File No: STD/1187

February 2006

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

ORASOL® YELLOW E-3G

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

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

Library
Australian Safety and Compensation Council
25 Constitution Avenue
CANBERRA ACT 2600
AUSTRALIA

To arrange an appointment contact the Librarian on TEL + 61 2 6279 1162 or email ascc.library@dewr.gov.au

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

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

Director
NICNAS

TABLE OF CONTENTS

FULL PUBLIC REPORT

ORASOL® YELLOW E-3G

1. APPLICANT DETAILS

APPLICANT(S)
Ciba Speciality Chemicals Pty Ltd (ABN: 97 005 061 469)
235 Settlement Rd,
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 Name
Other Names
CAS Number
Molecular Formula
Structural Formula
Means of Identification
Molecular Weight
Purity
Spectral Data
Methods of Detection and Determination
Impurities (Hazardous)
Import Volumes
Identity of Customers

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
The notified chemical is currently being notified to USA, Europe, Japan, Canada, Korea, China, and Philippines. It is not currently listed in any country.

2. IDENTITY OF CHEMICAL

OTHER NAME(S)
Solvent Yellow 41A
TKP 50073

MARKETING NAME(S)
ORASOL® YELLOW E-3G

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	Ultraviolet/Visible, Infrared, NMR Spectra, MS Spectra, GC, HPLC
Remarks	Reference spectra were provided.
TEST FACILITY	Ciba Specialty Chemicals Inc. (2004)

3. COMPOSITION

DEGREE OF PURITY
>98%

NON HAZARDOUS IMPURITIES (>1% by weight)
None.

ADDITIVES/ADJUVANTS
None.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported by sea in the form of a yellow powder with typical odour. The powder will be formulated into printing inks for decorative packaging.

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

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

USE
Colouring agent for printing inks.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Ciba Specialty Chemicals Pty Ltd
235 Settlement Road
Thomastown VIC 3074

TRANSPORTATION AND PACKAGING
The notified chemical (up to 100%) will be imported in 10-kg multi-wall paper sacks in a container load of mixed chemicals. The material will be transported by road from the dockside to the Ciba Specialty Chemical warehouse in Victoria and then supplied by road to printing ink manufacturers in Victoria and New South Wales for formulation into a range of decorative packaging printing inks. The decorative packaging printing inks are packed in 20 and 200 kg steel containers prior to distribution to printing press.

5.2. Operation Description

Formulation
The notified chemical will be manually loaded into a mixing tank along with other components, and cold stirred using a high speed stirring process to obtain coloured packaging ink preparations. The packaging ink formulation, containing 3 to 5 % notified chemical, will be filtered and packed into 20 kg and 200 kg steel containers for distribution to packaging printing companies.

Ink Application
Formulated ink product is transferred from supplied containers to printing press ink trays by either pumping or manual transfer from steel containers. Ink application will be applied using roller coating equipment for flexographic printing. Inks are filled under local exhaust ventilation and coating

equipment is also fitted with a filtered exhaust system.

5.3. Occupational Exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Waterside workers	2 – 3	None expected	None expected
Transport and storage workers	4 – 8	1 hour/day	10 – 15 days/year
Blender operators	5 – 10	6 – 8 hours/day	50 – 80 days/year
Quality Control staff	3 – 4	6 - 8 hours/day	50 – 80 days/year
Printer operators	50 – 100	8 hours/day	200 days/year

Exposure Details

Transport and Storage

Up to 11 dockside and warehouse workers will be involved in the transportation of the notified chemical by road in a mixed container load of chemicals from the wharf to the Ciba Specialty Chemical warehouse in Thomastown and the storage of the notified chemical in the appropriate racks. Warehouse workers may handle the paper sacks of the notified chemical for up to 15 days per year for 1 hour per day. The same warehouse workers would be involved in the loading of trucks for transporting notified chemical by road to customers across Australia.

