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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

CGI 113

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Ciba Specialty Chemicals P/L (ABN 97005061469) of 235 Settlement Road, Thomastown, Victoria 3074

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 identity information.
Import volume
Details of use
Identity of reformulation sites

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
Italy (2002), USA (2002)

2. IDENTITY OF CHEMICAL

OTHER NAME
TK 11005

MARKETING NAME
CGI 113

SPECTRAL DATA

ANALYTICAL METHOD	Infrared (IR) spectroscopy
Remarks	KBr pressed sample. Spectrum consistent with proposed structure.
TEST FACILITY	Ciba Specialty Chemicals (2002a).
ANALYTICAL METHOD	^{1}H nuclear magnetic resonance (NMR) spectroscopy
Remarks	Peak assignments were consistent with proposed structure.
TEST FACILITY	Ciba Specialty Chemicals (2002a).
ANALYTICAL METHOD	Mass spectroscopy (MS)
Remarks	Fragments and adductions observed were consistent with proposed structure.
TEST FACILITY	Ciba Specialty Chemicals (2002a).

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	NMR, IR, MS, elemental analysis, HPLC, GC
Remarks	Structure was confirmed by NMR, IR and Mass spectroscopy, levels of sodium, chlorine and sulphur by elemental analysis, impurities by HPLC and 2-propanol and n-hexane content by GC.

3. COMPOSITION

DEGREE OF PURITY
> 90%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)
One impurity > 1% detected.

ADDITIVES/ADJUVANTS
None

4. INTRODUCTION AND USE INFORMATION

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

Imported as a powder in 20 kg plastic lined steel drums.

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

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

USE
Component of UV-curable inks and coatings.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Ciba Specialty Chemicals

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in sealed plastic bags within 20 kg steel drums with clip-lock rings. It will be delivered to the notifier's warehouse and subsequently to ink and coating manufacturers who will ship inks and coatings to customers in 20 – 200 L steel drums. The notified chemical degrades in light and care must be taken to store in a cool, dark warehouse. Product storage requirements will be determined by components other than the notified chemical.

5.2. Operation Description

The notified chemical will be stored at the notifier's site and transported to up to three ink or coating manufacturing sites for reformulation into inks or coatings, containing 1 – 4 % notified chemical.

FORMULATION
In batch production of inks, the required quantity of the notified chemical will be weighed manually into a small scoop and added slowly with mechanical stirring to polymer resins in a 200 L stainless steel mixing tank (2 – 8 kg for each 200 kg batch) in a semi-closed process. After addition of the notified chemical, the tank will be closed for the rest of the mixing process. The method of formulation of coatings is expected to be similar. The formulated inks or coatings will be pumped in a closed process to 20 L pails or 200 L drums ready for sale to the end users.

END - USE
Inks or coatings will be applied to metal, paper or plastic substrates by standard printing or coating techniques, then exposed to UV light. During the curing process the notified chemical is partially consumed and residual traces are bound within the ink or coating matrix. Ink or coating containers and printing or coating components are washed and the aqueous wastes collected by liquid waste disposal contractors.

5.3. Occupational Exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Transport and Storage	6 – 8	2 -3 hours/day	10 – 15 days/year
Blending Operations	4	8 hours/day	50 days/year
Laboratory: QC and R&D	2	1 hour/day	20 days/year
Printing or coating	6 – 8 per site	4 hours/day	Daily

EXPOSURE DETAILS
Transport and storage
Transport and storage workers, including waterside workers, transport drivers and warehouse workers, will handle sealed containers of the notified chemical, and also of inks or coatings containing up to 4% notified chemical. No exposure is expected except in the case of an accident involving damage to the packages.

Formulation – Ink and coating manufacture
At each of the ink or coating manufacturing sites, the notified chemical will be manually weighed and slowly added to a 200 L stainless steel blending vessel and mixed with the other components of the printing ink or coating. Dermal, inhalation and accidental ocular exposure to the notified chemical as a powder is possible during this procedure although local exhaust ventilation will be available at the weighing station and mixing tanks. The blended ink or coating solution will then be piped to an automated filling system and dispensed into 20 L metal pails or 200 L drums. The only point where the notified chemical is handled outside the closed system is during weighing and addition to the blending vessel. Extraction ventilation will be used at this point. Workers will wear overalls, PVC coated cotton gloves and protective goggles. Respiratory protection may be used if conditions are dusty or high vapour concentrations are present.

End-use: Printing and coating
Exposure during end-use of the printing inks and coatings may vary depending on the nature and scale of the process. In general the ink or coating solutions containing up to 4 % notified chemical will be manually poured or pumped from the containers into reservoirs of the equipment designed to apply the ink or coating. Residual ink or coating will be scraped into the reservoir of from 20 L containers prior to the containers being washed. Larger vessels will be cleaned by drum reconditioning contractors. Dermal and accidental ocular exposure could occur during these processes, together with inhalation exposure to aerosols. From this point, the printing or coating process will be highly automated, and the ink or coating will be cured by UV exposure prior to the substrates being manually handled. This will decompose and immobilise the notified chemical, which will no longer be available for exposure. There may also be exposure to the notified chemical as part of the cleaning processes that occur during

the process or during cleaning of equipment at the end of a production run.

Workers will wear overalls, PVC coated cotton gloves and protective goggles while handling the inks or coatings. The inks or coatings contain prepolymers which polymerise under the UV curing conditions, and a number of these are known skin sensitisers, and a high level of precautions to avoid dermal exposure are required even in the absence of the notified chemical. Laboratory workers will be responsible for quality control measurements on the blended inks or coatings and for small scale testing of mixtures using up to 1 kg notified chemical. These workers will handle the notified chemical as well as formulated inks and coatings. Normal laboratory protective equipment (laboratory coats, safety glasses, protective gloves and fume hoods) would be expected to be used.

5.4. Release

RELEASE OF CHEMICAL AT SITE

It is estimated that a maximum of 0.5% of the notified chemical would be lost during spillage at formulation sites. This spillage may be vacuumed and the vacuum cleaner bags removed to landfill. It is estimated that a maximum of 1% of import volumes would remain in drums collected by a licensed waste disposal contractor.

