

Flammability Not highly flammable.

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks No ignition was observed in a dried sample of the notified chemical during 2 minutes of an applied Bunsen burner flame.
TEST FACILITY SafePharm (2006a)

Autoignition Temperature 317ºC

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
TEST FACILITY SafePharm (2006a)

Explosive Properties Does not have explosive properties.

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks Tests for thermal, shock and friction sensitivity gave negative results.
TEST FACILITY SafePharm (2006a)

Reactivity

Remarks Based on the chemical structure and experience in use the test material is predicted to be stable under normal conditions. The notified chemical decomposes above 315ºC.

Surface Tension 69.8 mN/m at 20.8 ± 0.5ºC (not surface-active)

METHOD EC Directive 92/69/EEC A.5 Surface Tension.
Remarks By the ISO 304 ring method, the surface tension of a 1.00 g/L solution of the notified chemical was determined using an interfacial tension balance with the result not being corrected using the Harkins-Jordan correction table as the correction was not considered applicable to the apparatus used. The notified chemical is not a surface-active substance.
TEST FACILITY SafePharm (2005a)

Oxidising Properties Negative (predicted)

METHOD EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks Based on the chemical structure of the notified chemical, it not predicted to display oxidising properties.
TEST FACILITY SafePharm (2006a)

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result		*Assessment Conclusion*
Rat, acute oral	LD50 > 2,000 mg/kg bw	low toxicity
Rat, acute dermal	LD50 > 2,000 mg/kg bw	low toxicity
Rabbit, skin irritation		slight irritant
Rabbit, eye irritation		slight irritant
Mouse, skin sensitisation (Local Lymph Node Assay)		non-sensitiser
Rat, oral repeat dose toxicity - 28 days.		NOEL = 27 mg/kg bw/day NOAEL = 160 mg/kg bw/day
Genotoxicity - bacterial reverse mutation		non mutagenic
Genotoxicity – *in vitro* mammalian cytogenicity		non genotoxic

7.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical (>80% pure)
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method. EC Directive 92/69/EEC B.1tris Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/Sprague-Dawley CD
Vehicle	Distilled water
Remarks - Method	Animals were evaluated for deaths or overt signs of toxicity 30 mins and 1, 2 and 4 hours after dosing, then once daily for fourteen days. At the end of the observation period, the animals were sacrificed and subjected to gross pathological examination.

RESULTS

Group	*Number and Sex of Animals*	*Dose* mg/kg bw*	*Mortality*
1	3F	300	0
2	3F	2,000	0
3	3F	2,000	0

* Administered to result in dose of the pure chemical shown.

LD50	>2,000 mg/kg bw
Signs of Toxicity	No signs of systemic toxicity were observed in any animals. No changes in the animals' bodyweight were observed at any dose level.
Effects in Organs	No abnormalities were observed at necropsy.
Remarks - Results	None.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	SafePharm (2005b)

7.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical (>80% pure)
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 CD
Vehicle	Dried arachis oil BP
Type of dressing	Semi-occlusive
Remarks - Method	The notified chemical was applied to ~10% of the total skin surface area of the test animal.

RESULTS

Group	*Number and Sex of Animals*	*Dose* mg/kg bw*	*Mortality*
1	5M	2,000	0
2	5F	2,000	0

* Administered to result in dose of the pure chemical shown.

LD50	>2,000 mg/kg bw
Signs of Toxicity - Local	No eschar or oedema was observed at the site of application. Red/brown-coloured staining was observed at all treatment sites 1 day after treatment, which prevented the evaluation of erythema.
Signs of Toxicity - Systemic	None. All animals showed the expected gains in body weight over the observation period.
Effects in Organs	No abnormalities were observed at necropsy.
Remarks - Results	None.

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

TEST FACILITY — SafePharm (2006b)

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	One male, two females
Vehicle	Distilled water
Observation Period	7 days
Type of Dressing	Semi-occlusive.
Remarks - Method	The test animals were exposed on the dorsal/flank area to the notified chemical for 3 minutes, 1 hour, or 4 hours. Observations were made at 1, 24, 48 and 72 hours, and at 7 days after exposure.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0	1	1	1	72 hours	0
Oedema	0	0.67	0.67	1	48 hours	0

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

Remarks - Results — The notified chemical induced a primary irritation index of 1.0.
All effects were fully reversible by 24 hours (1 rabbit) to 7 days (two rabbits) after exposure.

CONCLUSION — The notified chemical is a slight irritant to the skin.

TEST FACILITY — SafePharm (2005c)

7.4. Irritation – eye

TEST SUBSTANCE	Notified chemical (>80% pure)
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion. EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Observation Period	72 hours
Remarks - Method	The notified chemical was instilled as a 10% w/w aqueous preparation, with a pH of 8.9. Observations of effects were made at 1, 24, 48 and 72 hours after instillation. Practically none to moderate initial pain reactions were experienced by the test animals upon installation of the notified chemical solution. Local anaesthetic was administered to the third animal before treatment.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0	0.33	0.33	1	24 hours**	0
Conjunctiva: chemosis	0	0	0	0	0	0
Conjunctiva: discharge	0	0	0	1	1 hour**	0
Corneal opacity	0	0	0	0	0	0
Iridial inflammation	0	0	0	0	0	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.
** These observations had resolved by the next evaluation.