Dockside and warehouse workers routinely wear cotton industrial overalls and steel-capped boots. They are not expected to have any contact with the notified chemical, except in the case of an accident.

Formulation

Dermal, ocular and inhalation exposure to the notified chemical is possible when manually loading the notified chemical into a mixing vessel. The loading operation is carried out under a dust extractor and blending occurs in a closed mixing tank. Personal protective equipment (PPE) includes coveralls, dust mask, gloves and eye protection when carrying out the above activities.

Intermittent dermal exposure to the ink preparations containing 3–5% of the notified chemical is possible when collecting samples for quality testing. Laboratory workers will wear laboratory coats, gloves and eye protection.

Workers may also be exposed to the notified chemical at a concentration of 3–5% from drips and spills when drumming off ink preparations and ink products, and while connecting and disconnecting filling pipes, and during cleaning of equipment.

Ink application

Dermal and ocular exposure to the notified chemical (3–5%) may also occur during end-use when inks are transferred to the printer machine trays.

Maintenance workers and disposal workers may come into contact with the notified chemcial as residue on machinery and in containers respectively. Disposal workers may also be exposed to diluted chemical in waste ink.

Once the ink is dried the chemical is bound within an inert matrix and therefore is considered to be unavailable for exposure.

5.4. Release

RELEASE OF CHEMICAL AT SITE

No release of the notified chemical is expected during shipping and transport. During formulation of the printing ink preparation, < 100 kg/year of notified chemical waste, which are mainly from washing of mixing vessel and pump lines, will be generated. Less than 10 kg/year will remain as waste residues in import containers (paper sacks). It is expected these import sacks containing residual notified chemical will be collected by licensed hazardous waste contractor and disposed to licensed waste landfill site.

RELEASE OF CHEMICAL FROM USE
Release from the use of printing ink is estimated at < 1000 kg/year notified chemical.

Printers are cleaned periodically with a blend of ethanol, isopropanol and ethyl acetate solvent and waste from this process will be collected for solvent reclamation. The resulting solid will be disposed of to landfill. It is expected that formulation equipment will be cleaned in similar manner with the resulting waste disposed as described above.

The remainder of the notified chemical will be incorporated into ink and applied to packaging substances (e.g. fibreboard, plastics).

5.5. Disposal

The notified chemical should be disposed of via incineration in the presence of excess air. Non-recyclable waste arising from article manufacturing sites should be disposed to landfill.

The majority of the notified chemical will be applied to various fibreboard and plastic substrates, which at the end of the useful life, will be disposed to landfill.

The waste derived from the cleaning of formulation equipment, printing equipment and empty import containers will be disposed to landfill. Given the low water solubility, the notified chemical will be associated with the soil matrix and degrade slowly through abiotic and biotic processes.

5.6. Public Exposure

The public is unlikely to be exposed to the notified chemical during transport, storage, printing ink manufacture and printing ink application, except in the event of an accidental spill.

The printing inks are used for food and general packaging; however, the packaging is not in direct contact with food. The public may make dermal contact with the printed packaging material; however, the printed ink once dried and cured is firmly attached to the surface of the substrate and not available for exposure.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Yellow, crystalline powder with typical odour.

Melting Point/Freezing Point 165.6°C

METHOD	OECD TG 102 Melting Point/Melting Range. EC Directive 92/69/EEC A.1 and A.2 Melting/Freezing Temperature.
Remarks	Determined by Differential Scanning Calorimetry. Statement of GLP.
TEST FACILITY	RCC Ltd (2004a)

Boiling Point Decomposes before boiling point

METHOD	OECD TG 103 Boiling Point. EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	Decomposition of the notified chemical was observed at >260ºC before boiling occurred. The boiling point was estimated to be 443.3ºC using the Meissner's method (see Vapour Pressure) Statement of GLP.
TEST FACILITY	RCC Ltd (2004a)

Density 1310 kg/m^3 at 20˚C

METHOD	OECD TG 109 Density of Liquids and Solids. EC Directive 92/69/EEC A.3 Relative Density

Determined by gas comparison pycnometer

Remarks Statement of GLP.