RELEASE OF CHEMICAL FROM USE

Up to 2% of the ink or coating may be lost through spillage during transfer to reservoirs in the printing or coating machine. Any spilt ink or coating would be cleaned up with absorbent material and removed to landfill although a proportion may be hosed to sewer.

Once the chemical is within a curing coating it is likely to share the fate of the substrate which may involve recycling or landfill.

5.5. Disposal

All spilt or unused material would be expected to be removed to secured landfill or possibly incinerated.

5.6. Public exposure

The public may come into contact with the notified chemical in the event of a transport accident or on the substrates to which the cured coating is applied. In the latter case the chemical would not be bioavailable.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa Slightly yellow powder

Melting Point/Freezing Point 68.0°C

METHOD	OECD TG 102 Melting Point/Melting Range. EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	Test performed under red light. Samples lost mass during measurement. Melted samples were clear, yellowish.
TEST FACILITY	RCC (2002a)

Boiling Point > 270°C at 101.3 kPa

METHOD	OECD TG 103 Boiling Point. EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	Test performed under red light. Material decomposed from 270 °C. In the vapour pressure test, the boiling point was estimated to be approximately 471°C.
TEST FACILITY	RCC (2002b)

Density 1160 kg/m^3 at 20.0°C

METHOD	OECD TG 109 Density of Liquids and Solids.

EC Directive 92/69/EEC A.3 Relative Density.

Remarks Test performed under red light. Material dried before testing.

TEST FACILITY RCC (2002c)

Vapour Pressure 1.3 x 10^{-13} kPa at 25°C (estimated).

METHOD OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.

Remarks The boiling point was estimated using Meissner's method, based on atomic and structural contributions, to be approximately 471°C. This value was used to estimate the vapour pressure using a Modified Watson Correlation.

TEST FACILITY RCC (2002d)

Water Solubility 1.9 mg/L (±0.6 mg/L) at 20°C

METHOD OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.

Remarks Analytical Method: HPLC
The water solubility was determined using the column elution method. The test material was dissolved in ethyl acetate and loaded onto the glass bead carrier by evaporating the solvent under a stream of nitrogen. The beads were washed with a small volume of Milli-Q water and then Milli-Q water was circulated past the beads until the saturation concentration was established (as defined by at least 5 successive samples whose concentrations did not differ by more than 30%). The pH of the test samples ranged from 6.61-7.15. Samples of the eluent were analysed by HPLC with UV detection. Sample solutions were prepared under red light and stored in amber coloured glassware due to the light sensitivity of the test substance.

TEST FACILITY RCC (2002e)

Hydrolysis as a Function of pH

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

pH	*T (°C)*	*$t_{½}$ <hours or days>*
4	25	> 1year
7	25	> 1 year
9	-	-

Remarks Samples of the test substance (20 mg) were dissolved in methanol (2 mL) and diluted to 100 mL using the buffer solutions. After sonication for 5 minutes the samples were filtered through a 0.45 µm filter. The filtrate was diluted with an equal amounts of the buffer solutions. The initial measured concentrations in the test solutions were 103.8 and 2.2 mg/L at pH 4 and 7, respectively indicating that the test substance is considerably more soluble at low pH. At pH 9.0 the test material was not detectable in any of the test solutions. This variation in the concentrations of the test material with in the buffer solutions is indicative of protonation and deprotonation changing the water solubility of the chemical. The lack of detection of the test material at pH 9 may also be accounted for by rapid degradation (eg hydrolysis) of the test substance at high pH though this is less likely. Equilibration of samples was preformed in the dark due to the light sensitivity of the test substance. At the pH values of 4.0 and 7.0, less than 10% hydrolysis occurred after 50 days at 50°C in all test solutions.

TEST FACILITY RCC (2002f)

Partition Coefficient (n-octanol/water) log Pow at 20°C = 4.1

METHOD OECD TG 117 Partition Coefficient (n-octanol/water), HPLC Method.

EC Directive 92/69/EEC A.8 Partition Coefficient.

Remarks Analytical Method:HPLC
The partition coefficient was determined using HPLC. The retention time of the notified chemical was compared to those for six reference chemicals with known log Pow. The reference chemicals chosen covered a log Pow range of 2.1-4.7. Each standard was analysed six times and the test material was analysed three times.

TEST FACILITY RCC (2002g)

Adsorption/Desorption – main test log K_{oc} = 3.5

METHOD OECD TG 121 Estimation of the Adsorption Coefficient (Koc) on Soil and Sewage Sludge using High Performance Liquid Chromatography.

Remarks Analytical Method:HPLC
The adsorption coefficient (log K_{oc}) was determined using the HPLC Method, using a gradient elution method. The retention time of the notified chemical was compared to those for six reference chemicals with known log K_{oc} values. The reference chemicals chosen covered a log K_{oc} range of 1.86-5.63. Each standard was analysed six times and the test material was analysed three times.

TEST FACILITY RCC (2002h)

Dissociation Constant pKa = 10.2 (estimated)

METHOD Taft and Hammett Correlations

Remarks The molecular structure of the notified chemical was used to estimate the dissociation behaviour. The results of the calculation suggest that the notified chemical will be protonated under much of the environmental pH range (4-9) as indicated in the hydrolysis as a function of pH test above. This contrasts with the conclusion in the test report that the notified chemical does not dissociate or protonate in the environmentally relevant pH range (pH 4 to pH 9).

TEST FACILITY RCC (2002i)

Particle Size

METHOD According to the European Commission, Document ECB/TM/February 1996: "Particle Size Distribution, Fibre Length and Diameter Distribution" Guidance Document, using the laser diffraction method.

Range (μm)	*Weight (%)*
< 5	15.26
5 - 10	14.51
10 - 20	29.70
20 - 40	30.76
40 -60	7.81
60 - 80	1.62
> 80	0.34

Remarks The material is a fine white powder, with some lumpy, colourless, rod-shaped crystalline structures observed under the microscope at a magnification of 400.
The material was dispersed in water with 0.2 g/L sympatens SHO/400 before particle size determination by laser diffraction. Mass median diameter (MMD) was found to be 16.7 μm. The particle size distribution was approximately 0.3 μm to 100 μm. The inhalable fraction (≤ 100 μm) was 100% and the respirable fraction (< 10 μm) was 29.8%.