Remarks - Results	Brown staining of the fur was observed around all treated eyes during the observation period.
CONCLUSION	The notified chemical is a slight irritant to the rabbit eye.
TEST FACILITY	SafePharm (2005d)

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

TEST SUBSTANCE	Notified chemical (>80% pure)
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay. EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay).
Species/Strain	Mouse/CBA/Ca
Vehicle	Dimethyl formamide (DMF)
Remarks - Method	A preliminary screening study on a single mouse, treated with 10% (w/w) notified chemical, was performed to determine its toxicity potential. This mouse was treated on the dorsal surface of the ear daily for three days. In the main test, three groups of four mice were treated on the dorsal surface of the ear with 2.5, 5, or 10% (w/w) notified chemical in DMF for three consecutive days. A fourth group was treated with DMF alone. Five days after administration, all mice were injected with ^{3}H-methyl thymidine, five hours after this injection, the mice were sacrificed and their lymph node cells extracted. A laboratory historical positive control was used (recent relative to the study date).

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (SI) (Test/Control Ratio)*
Notified chemical		
0 (vehicle control)	704.63	N/A
2.5	679.52	0.96
5	764.89	1.09
10	1240.58	1.76
α-hexylcinnamaldehyde (positive control)		
5	Unknown	2.64
10	Unknown	8.36
25	Unknown	12.94

Remarks - Results

No deaths or signs of systemic toxicity were observed in any animals during the study. Black staining of the fur and ears was noted one hour post-dosing on all three days.

Despite an apparent dose-dependency in the observed SI values, the notified chemical is considered to be a non-sensitiser as no SI value was greater than 3 (in accordance with the test guideline).

The historical positive control yielded positive results. No explanation was given as to why a lower maximum concentration of the notified chemical (10% c.f. 25% positive control) was used in the test. It is unknown whether 25% notified chemical would yield an SI value >3. It was not stated why 10% was chosen as the highest dose, except that red staining of the ears was observed in the preliminary test.

CONCLUSION

At the concentrations of notified chemical used in the test, there was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY

SafePharm (2005e)

7.6. Repeat dose toxicity

TEST SUBSTANCE

Notified chemical (>80% pure)

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).
US EPA Health Effects Test Guidelines, OPPTS 870.3050 Repeated Dose 28-Day Oral Toxicity Study in Rodents.

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

Route of Administration: Oral – gavage

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

Vehicle: Dried arachis oil BP

Remarks - Method: No significant deviations from protocol.

RESULTS

Group	*Number and Sex of Animals*	*Dose* mg/kg bw/day*	*Mortality*
I (control)	5M, 5F	0	0
II (low dose)	5M, 5F	5	0
III (intermediate dose I)	5M, 5F	27	0
IV (intermediate dose II)	5M, 5F	160	1M, 1F
V (high dose)	5M, 5F	536	1M, 2F
VI (control recovery)	5M, 5F	0	0
VII (high dose recovery)	5M, 5F	536	0

* Administered to result in the dose of the pure chemical shown.

Mortality and Time to Death

One female receiving 536 mg/kg bw/day was killed *in extremis* on Day 27.

One male and one female of both the intermediate dose II and the high dose groups were found dead during the treatment period, apparently due to maladministration of the notified chemical during dosing.

Clinical Observations

One female showed hunched posture from Day 24. Marked deterioration of physical condition on Day 27 led to her death *in extremis*. Clinical signs included tiptoe gait, dehydration, staining around the eyes and anogenital region, and piloerection.

Increased salivation was observed in all high dose animals throughout most of the treatment period, and in three males and one female treated with 160 mg/kg bw/day on isolated occasions after Day 10. This was considered a common consequence of oral administration of an unpalatable or irritant chemical, and of no toxicological significance.

Functional Observations

No treatment-related changes in functional parameters were observed.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Females receiving 536 mg/kg bw/day showed increased white blood cells and decreased plasma albumin levels compared to controls.

Males receiving 536 mg/kg bw/day showed a reduced activated partial thromboplastin time (APTT) at the end of the treatment period. In addition, these animals showed increased levels of aspartate aminotransferase, alkaline phosphatase, creatinine, potassium and calcium, and an increased albumin/globulin ratio. Decreased levels of plasma sodium, total protein, triglycerides, and bilirubin were observed in these animals. After the recovery period, statistically significant differences from control levels were restricted to increased potassium levels. Decreased plasma sodium levels were also observed in males treated with 160 mg/kg bw/day.

An increase in micturition, with an accompanying decrease in urine specific gravity, was observed in high-dose animals.

Effects in Organs

Upon terminal sacrifice, the stomach and/or gastrointestinal tract contained dark red contents at 536 mg/kg bw/day, which was reversible after the recovery period. This was also observed for the female killed *in extremis*.

No treatment-related changes in organ weights were observed.

Kidney: Hypertrophy of the epithelial lining of the distal tubules and collecting ducts, and a higher incidence and severity of basophilic tubules was observed in high dose animals of both sexes. This condition had partially regressed after the recovery period.

Adrenal glands: Cortical vacuolisation was only observed in males treated with 536 mg/kg bw/day, and this condition had partially regressed after the recovery period.