TEST FACILITY RCC Ltd (2004b)

Vapour Pressure 2.3E-9 Pa at 25°C.

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

Remarks The vapour pressure of the notified chemical was estimated using the Modified Watson Correlation based on the boiling point (approximately 443.3°C) calculated using Meissner's method .
Statement of GLP.

TEST FACILITY RCC Ltd (2004c)

Surface Tension 66.7 mN/m at 20.7°C

METHOD OECD TG 115 Surface Tension of Aqueous Solutions.
EC Directive 92/69/EEC A.5 Surface Tension.

Remarks Determine in a 90% saturated solution in water with a tensiometer using the ring method. The notified chemical is not surface active.
Statement of GLP

TEST FACILITY RCC Ltd (2004d)

Water Solubility < 0.17 mg/L at 20°C

METHOD OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Column elution method
Analytical method: HPLC with UV detection (270 nm)

Remarks During the preliminary test the water solubility of notified chemical at room temperature was estimated by simplified flask method to be lower than the smallest calibration point of 0.1708 μg/mL. Therefore, the column elution method was used for the performance of the main test.
During the main test a set of six standards solutions were used to calibrate the HPLC system, having a concentration range of 0.1698 μg/mL to 37.73 μg/mL.
As no notified chemical could be detected in any of the column elutes, the water solubility was state to be below the smallest calibration point of a 0.1698 μg/mL.
Statement of GLP.

TEST FACILITY RCC Ltd (2004e)

Fat Solubility 1100 mg/100 g acetonitrile/acetone at 37°C

METHOD OECD TG 116 Fat Solubility of Solid and Liquid Chemicals.
EC Directive 84/449, A.7 Fat Solubility

Remarks Since the notified chemical was not miscible with the standard fat in a 1:1 ratio, a main test was performed. In the main test, the notified chemical in standard fat at 37^0C with a preliminary equilibration time at 30^0C and 50^0C was tested. The concentration found ranged from 9.8 g/kg to 11 g/kg for the different temperatures and incubation times. The average solubility obtained for the different temperature and incubation times was 11 g/kg.
Statement of GLP.

TEST FACILITY RCC Ltd (2004f)

Hydrolysis as a Function of pH Not determined.

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.

Analytical method: HPLC-UV

Remarks According to the 92/69/EEc, C7 the method is applicable only to water soluble substances. The solubility of the notified chemical in water is very low. It was not possible to increase the solubility of the notified chemical in buffer solutions pH 4.0, pH 7.0, pH 9.0 with the use of different solubilizers (acetone, acetonitrile, dimethylformamide and tetrahydrofuran). Peaks obtained, if any, were too small to allow quantification or even to follow a degradation curve. The notified chemical has a hydrolysable functionality but this is unlikely in the environmental pH range of 4 to 9.

TEST FACILITY RCC Ltd (2004g)

Partition Coefficient (n-octanol/water) log P_{ow} = 6.6 for the first peak at 20ºC
log P_{ow} = 7.3 for the second peak at 20ºC

METHOD OECD TG 117 Partition Coefficient (n-octanol/water), HPLC Method.
EC Directive 92/69/EEC A.8 Partition Coefficient.
Analytical method: HPLC

Remarks During the preliminary test (the ratio of solubility in water and n-octanol), the log Pow of notified chemical was estimated to be above 4.0. Therefore, the HPLC method was chosen to conduct the main test. Six common standards, which have log Pow values in the range of 3.0 to 6.2, were used as reference during the main test.
The chromatography of the notified chemical resulted in two main peaks eluted beyond the higher reference substance. The log Pow was calculated for which each peak using regression curve (log k' vs. log Pow) and was found to be 6.6 and 7.3, respectively.