TEST FACILITY RCC (2002j)

Flash Point 178ºC at 101.3 kPa

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks Material was heated to approximately 80^0C before testing, to liquefy.
TEST FACILITY RCC (2002k)

Flammability Testing indicated that material is not highly flammable.

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks Could not be ignited with the flame during the preliminary test. No main test was performed.
TEST FACILITY RCC (2002l)

Autoignition Temperature Did not autoignite

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks Material changed from solid to liquid during heating process. Test conducted up to > 400^0C. At end of test a silver-black carbonised melt remained when the sample was emptied from the test cell.
TEST FACILITY RCC (2002m)

Explosive Properties Not considered to be explosive.

METHOD Testing was not carried out. The explosive properties were estimated on the basis of criteria set out UN Recommendations of the Transport of Dangerous Goods (Manual of Tests and Criteria, Annex 6, Orange Book, 3rd Edition, 1999).
Remarks
TEST FACILITY RCC (2002n)

Reactivity

Remarks The notifier advised that solutions of CGI 113 are light sensitive but that decomposition is relatively slow. The identity of the photodegradation products is not known.

Oxidizing Properties Not considered to be oxidising

Remarks Testing was not carried out. The oxidising properties were estimated on the basis of criteria for molecular formula and structure, set out UN Recommendations of the Transport of Dangerous Goods (Manual of Tests and Criteria, Annex 6, Orange Book, 3rd Edition, 1999).
TEST FACILITY RCC (2002o)

ADDITIONAL TESTS

Fat (or n-octanol) Solubility 27.53 (±0.43) g/100 g HB 307 at 37°C

METHOD OECD TG 116 Fat Solubility of Solid and Liquid Substances.
Remarks Analytical Method: HPLC
The fat solubility was examined in a simplified flask method. Samples of the test substance were mixed with a standard fat (HB 307). Initial incubation was at either 30 or 50°C for either 6 or 24 h. sample were then incubated at 37°C for either 6 or 24 h and quantified by HPLC. The raw data was corrected for the mass fraction of the test item in the fat samples.
TEST FACILITY RCC (2002p)

Surface Tension 70.4 mN/m at 20.3ºC

METHOD OECD TG 115 Surface Tension of Aqueous Solutions.
EC Directive 92/69/EEC A.5 Surface Tension.
Remarks Concentration: 90% saturation concentration in water.
Test material was suspended in double distilled water, subjected to ultrasonication for 10 minutes and stirred for 16 hours. After filtration the filtrate was diluted to 90% of its saturation concentration and tested by means of a tensiometer, using the ring method. Neither the pH of the test solutions or the concentrations of the test substance were determined. Based on the criteria as outlined in the OECD Test Guideline the notified chemical is not a surface active substance.
TEST FACILITY RCC (2002q)

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral	low toxicity: LD50 > 2000 mg/kg bw
Rat, acute dermal	low toxicity: LD50 > 2000 mg/kg bw
Rat, acute inhalation	no data submitted
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation - adjuvant test.	no evidence of sensitisation.
Rat, oral (gavage) repeat dose toxicity - 28 days.	NOAEL 15 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosome aberration	non genotoxic
Genotoxicity – in vivo	no data submitted
Pharmacokinetic/Toxicokinetic studies	no data submitted
Developmental and reproductive effects	no data submitted
Carcinogenicity	no data submitted

7.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical – commercial grade

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/HanBri: WIST (SPF)
Vehicle	PEG 300
Remarks - Method	Limit test. Administered by gavage

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3/sex	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity	Slight emaciation in 1 female on days 5 and 6.
Effects in Organs	No macroscopic findings
Remarks - Results	

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

TEST FACILITY: RCC (2001a)

7.2. Acute toxicity - dermal

TEST SUBSTANCE: Notified chemical, commercial grade, purity unknown

METHOD: OECD TG 402 Acute Dermal Toxicity – Limit Test.
EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.

Species/Strain	Rat/HanBri: WIST (SPF)
Vehicle	PEG 300
Type of dressing	Semi-occlusive.
Remarks - Method	

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*

1	5/sex	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	None
Signs of Toxicity - Systemic	None
Effects in Organs	No macroscopic findings
Remarks - Results	

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

TEST FACILITY RCC (2001b)

7.3. Acute toxicity - inhalation

Data not provided

7.4. Irritation – skin

TEST SUBSTANCE Notified chemical, 99.1%

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 (1 male, 2 female)
Vehicle	Material was moistened with purified water before application
Observation Period	72 h
Type of Dressing	Semi-occlusive.

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	0	0	0	-	0
Oedema	0	0	0	0	-	0

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

CONCLUSION The notified chemical is non-irritating to skin.

TEST FACILITY RCC (2001c)

7.5. Irritation - eye

TEST SUBSTANCE Notified chemical, 99.1% purity

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 (1 male, 2 females)
Observation Period	72 h
Remarks - Method	0.1g of notified chemical was applied as powder as supplied by sponsor and was not ground.

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	0.67	0.33	1	2 days	0
Conjunctiva: chemosis	0	0.33	0	2	1 day	0
Conjunctiva: discharge	0	0	0	0	0	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.

Remarks - Results Yellow remnants of chemical noted in eye or conjunctival sac after 1 h only.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY RCC (2001d)

7.6. Skin sensitisation

TEST SUBSTANCE Notified chemical of 99.1% purity. Tested in vehicle PEG 300. Tested as supplied, without grinding.

METHOD OECD TG 406 Skin Sensitisation - GPMT.
EC Directive 96/54/EC B.6 Skin Sensitization - GPMT.

Species/Strain Guinea pig/Himalayan spotted female

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 10% (slight irritation noted at all concentrations tested: 3, 5 and 10%)
topical: 50% (not irritating, but was maximum attainable concentration)

MAIN STUDY

Number of Animals Test Group: 10 Control Group: 5

INDUCTION PHASE Induction Concentration:
intradermal injection 10% in PEG 300
topical application 50% in PEG 300

Signs of Irritation Slight irritation at 24 h and 48 h for both intradermal and topical application. SLS pre-treatment used for topical application, as no primary irritation had been observed in preliminary study.