Stomach: Acanthosis/hyperkeratosis of the limiting ridge was seen in high dose animals of either sex. In addition, agglomeration of secretion in mucosal cells, and superficial mucosal basophilia was observed in a few animals of either sex, but was not convincingly related to treatment. Regression of gastric changes was observed amongst the animals of the high

dose recovery group.

Mesenteric lymph node: Accumulations of red/brown pigment within the lymph node were seen in animals of either sex from the high dose treatment group, and this condition persisted until the end of the recovery period.

Remarks – Results

All of the adverse effects were observed in animals treated with the high dose, 536 mg/kg bw/day. Many of the findings at this dose seem to be related to the irritant nature of the notified chemical (eg stomach and renal tubule changes). Many irritant effects were more pronounced in males; this may be explained by their higher relative body weights resulting in a greater actual dose.

Although treatment-related effects such as decreased plasma sodium were observed at 160 mg/kg bw/day, these were considered to be reversible, based on the fact that this result was reversible in the 536 mg/kg bw/day recovery group. Increased salivation after Day 10 was considered normal after oral dosing of an irritant chemical. Due to the absence of degenerative changes, the effects observed at 160 mg/kg bw/day dose were not considered adverse effects.

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) was established as 160 mg/kg bw/day in this study, based on the absence of the more serious adverse effects seen at higher doses.

The No Observed Effect Level (NOEL) was considered to be 27 mg/kg bw/day in this study, based on the absence of any toxicologically relevant effects at this dose.

TEST FACILITY SafePharm (2006c)

7.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical (>80% pure)

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100
E. coli: WP2uvrA$^-$

Metabolic Activation System Phenobarbitone/β-naphthoflavone-induced rat liver S9 microsome mix

Concentration Range in Main Test a) With metabolic activation: 50-5,000 µg/plate*
b) Without metabolic activation: 50-5,000 µg/plate*

* A correction factor was applied to achieve the concentration of pure chemical shown.

Vehicle DMSO

Remarks - Method As the notified chemical is an azo compound, the OECD test method strongly recommends the use of a modified Ames test with a reducing pre-incubation step to improve sensitivity (eg Prival and Mitchell, 1982). However, such a modification was not used in this test.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	>5,000	>5,000	>5,000	>5,000
Test 2	-	>5,000	>5,000	>5,000
Present				
Test 1	>5,000	>5,000	>5,000	>5,000
Test 2	-	>5,000	>5,000	>5,000

Remarks - Results A red colour in the plates was observed at doses of ≥50 µg/plate, but this

did not interfere with the scoring of the revertant colonies. The positive controls yielded positive results, indicating that the test system was functioning appropriately.

As a reductive pre-incubation step was not used in this study, the result (non-mutagenic) is indicative only of the conditions of this particular Ames test. Many carcinogenic azo dyes test negative in Ames tests without the use of a modified test (SCCNFP, 2002).

CONCLUSION

The notified chemical was not mutagenic to bacteria under the conditions of the test. However, this negative result does not take into account reductive metabolism, and the test is therefore considered inconclusive.

TEST FACILITY

SafePharm (2005f)

7.8. Genotoxicity – *in vitro*

TEST SUBSTANCE

Notified chemical (>80% pure)

METHOD

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

Cell Type/Cell Line	Chinese Hamster Lung (CHL) cell line
Metabolic Activation System	Phenobarbitone/β-naphthoflavone-induced rat liver S9 microsome mix
Vehicle	Eagle's Minimal Essential Medium (MEM)
Remarks - Method	Positive controls used were mitomycin C (0.05-0.1 µg/mL; used without metabolic activation) and cyclophosphamide (5 µg/mL; used with metabolic activation). The concentration of S9 mix was reduced from 5% in Test 1 to 2% in Test 2, but no explanation was given for why this modification was made.

Metabolic Activation	*Test Substance Concentration (µg/mL)***	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 156.25*, 312.5*, 625*, 1250, 2500, 5000	6 hrs	24 hrs
Test 2	0*, 19.53, 39.06, 78.13*, 156.25*, 234.38, 312.5*	24 hrs	24 hrs
Present			
Test 1 (5% S9)	0*, 156.25*, 312.5*, 625*, 1250, 1875, 2500	6 hrs	24 hrs
Test 2 (2% S9)	0*, 78.13, 156.25, 312.5*, 468.75, 625*, 937.5*	6 hrs	24 hrs

*Cultures selected for metaphase analysis.
** A correction factor was applied to achieve the concentration of pure chemical shown.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	>5,000	>625	>5,000	negative
Test 2	>156.25	>156.25	>312.5	negative
Present				
Test 1	>1,250	>625	>2,500	negative
Test 2	>1,250	>625	>937.5	negative