TEST FACILITY RCC Ltd (2004h)

Adsorption/Desorption – screening test log K_{oc} = 6.3 for the first peak at 25°C.
log K_{oc} = 6.9 for the second peak at 25°C.

METHOD OECD 121 Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography
EC Directive 2001/59/EC C.19 Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography

Remarks Six reference items were used in the analyses having a range of log Koc between 1.25 to 5.63. As it eluted beyond the higher reference substance, the log K_{oc} for the notified chemical was calculated using a regression curve (log k' vs. log K_{oc}) and was found to be 6.3 for the first peak and 6.9 for the second peak.
The above values indicate that the notified chemical is immobile and will be strongly adsorbed to soil.

TEST FACILITY RCC Ltd (2004i)

Dissociation Constant Not applicable

METHOD Expert Statement

Remarks The notified chemical has no sites which can either be protonated or dissociated in the environmentally relevant pH range from 4 to 9.

TEST FACILITY RCC Ltd (2004j)

Particle Size Particle size distribution ranges from 0.5 µm to 2000 µm

METHOD EU Document ECB/TM/February 1996: "Particle Size Distribution, Fibre Length and Diameter Distribution" Guidance Document using a combined method of laser diffraction and sieving.

Range (µm)	*Mass (%)*
<5	0.87
<10	1.09
<50	29.68

<125	51.77
<250	61.58
<500	94.14
<1000	98.74
<2000	99.62

Remarks Mass median diameter (MMD) = 111.6 µm
Respirable fraction 1% < 10 µm
Inhalable fraction 49% < 100 µm
Statement of GLP.
TEST FACILITY RCC Ltd (2004k)

Flammability Limits Not highly flammable

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks The notified chemical could not be ignited with a flame during the preliminary test. Therefore, no main test was performed.
Statement of GLP.
TEST FACILITY RCC Ltd (2004k)

Autoignition Temperature No auto-ignition temperature (>166ºC).

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks Test conducted up to 166ºC. No self-ignition observed up to the melting point of the test substance (166ºC).
Statement of GLP.
TEST FACILITY RCC Ltd (2004l)

Explosive Properties Not explosive

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks None. Explosive potential was studied under heating, mechanical shock or mechanical friction conditions. No explosion was recorded in any test.
Statement of GLP.
TEST FACILITY Institute of Safety and Security (2004)

Oxidising Properties Non oxidizing.

METHOD Expert Statement
Remarks Based on the analysis of the functional groups and on the oxygen balance the notified chemical is considered to be non-oxidising.
TEST FACILITY RCC Ltd (2004m)

Reactivity Not reactive.

Remarks The notified chemical is considered to be non-oxidizing and is not capable of causing fire or enhancing the risk of fire when in contact with combustible material. No incompatible chemicals have been identified with the notified chemical. The product is not explosive when subjected to thermal sensitivity (flame) and mechanical impact (shock or friction). The product is considered to be stable under normal conditions of use. Typical decomposition products are oxides of carbon and oxides of nitrogen, no other toxic gases/vapours have been identified.

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
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly rritating
Mouse, skin sensitisation - LLNA	no evidence of sensitisation.
Rat, oral repeat dose toxicity - 28 days.	NOAEL 50 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro – Chromosome aberration test	genotoxic
Genotoxicity – in vivo – Mouse micronucleus assay	non genotoxic

7.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method (Limit Test) EC Directive 96/54, B.1 tris Acute Oral Toxicity – Acute Toxic Class Method (Limit Test)
Species/Strain	Rat/HanBrI: WIST (SPF)
Vehicle	PEG (Polyethylene glycol) 300
Remarks – Method	No significant protocol deviations. Statement of GLP

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	3 F	2000 mg/kg bw	0
II	3 F	2000 mg/kg bw	

LD50	> 2000 mg/kg bw
Signs of Toxicity	There were no deaths or remarkable body weight changes during the study period. Slightly ruffled fur was noted in all animals of the first treated group from the 1 to 5 hour reading.
Effects in Organs	No macroscopic findings were recorded at necropsy.
Remarks – Results	The LD50 cut-off estimated using the flow chart in Annex 2d of the OECD TG423 would be 5000 mg/kg bw.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	RCC Ltd (2004n)

7.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	Rat/HanBrI: WIST (SPF)
Vehicle	PEG (Polyethylene glycol) 300 (test item diluted at a concentration of 0.5 g/mL)
Type of dressing	Semi-occlusive.
Remarks – Method	No significant protocol deviations.