CHALLENGE PHASE

1st challenge topical application: 50% in PEG 300

Remarks - Method Material was not ground. Maximum non-irritant concentration not determined for topical application. Positive control 2-mercaptobenzothiazole.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	50%	0/10	0/10	N/A	N/A
Control Group	50%	0/5	0/5	N/A	N/A

Remarks - Results It is possible that results were affected by the fact that the substance could

not be tested at higher than 50% concentration, because this was the highest attainable solubility.

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

TEST FACILITY RCC (2001e)

7.7. 28-Day repeat dose oral toxicity

TEST SUBSTANCE

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

Species/Strain	SPF-bred Wistar rats
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	PEG 300
Remarks - Method	Haematology included reticulocyte fluorescence ratios

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5 / sex	0	0
II (low dose)	5 / sex	15	0
III (low mid dose)	5 / sex	50	0
IV (high mid dose)	5 / sex	150	0
V (high dose)	5 / sex	450	0
VI (control recovery)	5 / sex	0	0
VII (high dose recovery)	5 / sex	450	0

Mortality and Time to Death
No mortality was observed during the treatment or recovery phases.

Clinical Observations
Clinical signs, outside cage observation, food consumption and body weights were recorded during the study, with changes predominantly limited to the high dose group. The effects included reduced food consumption in high dose animals, reduced mean body weights in high dose animals from day 8 and high mid dose males from day 22. Piloerection, hunched posture, emaciation and changes in faecal appearance were noted in some animals. During the recovery period, body weights of high dose animals remained lower than the controls, although mean body weight gain improved.

Dark faeces and pale faeces were noted in high dose animals from days 12-22 and days 24-28 of treatment respectively, the latter persisting for 2 days into the recovery period. These effects are considered likely to be related to haematological changes, attributed to compensated anaemia.

No treatment related changes were noted during the functional observational battery, including locomotor activity and grip strength, performed during week 4,

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Haematology
Haematology parameters were tested at 4 weeks, with treatment-related changes noted in high dose and high

mid dose males and females, and low mid dose females. These were considered to represent different compensated stages of anaemia with reticulocytosis, with compensatory reticulocytosis expressed more clearly in males.

Statistically significant reductions in haemoglobin and haematocrit were noted in both sexes at the high dose, and a reduction in haematocrit was also found in mid high dose females. In high dose males, mean corpuscular volume, mean cell haemoglobin and mean cell haemoglobin concentration were reduced. The red blood cell count was reduced in females from the low mid dose. Platelet count was increased in high and mid high dose males.

Higher absolute and relative reticulocyte counts, and a left-shift towards high fluorescence reticulocytes were observed in high dose males, with similar but less significant changes in mid high dose males. These effects were absent in females, but high dose females had increased methaemoglobin levels.

Increased leucocyte counts were observed in both sexes at high dose, and males at mid high dose. These were reflected primarily in high dose animals by increased absolute lymphocyte counts (both sexes) and segmented neutrophil counts (male). Shortened thromboplastin times were significant only in high dose females and mid high dose males and females.

Some effects persisted after the two week recovery period. In these animals previously treated with the high dose, red blood cell count remained lower than controls in females, while in males the mean cell haemoglobin concentration remained lower, absolute and relative reticulocyte counts higher, and the left shift in reticulocyte fluorescence ratios persisted.

Clinical chemistry
Test item related changes in high dose animals, measured at 4 weeks, are considered to be indicative of minor treatment-related changes in liver metabolism. These included increased creatinine (males), total bilirubin (males), total cholesterol (both sexes), triglycerides (both sexes), phospholipids (both sexes), albumin (males), total protein (males), gamma glutamyl transferase activity (females) and calcium (both sexes).

After the two week recovery period, the elevated albumin and total protein levels persisted in males, and the elevated gamma glutamyl transferase activity in females.

Urinalysis
At 4 weeks no test item related changes were found.

Pathology – Effects in organs, macroscopic and microscopic findings
Effects in Organs
Testes and epididymides weights were reduced in high dose males. Increased liver and kidney weights were observed in high dose and mid high dose males and females, and low mid dose females. In high dose recovery animals the reduced testes and epididymides weights and increased liver weight were not reversible after 2 weeks.

Macroscopic findings
Small testes were observed in high dose males after 4 weeks (5/5) and most (4/5) recovery males.

Microscopic findings
At the end of 4 weeks, all high dose males (5/5) showed moderate to marked reductions in spermatogenesis, 3/5 had slight to marked occurrence of spermatic giant cells, and 1/5 had marked tubular atrophy. Effects on the epididymides, namely reduced spermatozoa and occurrence of cellular debris, were also observed. Most effects on both organs persisted through the recovery period.

In bone marrow there was minimally increased incidence and grading of fatty atrophy in high dose males and females, that did not persist after the recovery period. Splenic extramedullary haematopoiesis increased in all dosed males except low dose, and remained higher after recovery in high dose males. Haemosiderosis in the spleen occurred in both control and treated animals and was not increased in treated animals.

Tubular hyaline changes were observed in high and mid high dose male kidneys, with some effect still noted after the recovery period. Slight hepatocellular hypertrophy observed in 3/5 high dose females did not persist after recovery. High dose females had a slightly increased average grading of the alveolar foam cells in the

lung, that persisted in high dose recovery animals.

Remarks – Results

The major effects from repeated dose testing were found in the male reproductive system and the haematopoietic system. At the high dose only, the testes showed macroscopic and microscopic changes and reduced spermatogenesis, with alterations in the epididymides consistent with these effects. Statistically significant alterations in several haematology parameters were found in both high and high mid dose males and females, and there was a reduced red blood cell count in low mid dose females. There was increased splenic extramedullary haematopoiesis in low mid dose, high mid dose and high dose males. Minimal increases in fatty atrophy of the bone marrow in both sexes were seen only at the high dose. The pattern of changes in the haematopoietic system is indicative of compensated anaemia observed at different stages in males and females, with compensatory reticulocytosis showing clearly in males but not in females. The type and cause of the anaemia cannot be determined from the data.