Remarks - Results

Low-level structural chromosomal aberrations, at higher levels than those observed in the negative controls, were observed in Test 1 at ≥156.25 µg/mL notified chemical in the absence or presence of S9 mix. This result was also seen in Test 2 without S9 mix; the highest levels were observed in the cells exposed for 24 hours. However, none of these apparent increases over control levels were found to be statistically significant, and

	often were not dose-dependent.
CONCLUSION	The notified chemical was not clastogenic to CHL cells treated *in vitro* under the conditions of the test.
TEST FACILITY	SafePharm (2006d)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Sewage treatment microorganisms
Exposure Period	28 days
Auxiliary Solvent	Nil
Analytical Monitoring	Dissolved Oxygen
Remarks - Method	An amount of test material (116 mg) was dissolved in culture medium with the aid of ultrasonication for approximately 5 minutes and the volume adjusted to 100 mL to give a 1,000 mg/L stock solution. An aliquot (24 mL) of this stock solution was dispersed in a final volume of 6 L of inoculated culture medium to give a test concentration of 4.0 mg/L. For the purposes of the test, a standard material, sodium benzoate, was used.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
3	7	3	59
7	15	7	73
14	12	14	80
21	13	21	81
28	12	28	82

Remarks - Results	The observed variation in degradation rates on different sampling days was considered to be due to variation in respiration rates between control and test vessels. The toxicity control attained 26% degradation after 14 days thereby confirming that the test material was not toxic to the sewage treatment microorganisms used in the study. The standard material, sodium benzoate, attained 80% degradation after 14 days and 82% degradation after 28 days thereby confirming the suitability of the test method and culture conditions.
CONCLUSION	The test material cannot be considered to be readily biodegradable under the strict terms and conditions of OECD Guideline 301D.
TEST FACILITY	SafePharm (2006e)

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 203 Fish, Acute Toxicity Test - semi-static. EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - semi-static.
Species	*Oncorhynchus mykiss*
Exposure Period	96 h
Auxiliary Solvent	Nil
Water Hardness	100 mg $CaCO_3$/L
Analytical Monitoring	HPLC analysis of test concentrations.
Remarks – Method	Based on the results of the range-finding test, a "limit test" was conducted at a concentration of 100 mg/L to confirm that at the maximum concentration given in the OECD/EEC Test Guidelines, no mortalities or sub-lethal effects of exposure were observed. An amount of test material (2,320 mg) was dissolved in dechlorinated tap water and the volume adjusted to 1 L to give a 2,000 mg/L stock solution. This was further diluted in a final volume of 20 L and stirred using a flat bladed mixer for approximately 1 minute to give the 100 mg/L test concentration.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
100	-	20	0	0	0	0	0

LC50	>100 mg/L at 96 hours.
NOEC	100 mg/L at 96 hours.
Remarks – Results	The control was observed to be a clear, colourless solution throughout the duration of the test. The 100 mg/L test preparation was observed to be a very dark red coloured solution throughout the duration of the test. Analysis of the test preparation at 0, 24 and 96 h showed measured test concentrations to range from 85% to 107% of nominal and so it was considered justifiable to estimate the LC50 values in terms of the nominal test concentrations only.
CONCLUSION	The notified chemical is not harmful to *Oncorhynchus mykiss*.
TEST FACILITY	SafePharm (2005g)

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. EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Nil
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC analysis of test concentrations.
Remarks - Method	Based on the results of the range-finding test, a "limit test" was conducted at a concentration of 100 mg/L to confirm that at the maximum concentration given in the OECD/EEC Test Guidelines, no

immobilisation or adverse reactions were observed.

An amount of test material (116 mg) was dissolved in dechlorinated tap water and the volume adjusted to 1 L to give the 100 mg/L test concentration.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
100	-	20	0	0

LC50	>100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks - Results	No immobilisation was observed at the test concentration of 100 mg/L. It was considered unnecessary and unrealistic to test at concentrations in excess of 100 mg/L. The control test media was observed to be a clear colourless solution and the 100 mg/L test media was observed to be a dark red coloured solution throughout the duration of the test. Analysis of the test preparation at 0 and 48 h showed measured test concentrations to range from 83 to 102% of nominal and so it was considered justifiable to estimate the LC50 values in terms of the nominal test concentrations only.

CONCLUSION — The notified chemical is not harmful to *Daphnia magna*.

TEST FACILITY — SafePharm (2006f)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE — Notified chemical.

METHOD — OECD TG 201 Alga, Growth Inhibition Test.
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species	*Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 100 mg/L Actual: 104-108% of Nominal
Auxiliary Solvent	Nil
Analytical Monitoring	HPLC
Remarks - Method	Based on the result of the range-finding test a “limit-test” was conducted at a concentration of 100 mg/L to confirm that at the maximum concentration given in the OECD/EEC Test Guidelines no effect on algal growth was observed. An amount of test material (116 mg) was dissolved in culture medium and the volume adjusted to 500 mL to give a 200 mg/L stock solution. An aliquot (250 mL) of this stock solution was mixed with algal suspension (250 mL) to give the required test concentration of 100 mg/L. A Student’s t-test incorporating Bartlett’s test for homogeneity of variance was carried out on the area under the growth curve data at 72 h for the control and the 100 mg/L test concentration to determine any statistically significant differences between the test and control groups.

RESULTS

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

Remarks - Results

Analysis of the test preparation at 0 and 72 hours showed measured test concentrations to range from 104% to 108% of nominal and so it was considered justifiable to estimate the EC50 values in terms of the nominal test concentrations only. It was considered unnecessary and unrealistic to test at concentrations in excess of 100 mg/L.