Statement of GLP.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5 males	2000	0
II	5 females	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	Slight yellow discolouration produced by the test item was noted in all male and female animals from test day 2 to 7 and persisted in one male and one female up to test day 8, in one male and two females up to test day 9, in one male up to test day 10 and in one female animal up to test day 13. Slight violet discolouration was seen in one male and four females on test day 2 and in the male and two females also on test day 3. Slightly focal erythema was observed in two males and one female on day 2 and persisted in the female up to test day 4. Slight scaling was noted in one male from test day 7 to 13.
Signs of Toxicity - Systemic	There were no deaths or test substance related clinical signs or remarkable body weight changes during the study period.
Effects in Organs	No macroscopic findings were observed at necropsy.
Remarks – Results	None.

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

TEST FACILITY RCC Ltd (2004o)

7.3. Acute toxicity – inhalation

REMARKS Not determined

7.4. 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, SPF
Number of Animals	3
Vehicle	Test substance moistened with purified water
Observation Period	7 days
Type of Dressing	Semi-occlusive.
Remarks – Method	No significant protocol deviations. Statement of GLP.

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	-	-	-
Oedema	0	0	0	-	-	-

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

Remarks – Results Slight orange staining of the treated skin in all animals from 1 to the 48

hour examination and persisted up to the 72-hour examination in one animal. No corrosive effects were noted on the treated skin of any animal. There were no deaths or test substance related clinical signs or remarkable body weight changes during the study period.

CONCLUSION The notified chemical is non-irritating to skin.

TEST FACILITY RCC Ltd (2004p)

7.5. Irritation – eye

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain Rabbit/New Zealand White, SPF
Number of Animals 3
Observation Period 72 hours
Remarks – Method No significant protocol deviations.
Statement of GLP.

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	1	< 2 days	0
Conjunctiva: chemosis	0	0	0	1	< 1 day	0
Conjunctiva: discharge	0	0	0	1	< 1 day	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 The instillation of the notified substance into the eye resulted in mild, early-onset and transient ocular changes, such as reddening of the conjunctivae and sclerae, discharge and chemosis. These effects were reversible and were no longer evident 48 hours after treatment. No abnormal findings were observed in the cornea or iris of any animal at any of the examinations. No corrosion was observed at any of the measuring intervals. No staining of the treated eyes by the notified chemical was observed and no clinical signs were observed.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY RCC Ltd (2004q)

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

TEST SUBSTANCE Notified chemical

METHOD OECD 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/CBA/CaOlaHsd
Vehicle Acetone:olive oil, 4:1 (v/v)
Remarks – Method No significant protocol deviations.
Statement of GLP.
The maximum practical dose was reported to be 10% w/v. alpha-hexylcinnamaldehyde was used as the positive control.

RESULTS

Concentration	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0% (control)	592	-
2.5%	533	0.9
5.0%	455	0.8
10%	513	0.9
Positive Control		
5%	504	1.5
10%	755	2.3
25%	2804	8.4

Remarks – Results: There were no deaths or test substance related clinical signs or remarkable body weight changes observed during the study period.

CONCLUSION: There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY: RCC Ltd (2004r)

7.7. Repeat dose toxicity

TEST SUBSTANCE: Notified chemical

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: Rat/SPF-bred Wistar

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: Corn oil

Remarks – Method: No significant protocol deviations.
Statement of GLP.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5/sex	0	0
II (low dose)	5/sex	50	0
III (mid dose)	5/sex	200	0
IV (high dose)	5/sex	1000	0
V (control recovery)	5/sex	0	0
VI (high dose recovery)	5/sex	0	0

Mortality and Time to Death

All animals survived until scheduled necropsy.