Tubular hyaline changes in the male kidney are attributed to $\propto_{2\mu}$-globulin accumulation, which is a sex and species specific effect. Increases in liver weights from the low mid dose and above may to be primarily related to metabolism of the xenobiotic, as the only microscopic changes observed in the liver were slight centrilobular hepatocellular hypertrophy in high dose females. Relative increases in kidney weights are likely to be related to the drop in body weight of the treated animals.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 50 mg/kg bw/day in this study, based on effects at 150 mg/kg bw/day on the haematopoietic system. The slight effects seen at 50 mg/kg bw/day in females are not considered to be toxicologically significant.

TEST FACILITY RCC (2001f)

7.8. Genotoxicity - bacteria

TEST SUBSTANCE CGI 113 99%

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 and pre incubation procedure used.

Species/Strain *S. typhimurium*:
TA1535, TA1537, TA98, TA100.
E. coli: WP2 uvrA.

Metabolic Activation System S9 fraction from Phenobarbital / β-Naphthoflavone induced rat liver

Concentration Range in Main Test With and without metabolic activation:
Experiment 1: 3 - 5000 µg/plate.
Experiment 2: 33 - 5000 µg/plate.

Vehicle DMSO

Remarks - Method Pre-test was used as Experiment 1, and was based on plate incorporation method. As its results were negative, Experiment 2 was performed as a pre-incubation assay.

RESULTS

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

Test 1	Slight at 5000 µg/plate for TA 1537	> 5000 µg/plate	> 5000 µg/plate	negative
Test 2	> 5000 µg/plate	> 5000 µg/plate	> 5000 µg/plate	negative

Remarks - Results: No precipitation was reported. Slight toxicity was reported at only one concentration and strain, with activation. The test substance did not cause a marked increase either in the presence or absence of microsomal enzymes prepared from Phenobarbital / β-Naphthoflavone induced rat liver (S9). All negative controls were within historical limits, except for Experiment 1, TA 1535 with activation, where the negative control fell slightly short of the historical range. Positive controls confirmed the sensitivity of the test system.

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

TEST FACILITY: RCC (2002r)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE: CGI 113 99%

METHOD: OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.
EC Directive 2000/32/EC 2000/32/EC, L1362000, Annex 4A

Cell Type/Cell Line: Chinese Hamster V79 cells.
Metabolic Activation System: S9 fraction from Phenobarbital/β-naphthoflavone-treated rat liver.
Vehicle: DMSO
Remarks - Method: Pre-test was carried out to determine toxicity of the test item.
Test 1 4 h/18 h with S9 and Test 2 18 h/18 h without S9 were repeated because of strong toxicity, and the results of the second test were used.
Cyclophosphamide (with metabolic activation) and ethylmethane sulphonate (without metabolic activation) were used as positive controls.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	3.1, 6.3*, 12.5*, 25*, 50, 100	4 h	18h
Test 2	0.6, 1.3, 2.5*, 5.0*, 7.5, 10*	18 h	18 h
	12.5*, 25, 50, 100	28 h	28 h
Present			
Test 1	5, 10*, 20*, 30*, 40, 60	4 h	18 h
Test 2	3.1, 6.3, 12.5*, 25*, 50*, 100	4 h	28 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	23.4	≥ 25	> 12.5	not observed
Test 2		≥ 10	> 25	not observed
Present				
Test 1	46.9	> 30	60	not observed
Test 2		≥ 50	> 12.5	slight effect at 12.5

Remarks - Results	The aberration rates of treated cells exclusive of gaps (0.5 – 3%) were close to those of the solvent controls (0 – 2.0%) and within the range of historical control data (0 – 4.0%). One statistically significant response (2.5% aberrant cells) was seen in one dose and condition: 12.5μg/mL in experiment 2, 4 h/28 h only and is not considered biologically significant as the response was not dose related and aberration rates were within historical control data. Positive controls showed distinct increases in aberrant cells.
CONCLUSION	The notified chemical was not clastogenic to Chinese Hamster V79 cells treated in vitro under the conditions of the test.
TEST FACILITY	RCC (2002s)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Aerobic activated sludge.
Exposure Period	28 days.
Auxiliary Solvent	None.
Analytical Monitoring	Inorganic Carbon analysis using a Shimadzu TOC-500 Analyzer
Remarks - Method	Inoculum was aerated overnight in culture medium prior to the addition of test materials. Samples were collected from the first CO_2 absorber vessel on Days 2, 5, 7, 9, 12, 14, 19, 23, 27, 28 and 29. On day 28 test vessels were treated with 1 mL of concentrated hydrochloric acid to drive of any inorganic carbonates formed.

RESULTS

Test substance		*Sodium Benzoate*	
Day	*% degradation*	*Day*	*% degradation*
28	0	28	78.4

Remarks - Results	The extent of degradation of the reference material validates the test. A toxicity control containing test material and sodium benzoate reached 21% degradation on day 28 indicating that the notified chemical may be slightly toxic to sewage treatment organisms since it is <25% as required. However, this toxicity is not observed in the Activated Sludge Respiration test (OECD Test Guideline 209).
CONCLUSION	The notified chemical is not readily biodegradable under the conditions of the test.
TEST FACILITY	RCC (2002t)

8.1.2. Bioaccumulation

According to the general characteristics of bioaccumalative organic chemicals (Connell 1990) the notified chemical has a moderate to high potential to bioaccumulate. The notified chemical contains a high proportion of aliphatic and aromatic carbon-carbon bonds, has a molecular weight around 350, a log Pow of 4.1 and a water solubility of around 0.05 moles/m^3 and low estimated potential to ionise. This will be offset by the chemical's instability toward light and limited environmental exposure.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static. EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - static.
Species	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks – Method	A supersaturated dispersion the test substance at 100 mg/L was prepared and stirred for three hours. The solution was then passed through a membrane filter (pore size 0.45 μm). The concentration of the test material in the filtrate was determined by HPLC to be 0.17 mg/L, which was considerably lower than the levels observed in the water solubility study using the column elution method (OECD Test Guideline 105). The pH of the test media in this study was slightly basic (pH 7.9) which may in part account for the reduced solubility of the test material (see comments under hydrolysis as a function of pH test). The undiluted filtrate was used as the test medium. Water quality parameters of pH, water temperature, O_2 content were within normal limits throughout study.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
control		7 per sample	0	0	0	0	0
100	0.17	7 per sample	0	0	0	0	0