There were no statistically significant differences (P≥0.05) between the control and 100 mg/L test group and therefore, the NOEC was 100 mg/L.

The cell concentration of the control cultures increased by a factor of 21 after 72 hours, which was in line with the OECD Guideline that states that any enhancement must be at least by a factor of 16 after 72 hours.

CONCLUSION

The notified chemical is not harmful to *Scenedesmus subspicatus.*

TEST FACILITY

SafePharm (2005h)

8.2.4. 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
US EPA Draft Ecological Effects Test Guidelines OPPTS 850.6500.

Inoculum

Activated sewage sludge.

Exposure Period

3 hours

Concentration Range

Nominal: 1,000 mg/L

Remarks – Method

Based on the results of a range-finding test, a "limit test" was conducted at a concentration of 1,000 mg/L (three replicates) to confirm that at this concentration no effect on respiration of the activated sewage sludge was observed.

An amount of test material (2,320 mg) was dissolved in water and the volume adjusted to 1000 mL to give a 2000 mg/L stock solution. An aliquot (250 mL) of this stock solution was dispersed with synthetic sewage (16 mL), activated sewage sludge (200 mL) and water, to final volume of 500 mL, to give the require concentration of 1,000 mg/L. Analysis of the concentration, homogeneity and stability of the test material in the test preparations was not appropriate to the Test Guidelines. For the purpose of the test a reference material, 3,5-dichlorophenol was used.

RESULTS

IC50

>1,000 mg/L

NOEC

1,000 mg/L

Remarks – Results

The test validation criteria were satisfied. Observations made throughout the test period showed that at the test concentration of 1,000 mg/L no undissolved test material was visible. Validation criteria were satisfied for the test.

CONCLUSION

The notified chemical is not harmful to activated sludge microorganisms.

TEST FACILITY

SafePharm (2006g)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Manufacture, reformulation and packaging into end-use containers occurs overseas, and release is not expected. After use, printed paper may be disposed of by incineration, to landfill or be recycled. Notified chemical disposed of to landfill may be mobile, however, the low proposed annual import volume, and diffuse release throughout Australia will mitigate any potential exposure while the notified chemical slowly degrades.

In Australia, approximately 50% of printed paper is recycled. The following Predicted Environmental Concentration calculation assumes this 50% recycling, and as a worst case scenario assumes no recovery within STPs:

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	365	days/year
Daily chemical release	1.37	kg/day
Water use	200	L/person/day
Population of Australia (millions)	20.496	million
Removal within STP	0%	
Daily effluent production	4,099	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River	0.33	µg/L
PEC - Ocean	0.03	µg/L

9.1.2. Environment – effects assessment

Aquatic ecotoxicity data were provided for three trophic levels, with all trophic levels having an EC50 value >100 mg/L. The following Predicted No-Effect Concentration has been calculated using an assessment factor of 100.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50	>100	mg/L
Assessment Factor	100	
PNEC	>1,000	µg/L

9.1.3. Environment – risk characterisation

Based on the above PEC and PNEC values, the following Risk Quotient has been calculated.

Risk Assessment	PEC (µg/L)	PNEC (µg/L)	Q
Q - River:	0.33	>1,000	<0.00033
Q - Ocean:	0.03	>1,000	<0.00003

This indicates that the current import volume and use pattern is expected to pose an acceptable risk to the aquatic environment.

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 will not be exposed to the notified chemical except in the unlikely event that packaging and cartridges are accidentally breached.

There is low potential for office workers to be exposed to the notified chemical in inks (<5%

concentration) when replacing spent cartridges. The design of the cartridges is expected to be such that they can be easily replaced without dermal exposure to ink. Accidental contact is expected to be minimal, but may occur. Workers are expected to avoid direct contact with inks to avoid staining of their skin and/or clothing.

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. The extent of binding of the notified chemical within the ink matrix on media is expected to be based on the other components of the ink (eg polymers) and the components and properties of the media (eg absorbency, hydrophobicity, paper coatings or other ingredients). The extent of binding is therefore likely to be a combination of how well integrated the notified chemical will become with these components upon drying of the ink. The components of the ink are likely to be more important for the purposes of risk assessment, as a wide range of media is available for use inkjet printers. It is expected that overall, inks will be designed to maximise fastness of dye components, to extend the life of inkjet prints. Therefore, minimal dye might be expected be released from dried prints upon contact with skin.

The most probable exposure of office workers to the notified chemical will be to wet ink on freshly printed media. The extent of dermal exposure of workers to wet ink on paper or other non-absorbent substrate has been estimated by the notifier. One kilogram of pure dye would be expected to produce several million sheets of A4 coloured text or graphics. Under worst-case conditions, each piece of A4 paper could be assumed to incorporate a maximum of 1 mg of notified chemical. Based on a 50% transfer on contact when handling printed paper or other substrate (assuming partially dry ink), and the relative contact area of fingertips and paper size:

Area of contact with finger ends (four fingers on one hand) = 8 cm^2
A4 sized paper = ~600 cm^2
% Removal = (8/600) × 0.5 × 100 = <1%
∴ Exposure to fingertips per event = <1% of 1 mg = <u><0.01 mg per event</u>.