Clinical Observations

Pale to orange faeces was observed in males and females treated with 50 mg/kg/day or 200 mg/kg/day of the test substance on treatment day 20, and in animals treated with 1000 mg/kg/day of the test substance on day 20 and from day 22 to 28 in males and from day 22 to 24 in females.

Slight salivation was seen in two males treated with 1000 mg/kg/day on treatment days 18/19 and in up to five males of this dose group on days 21 to 28. In one female of this dose group it was seen on treatment day 16

and up to 5 females it was seen from day 18-28. It could not be excluded that this finding was related. No other treatment related clinical signs were noted daily or weekly in males or females.

Functional Observational Battery
No related clinical signs were noted in males or females in treatment week four.

Grip Strength
No treatment related differences in the mean fore- and hindlimb grip strength were noted when compared with controls after four weeks of treatment.

Locomotor Activity
No treatment related differences in the mean locomotor activity were noted when compared with controls after four weeks of treatment.

Food Consumption
Slight (<10%) dose-related increases in feed consumption were observed in treated males and females from week 2 to 4 and during the 2-week recovery period in high dose males when compared to controls.

Body Weight
A dose-related decrease in body weights was observed in treated males when compared to controls.
The mean absolute body weights of males treated with 1000 mg/kg/day were significantly decreased ($p<0.05$) in treatment week four, with the mean body weight gain significantly decreased ($p<0.01$) from treatment week two to four in males of this dose group and in males treated with 200 mg/kg/day (in treatment week two: $p<0.01$; in week three: not significant; in week four: $p<0.05$) when compared with the controls. This effect was not significant after the two weeks treatment free recovery period. It could not be excluded that this decrease was test item related. No similar effect was observed in females. The slightly decreased ($p<0.05$) mean body weight of females treated with 50 mg/kg/day on treatment day 22 was considered to be incidental because no dose-response relationship was observed.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Clinical Chemistry
The mean activity of aspartate aminotransferase was significantly increased ($p<0.01$) in males treated with 200 (64%) or 1000 (73%) mg/kg/day and in females treated with 50 (62%), 200 (74%) or 1000 (52%) mg/kg/day ($p<0.05$, $p<0.05$, $p<0.01$, respectively). The mean activity of alanine aminotransferase was increased ($p<0.01$) in males and females treated with 200 or 1000 mg/kg/day, when compared with controls after four weeks of treatment. The mean activity of creatine kinase was increased ($p<0.01$) in males treated with 200 or 1000 mg/kg/day, and in females treated with 50 mg/kg/day ($p<0.05$) when compared with controls after four weeks of treatment. The mean activity of bilirubin was significantly increased ($p<0.01$) in males treated with 200 (52%) or 1000 (48%) mg/kg/day and in females treated with 200 (29%, not significant) or 1000 (118%, $p<0.01$) mg/kg/day. The mean activity of globulin was significantly decreased in males treated with 50 (11%), 200 (19%) or 1000 (19%) mg/kg/day ($p<0.05$, $p<0.01$, $p<0.01$ respectively) and significantly decreased in females ($p<0.5$) treated with 50 (10%), 200 (12%) and 1000 (8%) mg/kg/day. The mean activity of triglycerides was significantly increased in males treated with 200 (287%) or 1000 (110%) mg/kg/day ($p<0.01$, $p<0.05$ respectively) and significantly in females ($p<0.5$) treated with 1000 (89%) mg/kg/day. These changes were reversible after the two weeks treatment free recovery period except for aspartate aminotransferase in females.

No other test item-related changes in parameters of clinical chemistry were noted.