LC50	>0.17 mg/L mg/L at 96 hours.
NOEC	0.17 mg/L mg/L at 96 hours.
Remarks – Results	The results of the limit study showed that no mortalities or sub-lethal effects were observed in any of the test vessels. The 96-hour NOEC for the test material and its degradation products was determined in the report to be at the highest test level with a nominal concentration of 100 mg/L (actual 0.17 mg/L). The true value of the NOEC may be higher but concentrations in excess of 0.17 mg/L could not be achieved due to the low water solubility of the test substance. Similarly, the 96-hour LC50 for the test substance could not be determined for *Brachydanio rerio* as the test substance and its degradation products showed had no toxic effect on the test fish up to its highest concentration which could be achieved in the test media. Hence, the 96-hour LC50 is greater than 0.17 mg/L.
CONCLUSION	The notified chemical is not toxic to Zebra fish up to the limit of its water solubility in the test media.
TEST FACILITY	RCC (2002u)

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	None.
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	A supersaturated dispersion the test substance at 100 mg/L was prepared and stirred for three hours. The solution was then passed through a membrane filter (pore size 0.45 μm). The undiluted filtrate was used as the test medium. The analytically measured test item concentrations in the test media were below the level of quantification (LOQ of HPLC, 0.0643 mg/L) which is significantly lower than that measured by the column elution method (OECD Test Guideline 105). The pH of the test media in this study was slightly basic (pH 7.9) which as noted above may in part account for the reduced solubility of the test material. Water quality parameters of pH, water temperature, O_2 content were within normal limits throughout the study.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h [acute]*	*48 h [acute]*
control		20	0	0
100	< 0.0643 mg/L	20	2	2

EC50	> 0.0643 mg/L at 48 hours
LOEC	100 mg/L (nominal) at 48 hours
Remarks - Results	The results of the limit study showed that no immobilities or sub-lethal effects were observed in any of the test vessels. The 48-hour NOEC for the test material and its degradation products was determined in the report to be at the highest test level with a nominal concentration of 100 mg/L (actual < 0.0643 mg/L). The true value of the NOEC may be higher but concentrations in excess of 0.0643 mg/L could not be achieved due to the low water solubility of the test substance. Similarly, the 48-hour EC50 for the test substance could not be determined for *Daphnia magna* as the test substance and its degradation products showed had no toxic effect on the test daphnia up to its highest concentration which could be achieved in the test media. Hence, the 48-hour EC50 is greater than 0.0643 mg/L.
CONCLUSION	The notified chemical is not toxic to daphnia up to the limit of its water solubility in the test media.
TEST FACILITY	RCC (2002v)

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	0 - 100 mg/L
Concentration Range Actual	0.0154 (non-aged) – 0.165 (aged) mg/L
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	A supersaturated dispersion the test substance at 100 mg/L was prepared and stirred for three hours. The solution was then passed through a membrane filter (pore size 0.45 μm). The undiluted filtrate was used as the test medium along with dilutions 1:2, 1:4, 1:8 and 1:16. The mean measured concentration of the undiluted filtrate was 90 μg/L, an dthus solutions ranged from 5-90 μg/L. This measured concentration was considerably lower than the levels observed in the water solubility study using the column elution method (OECD Test Guideline 105). The pH of the test media in this study was basic (pH 7.9-9.5) which accounts for the reduced solubility of the test material (see above). Water quality parameters of pH, water temperature, O_2 content were within normal limits throughout study.

RESULTS

Biomass	*Growth*	*NOEC*
E_bC50 mg/L at 72 h	*E_rC50 mg/L at 72 h*	*mg/L at 72 h*
>0.09	>0.09	0.09

Remarks - Results	The results of the limit study showed that no inhibitory effect on the growth of *Scenedesmus subspicatus*. The 72-hour NOEC for the test material and its degradation products was determined in the report to be at the highest test level with a nominal concentration of 100 mg/L (actual 0.09 mg/L). The true value of the NOEC may be higher but concentrations in excess of 0.09 mg/L could not be achieved due to the low water solubility of the test substance. Similarly, the 48-hour E_bC50 and E_rC50 for the test substance could not be determined for *Daphnia magna* as the test substance and its degradation products showed had no inhibitory effect on the test algae up to its highest concentration which could be achieved in the test media. Hence, both the 48-hour E_bC50 and E_rC50 are greater than 0.09 mg/L.
CONCLUSION	The notified chemical is not toxic to algae up to the limit of its water solubility in the test media.
TEST FACILITY	RCC (2002w)

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
Inoculum	Aerobic activated sludge from a wastewater treatment plant treating predominantly domestic wastewater.
Exposure Period	3 hours
Concentration Range Nominal	6.25, 12.5, 25, 50, 100 mg/L
Remarks – Method	

RESULTS	The activated sludge study was conducted using sludge obtained from sewage treatment plant in Füllensdorf, Switzerland. The reference material used in the study was 3,5-dichlorophenol. The 3-hour EC50 for the notified substance to activated sludge could not be quantified as there was <15% inhibition at the highest nominal test concentration. However, the 3-hour EC50 for the notified chemical to activated sludge is expected to be greater than 100 mg/L. The EC50 of the reference substance was 12 mg/L, therefore confirming the suitability of the activated sludge.
IC50	> 100 mg/L
NOEC	> 100 mg/L
CONCLUSION	The notified chemical is not inhibitory to activated sludge up to 100 mg/L suspension.
TEST FACILITY	RCC (2002x)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The majority of the notified chemical will be consumed during curing or remain bound within cured inks at low levels on metal, paper or plastic substrates.

The main potential for environmental hazard would arise from release of the notified chemical during storage or transport. The use of bunded containment minimises the risk of release at storage sites. Less than 90 kg of notified chemical may be released landfill annually via spills, with the possibility a small portion of this may be hosed into the sewer. This release is expected to be distributed across several sites and will not be restricted to a single site, thus minimising the degree of risk to the environment at any given time. The compound is not readily biodegradable, has a high partition coefficient and low water solubility, all indicating that any material released would partition to sediments, where it is expected to persist. Empty containers containing less than 40 kg of the notified chemical will be consigned to licensed waste disposal contractors residues for disposal.