For extensive contact with wet ink on paper or other substrate (i.e. >10 events per day) the daily exposure, assuming no washing between events, a 70 kg person and conservative estimate of 100% absorption, would be:

Daily exposure = (<0.01 (mg/event)×10) ÷ 70 = <u>~0.0014 mg/kg bw/day</u>.

It is not possible to estimate the level of exposure that is expected for the smaller arylamine species that may be derived from the notified chemical.

Service technicians may occasionally experience skin contact with the notified chemical (<5% in the ink) during maintenance of inkjet printers. The exposure of these workers to the notified chemical might be expected to be quite frequent; however, these workers may service a great variety of different inkjet printers during a day, most of which would not contain inks formulated with the notified chemical. In addition, their exposure is likely to be limited to contact of inks with their fingertips during the handling and cleaning of printer components. Therefore, the exposure of these workers is expected to be minimal and infrequent.

9.2.2. Public health – exposure assessment

Public exposure through importation, transportation or storage is expected to be negligible. Such exposure could only occur in the extremely unlikely event of an accident where crates, boxes, packaging and cartridges were ruptured, liberating inks containing the notified chemical.

The exposure of the public to the notified chemical through the use of inkjet printer inks is expected to be identical to that experienced by office workers during the changing of cartridges, printing onto paper and other media, and handling dried, printed pages. Members of the public may be expected to change inkjet printer cartridges less frequently than would office workers, as domestic applications are often smaller.

9.2.3. Human health – effects assessment

Toxicokinetics, metabolism and distribution:

Many azo dyes are unlikely to be absorbed through the skin, as intact azo dyes often do not penetrate the skin because of their size and polarity (Øllgaard *et al*, 1998). These smaller species may undergo percutaneous absorption, dependent on their properties. There was no evidence

from the toxicological investigations to suggest that the notified chemical was absorbed following dermal exposure. However, bacterial skin microflora have been speculated to be able to break down azo dyes into smaller species through azo reduction, which may be more readily absorbed (SCCNFP, 2002).

Highly sulfonated azo dyes are generally poorly absorbed from the intestine after oral intake. However, cleavage of the azo linkage takes place in the gastrointestinal tract, through the action of azo reductases (see below). The sulfonated aromatic amines are rapidly absorbed. Given the the systemic effects observed in the repeated dose oral toxicity study (SafePharm, 2006c), it is clear that the notified chemical can be absorbed from the gastrointestinal tract following oral exposure. It is not clear if it is absorbed intact or degraded prior to absorption, perhaps through the action of intestinal microflora.

Ultimately, the metabolites of azo dyes are excreted in the urine and bile (Brown & DeVito, 1993, referenced in Øllgaard *et al*, 1998).

General toxicity:
The notified chemical was of low acute oral and dermal toxicity in rats (LD50 >2,000 mg/kg bw). The NOAEL in a 28-day oral repeat dose study in rats was 160 mg/kg bw/day on the basis of a lack of degenerative effects at or below this dose level, and the NOEL was 27 mg/kg bw/day. Systemic adverse effects were observed in experimental animals following only high oral doses of the notified chemical (536 mg/kg bw/day), suggesting that it may display only very weak toxic properties.

In addition, the notified chemical was found to be a mild irritant, when administered in high concentrations to the skin or eye. In addition, many of the adverse effects observed in the test animals of the repeat dose oral study were thought to be due to the irritant nature of the notified chemical.

The notified chemical was not found to be a skin sensitiser, under the conditions of the mouse local lymph node assay used. However, no justification was given for why lower doses of the notified chemical were used in comparison with those of the positive control. Several azo dyes have been demonstrated to be skin sensitisers in humans, using clinical patch tests, and others have been associated with causing allergic contact dermatitis (Øllgaard *et al*, 1998). However, the structure and chemistry of the notified chemical do not resemble the structures of these sensitising azo dyes. Therefore, in combination with the negative mouse LLNA test result, the notified chemical is unlikely to cause skin sensitisation in exposed humans.

Mutagenicity:
Azo dyes as a class are a concern for their potential induction of mutagenicity and carcinogenicity. The azo linkage is the most labile portion of an azo dye molecule, and it is readily enzymatic metabolised in mammals, including man (SCCNFP, 2002). Liver azo reductase enzymes reductively cleave the molecule into component amines. Some metabolism may also occur in the cells of the bladder wall, and during percutaneous absorption. Anaerobic intestinal bacteria are also capable of catalysing reductive cleavage of the azo bond.

The aromatic amines that arise from the azo reduction of azo dyes are thought to be activated through their *N*-oxidation by cytochrome P450 isozymes (SCCNFP, 2002). These *N*-hydroxylarylamines may be further glucuronated (activated) or acetylated (inactivated), which may influence their mutagenicity (Bartsch, 1981). Under acidic pH, they form reactive nitrenium ions that can alkylate bases in DNA, particularly the nucleophilic centres in guanine. This mechanism is thought to contribute to the carcinogenicity of many azo dyes.