Haematology
No test-item related changes in parameters of haematology were noted when compared with control animals after four weeks of treatment and after two weeks treatment free recovery period. Observed effects were either not dose-related or within historical controls and therefore considered incidental.

Urinalysis
No test-item related changes in parameters of urinalyses were noted when compared with controls after four weeks of treatment and after the two weeks treatment free recovery period.

Effects in Organs
Organ weights

A significant increase in the relative (liver to body weight) liver weight was observed in males treated at 200 (18%, p<0.01) and 1000 (11%, p<0.05) and females treated at 50 (18%, p<0.01) and 200 (28%, p<0.01) and 1000 mg/kg/day (24%, p<0.01). The mean liver weights, liver to body weight ratios and liver to brain weight ratios were still increased in females after the two weeks treatment free recovery period. This finding was considered to be test-item related because it could be correlated with the microscopic changes. No other test-item related changes in mean organ weights, organ to body weight ratios and organ to brain weight ratios were noted.

Macroscopic/Microscopic Findings
At necropsy, at the end of the treatment and recovery periods a yellowish discoloration of the mammary glands and of the adipose tissue of the body cavities was recovered in all treated male and female groups. At histopathological examination performed at the end of the treatment and following recovery period related microscopic changes were observed in the liver and thymus. The changes consisted of an increased incidence of single cell necrosis of the hepatocytes in males treated with 200 (4/5 animals) or 1000 mg/kg/day (5/5, only 1/5 animals scored a higher grade in severity compared with the control group) animals compared with the control group of which liver necrosis was observed in 3/5 animals, hepatocytic vacuolation in females treated with 1000 mg/kg/day and lymphoid depletion in the thymus of male rats treated with 1000 mg/kg/day. These findings were considered to be test-item related. After two weeks of recovery period, both liver and thymus returned to normal.

Remarks – Results
Clinical Chemistry
With the exception of increased alanine aminotransferase in females, none of the differences observed in the clinical chemistry parameters during treatment were observed at the end of the recovery period.

Organ Weight
The increased liver weights correlated with changes in clinical chemistry parameters indicative of hepatoxicity (increased aspartate aminotransferase and alanine aminotransferase, increased bilirubin, decreased globulin, increased triglycerides) and histopathological findings in animals treated with ≥ 200 mg/kg/day is considered to be potentially adverse, although as the effects appeared to reverse during the recovery period these changes may represent a metabolic adaptation.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 50 mg/kg bw/day based on the effects in the liver observed at 200 mg/kg bw/day.

TEST FACILITY RCC Ltd (2004s)

7.8. Genotoxicity – *S. typhimurium*

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Pre-incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2 *uvrA*.
Metabolic Activation System	Phenobarbital / beta-Naphthoflavone induced rat liver S9
Concentration Range in Main Test	<u>Test 1</u> a) With metabolic activation: Test 1: 25 - 400 µg/plate b) Without metabolic activation: Test 1: 25 - 400 µg/plate <u>Test 2</u> a) With metabolic activation: Test 1: 5 - 200 µg/plate b) Without metabolic activation: Test 1: 5 - 200 µg/plate
Vehicle	DMSO (dimethyl sulfoxide)
Remarks – Method	No significant protocol deviations. Statement of GLP. Doses selected based on precipitation observed in preliminary test.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	>1000	>400	≥25	Negative
Test 2	>1000	>200	>10	Negative
Absent				
Test 1	>1000	>400	≥25	Negative
Test 2	>1000	200 (TA1535)	>10	Negative

Remarks – Results: The test substance did not cause a marked increase in the number of revertants per plate of any of the tester strains, either in the presence or absence of activation in either test. Negative controls were within historical limits. 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: GenPharmTox Bio Tech AG (2004a)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.
Cell Type/Cell Line: V79MZ Chinese hamster cells
Metabolic Activation System: Phenobarbital/beta-Naphthoflavone induced rat liver S9
Vehicle: DMSO (Dimethyl sulfoxide)
Remarks – Method: No significant protocol deviations.
Statement of GLP.
Doses selected based on precipitation observed in preliminary test.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Present			
Test 1	25*, 10*, 5*, 2.5, 1.25	3	18
Absent			
Test 1	50*, 25*, 10*, 5, 2.5	3	18

*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*
Present				
Test 1	25	>25	25	Positive
Absent				
Test 1	50	>50	≥25	Equivocal

Remarks – Results: Cytotoxicity was not observed at any test concentration. Positive controls confirmed the sensitivity of the test system.