The notified substance will ultimately suffer the same fate as the finished article at the end of its useful life, ie be disposed of to landfill. Since it will be incorporated into the inert matrix of the cured ink it will pose minimum risk to the environment.

According to the general characteristics of bioaccumulative organic chemicals (Connell 1990), the notified chemical has a moderate to high potential to bioaccumulate. However, bioaccumulation is not expected due to the notified chemical's instability to UV light and its low exposure expected to the aquatic environment.

9.1.2. Environment – effects assessment

The notified chemical is non-toxic to fish, daphnia, algae and sewage micoorganisms up to the limit of its water solubility. Since LC50 and EC50 levels could not be determined, estimation of a PNEC is not possible.

9.1.3. Environment – risk characterisation

The notified chemical will be used as a component of UV curable inks. Once these inks have been cured the notified chemical is expected to remain within the product matrices. Hence, the majority of the notified chemical will share the fate of the articles into which it is incorporated. It is anticipated that these will be disposed of to landfill or incinerated at the end of their useful lifetime. In landfill it is expected that the notified chemical will remain immobile within the matrices. Incineration of the notified chemical will result in the formation of water vapour and oxides of carbon and nitrogen.

Very little will be released to water and it is not possible to calculate a reasonable predicted environmental concentration (PEC). However, as the notified chemical is not toxic to aquatic organisms up to the limit of its water solubility it is estimated the risk quotient (PEC/PNEC) should be very small.

The above considerations indicate minimal risk to the environment when the notified chemical is used in the manner and levels indicated by the notifier.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

The imported notified chemical is a fine powder and will be used at 1 – 4% in liquid ink or coating formulations. Exposure during transport and storage would only occur through accidental breaching of the containers containing the chemical or inks containing it. The chance of exposure to the powder through accident is reduced through the double layer of packaging, with the chemical contained in a plastic bag within a steel drum.

Exposure during formulation of inks and coatings

There is potential for dermal, ocular and inhalation exposure to workers during the manual weighing and transfer of the notified chemical into the formulation tank, especially if dust is produced, as all of the particles are in the inspirable range, and 30% are in the respirable range. Local exhaust ventilation is available for weighing and addition to the tank and PPE would be worn. After addition of the chemical to the mix, the lid is replaced and the remainder of the formulation and filling process occurs within a closed system. EASE modelling was carried out to estimate the potential dermal and inhalation exposure of formulation workers to the notified chemical. The model is a conservative one and may overestimate exposure, and it estimates exposure in the absence of personal protective equipment. Exposure of up to 0.1 mg/cm^2/day of the notified chemical was predicted on the basis of incidental dermal contact. Using the area of the hands (840 cm^2) and 70 kg body weight, this is 1.2 mg/kg/day. Additional potential exposure through inhalation was estimated at up to 0.093 mg/kg/day with local exhaust ventilation, and 0.93 mg/kg/day in the absence of local exhaust ventilation, if exposure occurs for 1 h/day. Combined dermal and inhalation exposure is potentially up to 1.3 mg/kg/day with local exhaust ventilation, and 2.1 mg/kg/day in its absence.

Exposure during use of inks and coatings

A range of equipment may be used for application of the inks or coatings, depending on the type of process and the scale of use. The NICNAS PEC assessment of N-vinyl pyrrolidone, used in similar processes, identified a variety of control measures in use in different companies. The notifier has stated that the printing and coating processes are highly automated, and this is likely to be the case at many sites, with some sites containing less automated equipment and fewer engineering controls. Once the chemical is incorporated into inks or coatings, dermal or ocular exposure could occur during charging of the printing and coating machines, and during cleaning processes. Unless aerosols are generated, inhalation exposure during ink or coating use is expected to be very low because of the high boiling point and estimated very low vapour pressure of the notified chemical, however aerosols could be generated during addition to machines.

Using the upper level of 4% notified chemical in inks or coatings, and skin area of 840 cm^2 (both hands), the maximum predicted worker dermal exposure to the notified chemical in inks or coatings is 33.6 mg/day, or 0.48 mg/kg/day, assuming a body weight of 70 kg and intermittent contact with the formulation. Inhalation exposure would be expected only if aerosols are formed, and may be up to 0.74 mg/kg/day in a scenario where local exhaust ventilation is absent, based on 1 h/day exposure. Combined dermal and inhalation exposure is predicted to be up to 1.22 mg/kg/day.

The notifier has stated that printing/coating workers and laboratory personnel will wear personal protective equipment to protect skin and eyes from exposure to the inks, some of which contain sensitisers. Therefore the amount of dermal contact predicted by the EASE model would be an overestimation. Similarly the potential for inhalation exposure is reliant on the formation of aerosols of the formulation being used for printing or coating.

Once the inks or coatings have been applied and cured by UV, the notified chemical will not be available from handling the substrate, as it will be consumed and/or become immobilised through the curing process.

9.2.2. Public health – exposure assessment

The public is not expected to come into contact with the notified chemical or inks/coatings containing it, unless exposed through a transport accident. No exposure is expected from contact with the final printed or coated articles, as the chemical and/or its decomposition products will be bound within the substrate.

9.2.3. Human health - effects assessment

The notified chemical is of low acute oral and dermal toxicity. It is not a skin irritant but is slightly irritating to the eye. For skin sensitisation a negative result was obtained in a guinea pig maximisation test at 50%, the highest level that could be solubilized for testing.

The notified chemical was not mutagenic when tested in the bacterial reverse mutation test, nor

genotoxic in an in vitro chromosome aberration test.

In a 28-day oral repeat dose study on rats, adverse effects on the male reproductive system were found at the highest dose tested, 450 mg/kg bw/day. These included macroscopic and microscopic changes and reduced spermatogenesis, with effects persisting in 14-day recovery animals. Dose related effects on the haematopoietic system were found that are indicative of compensated anaemia, with some minor changes occurring down to 50 mg/kg bw/day. The effects observed at 50 mg/kg bw/day are not considered toxicologically significant. Haematopoietic effects were also observed in recovery animals. The NOAEL was set at 50 mg/kg bw/day, based on effects on the haematopoietic system at 150 mg/kg bw/day. Effects were observed in other organs, namely the kidneys and liver, primarily at the highest dose tested, 450 mg/kg bw/day.