The notified chemical is not to expected to be reductively cleaved to release any of the restricted aromatic amines specified in either the Appendix to EC Directive 76/769/EEC (EC, 2004) or the annexes of EU SCCNFP/0495/01 (SCCNFP, 2002). However, the notified chemical can be broken by azo reduction into a number of arylamine species, all of which potentially could be mutagenic. The structure of two of these arylamine species resembles those of known human carcinogens (SCCNFP, 2002; RoC, 2005). However, the significant structural modification of these species indicates that they may be of lower concern as potential carcinogens (SCCNFP, 2002; US EPA, 2002).

In addition, azo dyes are renowned for their content of impurities, particularly for the presence of component arylamines (SCCNFP, 2002; Øllgaard *et al*, 1998). Such impurities are thought to contribute to their carcinogenicity, as these species may be more readily absorbed, and activated

as carcinogens. The HPLC trace provided by the notifier indicates that the sample of the notified chemical used contains low levels of a number of contaminants that are either more hydrophobic or more hydrophilic than the notified chemical itself (Fuji Photo Film Co. Ltd., 2005). The identity of only some of these species is known. The identified impurities are likely to display similar toxicological properties to the notified chemical. The identity of the remainder of the impurities is unknown, but these could be aromatic amine species.

The notifier supplied test results showing that the notified chemical was found to be not mutagenic in bacteria (under the conditions of the Ames test used), and it did not induce chromosomal aberrations in mammalian cells *in vitro*. However, while these results are suggestive, they do not rule out the notified chemical as a possible carcinogen. In general, the degree of correlation between mutagenicity study results and the carcinogenicity of azo dyes as a class is poor, likely due to their complex metabolism *in vivo* (Brown and DeVito, 1993, referenced in Øllgaard *et al*, 1998).

The Ames test performed was a standard test, according to OECD Test Guideline 471. However, the test guideline strongly recommends the use of alternative procedures for the detection of mutagenicity of azo dyes, as it is recognised that the standard procedure is not sufficiently sensitive for these chemicals. Modified tests, such as that of Prival and Mitchell, utilise a reductive pre-incubation step (during which the azo dye is reduced to amine species) before the test is carried out (Prival and Mitchell, 1982). This modified test is thought to yield a greater detection of mutagenic azo dyes. Because of this, NICNAS has required the notifier to perform a modified Ames test according to Prival and Mitchell, and to provide data when they are available. Based on the result of this study, further testing may be requested from the notifier.

Conclusion:
Based on the currently available data, the notified chemical cannot be classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004).

9.2.4. Occupational health and safety – risk characterisation

The notified chemical will be imported in pre-packed sealed cartridges. In addition, the notified chemical is present in the ink at <5%, and is not likely to be toxic at the highest levels of probable exposure (worst-case exposure estimate of ~0.0014 mg/kg bw/day, compared with a NOAEL of 160 mg/kg bw/day). Therefore, discounting any possibility of a risk from carcinogenicity, the expected risk of the notified chemical to the health and safety of workers is expected to be minimal.

During most operations, the probable exposure of workers to the notified chemical is expected to be low, and thus the probable OHS risk is likely to be low. Transport, storage and retail workers are unlikely to be exposed to the notified chemical except when cartridges are accidentally breached. There is low potential for office workers to be exposed to the notified chemical when replacing spent cartridges, as the notified chemical is sealed within the cartridge, and the cartridges are designed to prevent leakage. Service technicians will generally experience only infrequent exposure to the notified chemical, at levels below the levels of exposure indicated by the worst-case estimate above.

Likewise, the exposure of workers to the notified chemical on dried, printed paper is expected to be low, as the dye should remain bound within the ink matrix. Therefore, the risk to workers handling dried inkjet prints containing the notified chemical is expected to be minimal if not negligible.

However, the OHS risk of the notified chemical cannot be established without a consideration of its likelihood of degradation into potentially carcinogenic aromatic amines. Breakdown of similar azo dyes to the notified chemical has been reported, following their exposure to heat or sunlight (Brown and DeVito, 1993, referenced in Øllgaard *et al*, 1998). Given that inkjet prints are likely to be exposed to light for prolonged periods, and that preparations of the notified chemical may already contain traces of aromatic amine species, the risk presented by these species must be considered.

Chemicals which may release specific carcinogenic amines (as specified the Appendix of EU SCCNFP/0495/01) upon azo reduction are restricted in the EU (SCCNFP, 2002):

"*Azo-dyes that may release, by reductive cleavage of one or more azo groups, one or more of the aromatic amines listed in Appendix, in concentrations above 30 ppm in the finished articles, according to the testing method specified in Appendix, may not be used in textile and leather articles which have the potential of coming into direct and prolonged contact with the human skin or oral cavity.*"

While the notified chemical is not expected to break down into one of the SCCNFP-specified arylamines, it is expected to break down into species that resemble these arylamines. These species may have very different properties to the notified chemical, and they may not be as readily bound, for example, within the matrices of a dried inkjet print. It is not possible to derive any conclusions without greater knowledge of their properties. Nevertheless, the expected exposure to these species is expected to be less than that specified by the SCCNFP (30 ppm), and is likely to be less frequent than "direct and prolonged". Therefore, the risk from these breakdown species is expected to be low.

9.2.5. Public health – risk characterisation

The exposure and hazard of the notified chemical to the members of the public during the use of inkjet printers are expected to be identical or similar to that experienced by office workers. Therefore, the risk of the notified chemical to the health of the public is assessed to be low. The unlikely but potential public exposure through accidents during importation, transportation or storage is assessed as negligible.

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

10.1. Hazard classification

Based on the available data the notified chemical cannot be classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances.*

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio, the notified chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

The notified chemical is expected to present an acceptable risk to occupational health and safety when used as a component of inkjet printer inks.

10.3.2. Public health

The notified chemical presents an acceptable risk to public health when used as a component of inkjet printer inks.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical and products containing the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). They are 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 the product containing the notified 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

CONTROL MEASURES
Occupational Health and Safety

- A copy of the MSDS should be easily accessible to employees.
- Service personnel should wear cotton or disposable gloves during routine maintenance and repairs of inkjet printers.
- 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.

Public Health

- Products containing the notified chemical should be labelled with the following safety direction:
  - Avoid skin or eye contact with ink.

Disposal

- The notified chemical should be disposed of by incineration or to landfill.

Emergency procedures

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

12.1. 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 regardless of whether the notified chemical has been listed on the Australian Inventory of Chemical Substances (AICS).

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

(1) Under Section 64(1) of the Act; if
  - the importation volume exceeds one tonne per annum notified chemical; or
  - if the notified chemical is imported in any fashion other than within an inkjet ink cartridge.
  - additional mutagenicity test data is to be provided to NICNAS when it is available.

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

The Director will then decide whether a reassessment (i.e. a secondary notification and

assessment) is required.

13. BIBLIOGRAPHY

Bartsch H (1981) Metabolic Activation of Aromatic Amines and Azo Dyes. *IARC Sci Publ*. (40):13-30.

EC (2004) EC Directive 76/769/EEC, Office for Official Publications of the European Communities http://europa.eu.int/comm/enterprise/chemicals/legislation/markrestr/consolid_1976L0769_en.pdf

Fuji Photo Film Co. Ltd. (2005) (Unpublished data provided by the notifier)

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 (2004) Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

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.

Øllgaard H, Frost L, Galster J and Hansen OC (1998). Survey of Azo-Colorants in Denmark: Consumption, Use, Health and Environmental Aspects. Danish Technological Institute, Environment, Danish Environmental Protection Agency.

Prival MJ and Mitchell VD (1982) Analysis of a Method for Testing Azo Dyes for Mutagenic Activity in *Salmonella Typhimurium* in the Presence of Flavin Mononucleotide and Hamster Liver S9. *Mutat Res*. 97(2): 103-16.

RoC (2005) Report on Carcinogens, Eleventh Edition; U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program.

Safepharm (2005a), FSM-004Y: Determination of General Physico-Chemical Properties, SPL project number: 2125/0029. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005b), FSM-004Y: Acute Oral Toxicity in the Rat – Acute Toxic Class Method, SPL project number: 2125/0031. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005c), FSM-004Y: Acute Dermal Irritation in the Rabbit, SPL project number: 2125/0032. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005d), FSM-004Y: Acute Eye Irritation in the Rabbit, SPL project number: 2125/0033. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005e), FSM-004Y: Local Lymph Node Assay in the Mouse, SPL project number: 2125/0034. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005f), FSM-004Y: Reverse Mutation Assay "Ames Test" Using *Salmonella typhimurium* and *Escherichia coli*, SPL project number: 2125/0037. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005g) FSM-004Y: Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*). SPL project number: 2125/038. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2005h) FSM-004Y: Algal Inhibition Test. SPL project number: 2125/040. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006a), FSM-004Y: Determination of Hazardous Physico-Chemical Properties, SPL project number: 2125/0030. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006b), FSM-004Y: Acute Dermal Toxicity (Limit Test) in the Rat, SPL project number: 2125/0063. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006c), FSM-004Y: Twenty-eight Day Repeated Dose Oral (Gavage) Toxicity Study in the Rat, SPL project number: 2125/0035. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006d), FSM-004Y: Chromosome Aberration Test in CHL Cells *In Vitro*, SPL project number: 2125/036. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006e) FSM-004Y: Assessment of Ready Biodegradability; Closed Bottle Test. SPL project number: 2125/041. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006f) FSM-004Y: Acute Toxicity to *Daphnia magna*. SPL project number: 2125/039. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SafePharm (2006g) FSM-004Y: Assessment of the Inhibitory Effect on the Respiration of Activated Sewage Sludge. SPL project number: 2125/0028. Safepharm Laboratories Limited, Shardlow Business Park, Shardlow, Derbyshire, UK. (Unpublished report supplied by the notifier)

SCCNFP (2002) The Safety Review Of The Use Of Certain Azo-Dyes In Cosmetic Products: Opinion Of The Scientific Committee On Cosmetic Products And Non-Food Products Intended For Consumers.. SCCNFP/0495/01 (prepared in the context of Directive 76/768/EEC).

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.

US EPA (2002). TSCA New Chemicals Program (NCP) Chemical Categories. http://www.epa.gov/opptintr/newchems/pubs/cat02.htm.

Zeiger E, Anderson B, Haworth S, Lawlor T and Mortelmans K (1988) Salmonella Mutagenicity Tests: IV. Results from the Testing of 300 Chemicals. *Environ Mol Mutagen* 11(Suppl.12): 1-158