The notified chemical is approved for use in some other countries, and the notifier advised that no adverse effects of the chemical in use had been noted.

Based on the data above showing adverse effects on the male reproductive system at 450 mg/kg/day, the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances.* It is classified as Category 3 for effects on fertility, with the risk phrase R62 "Possible risk of impaired fertility". The results of the 28-day repeat dose oral toxicity study provide sufficient evidence to cause a strong suspicion of impaired fertility occurring at around the same dose levels as other toxic effects. While possible systemic effects were recognised at 450 mg/kg/day, eg, 11% reduced body weight in comparison with the controls, the following effects were seen in the testes: reduced spermatogenesis, 50% weight reduction in comparison with controls, occurrence of giant cells in 3/5 animals, tubal atrophy in 1/5 animals. The observed effects on the testes, which persisted during the recovery period, are not considered to be a secondary non-specific consequence of other toxic effects. It is agreed with the study authors that the effects on the epididymides are a secondary consequence of testicular toxicity. Consequently the data are sufficient to justify classification as harmful with risk phrase R62.

At the 150 mg/kg bw/day dose level in the 28-day repeat dose study, male reproductive effects were absent, and haematopoietic changes were not considered severe enough to warrant classification with the risk phrase R48. The health effects from repeated exposure and in particular the effects on the haematopoietic system may be better characterised by longer animal testing, eg 90 day test.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is imported as a powder of small particle size that is incorporated in UV printing and coating formulations. In preparation of the ink and coating formulations, there is potential for both dermal exposure and inhalation exposure to the notified chemical in powder form. Based on EASE estimates of exposure and the NOAEL of 50 mg/kg/day for haematopoietic effects after repeated exposure, the margin of exposure (MOE) would be 38 if local exhaust ventilation is used during formulation processes, and the MOE would be 24 in absence of local exhaust ventilation. In the end-use of the formulated inks and coatings there is potential for dermal and ocular exposure to the notified chemical in solution, and potential for inhalational exposure if aerosols are formed. Combined dermal and inhalational exposure could lead to a MOE of 41 under some circumstances of use. Accidental spillage could also lead to worker exposure. Taking into account the conservative nature of the exposure estimates, the MOE above represent a low concern for workers during formulation and end-use. The extent of potential dermal, ocular and inhalation exposure is reduced by the use of engineering controls and PPE, described as being standard in formulation and use of UV inks and coatings.

Based on available animal testing, the acute effects of the chemical are expected to be low. Overall, the risk to workers is considered low if available measures to reduce exposure during formulation and printing/coating are in place.

9.2.5. Public health – risk characterisation

The public is not expected to have significant exposure to the notified chemical or inks/coatings containing it. The public will have contact with articles with cured print or coatings containing the chemical, but it will be immobilised in these media. The possibility of public contact with accidentally spilt chemical is considered very low. Because of low exposure, the public health risk is considered very low.

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 is Harmful X_n with the following risk phrase:
R62: Possible risk of impaired fertility.

The submitted MSDS for the notified chemical contains the following environmental risk and safety phrases:
R53: May cause long-term adverse effects in the aquatic environment
S61: Avoid release to the environment. Refer to special instructions / safety data sheets.

According to the Globally Harmonised System for the Classification and Labelling of Chemicals (UN, 2003), the notified chemical is classified as:

	Hazard category	***Hazard statement***
Reproductive toxicants	2	Suspected of damaging male fertility.

For the environment it is not possible to categorise the notified chemical according to the Globally Harmonised System for the Classification and Labelling of Chemicals.

10.2. Environmental risk assessment

The 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

There is Low Concern to occupational health and safety under the conditions of the occupational settings described, dependent on controls being in place.

10.3.2. Public health

There is Negligible Concern to public health when used in UV cured inks and coatings.

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, 1994a). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

NICNAS has recommended that the MSDS be revised in accordance with the recommended hazard classification. Details are in section 12.

11.2. Label

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

12. RECOMMENDATIONS

REGULATORY CONTROLS
Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - R62: Possible risk of impaired fertility.

- Use the following risk phrase for products/mixtures containing the notified chemical:
  - ≥ 5.0%: R62: Possible risk of impaired fertility.

FURTHER TESTING
It is recommended that a 90-day repeat dose study be carried out, to better characterise the effects found in the 28-day study, especially the effects on the haematopoietic system.

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - For formulation, local exhaust ventilation should be used in weighing and mixing areas, to minimise exposure to the notified chemical as a powder.
  - For both formulation and printing/coating operations, the process should be enclosed as much as possible to reduce dermal exposure and the possibility of exposure to aerosols.

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced or in products:
  - In handling notified chemical, avoid spills and dust generation.
  - In handling inks/coatings containing the notified chemical, avoid spills, splashes or aerosol generation that would increase exposure.
  - Avoid direct handling of the notified chemical and products where possible

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced or in products:
  - Respiratory protection capable of filtering out respirable particles, if exposure to dust is likely
  - Gloves
  - Protective clothing
  - Safety eye protection

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

- The MSDS should be revised according to the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003) to reflect the new toxicity data and the recommended human health hazard classification of R62.

- 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.

Environment

- The following control measures should be implemented by end-users to minimise environmental exposure during use of the notified chemical:
  - Do not allow material or contaminated packaging to enter drains, sewers or water courses.

Disposal

- The notified chemical should be disposed of into landfill or incinerated.

Emergency procedures

- Spills/release of the notified chemical should be handled by damping down, scooping up and placing in marked containers for disposal.

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 sub-section 64(1) of the Act; if
- the use pattern of the notified chemical changes in such a way as to increase the exposure of the chemical to the aquatic compartment. A secondary notification will allow a more detailed risk assessment of the changed use pattern.*)*
- the use pattern of the notified chemical changes in such a way as to increase occupational exposure, either through inhalation or dermal contact eg change to a dispersive use, or use where aerosols are formed.
- Further toxicological data on the notified chemical becomes available eg a 90-day repeated dose study.

or

(2) Under sub-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.

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