Statistically significant increases in the percentage of aberrant cells above

the vehicle control levels were recorded in the presence of metabolic activation and all concentrations of the notified chemical. A clear dose-response relationship was observed over the analysed concentrations. Slight but not significant increases in the number of structural chromosome aberrations at all concentrations were observed in the absence of metabolic activation however there was no clear dose-response relationship.

At the test-substance concentration of 25 µg/mL in the absence of metabolic activation, one polyploid cell was observed. This finding was within historical control data and therefore no aneugenic potential was assumed.

CONCLUSION The notified chemical was clastogenic to V79 Chinese hamster cells treated in vitro under the conditions of the test.

TEST FACILITY GenPharmTox BioTech AG (2004b)

7.10. Genotoxicity – in vivo

TEST SUBSTANCE Notified chemical

METHOD OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
EC Directive 2000/32/EC, Annex 4C, Micronucleus Assay in Bone Marrow cells

Species/Strain Mouse/NMRI
Route of Administration Oral – gavage
Vehicle PEG (Polethylene glycol) 400
Remarks – Method Test substance administered once.
Only 5 animals/sex/dose group were evaluated for the occurrence of micronuclei.
Statement of GLP.
Deviations from the study plan:
1. The relative humidity under which the experiment was conducted ranged between 18 – 70% and not between 30 – 70% as described in the study plan; the historical control range was updated.
2. The animals of all dose groups were examined for acute toxic symptoms at intervals of around 1h, 2 – 4 h, and 24 h after administration of the test item.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time Hours*
Control	6/sex	0	24 h
Positive Control (CP)	6/sex	40	24 h
I	6/sex	2000	24 h
II	6/sex	2000	48 h
III	6/sex	1000	24 h
IV	6/sex	500	24 h

CP=cyclophosphamide. M=mitomycin C.

RESULTS

Doses Producing Toxicity Generally, the toxic symptoms were significantly reduced at the 1000 and 500 mg/kg bw after 24 h post-dosing. At the 2000 mg/kg bw all toxic reactions accept abdominal position were present 24 h post-dosing with a slight increase in the number of animals exhibiting these symptoms.
Cytotoxic effects were noted only at the highest test concentration of the notified chemical (2000 mg/kg bw) as a slight decrease in the mean number of polychromatic erythrocytes (PCEs) per 2000 erthyrocytes was observed compared to the vehicle control.

Genotoxic Effects	No statistically or biologically significant increase in the frequency of the detected micronuclei at any preparation interval or dose level in comparison with the vehicle control was observed. The mean values of micronuclei observed after treatment with the notified chemical were below or near to the value of the control group. Positive controls confirmed the sensitivity of the test system.
Remarks – Results	Several animals of both sexes within each test-item treated group exhibited reduction in spontaneous activity, abdominal position, eyelid closure and ruffled fur immediately after dosing. The decrease in the number of PCEs is indicative that the test substance reached the bone marrow.
CONCLUSION	The notified chemical was not clastogenic in this in vivo micronucleus assay under the conditions of the test.
TEST FACILITY	RCC Ltd (2004t)

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: Activated sludge (ARA Ergolz II, Fullinsdorf, Switzerland)
- Exposure Period: 28 days
- Auxiliary Solvent:
- Analytical Monitoring: none
- Remarks - Method: For abiotic control and abiotic control blank, the untreated test medium was poisoned with mercury dichloride at a concentration of 10 mg/L.
The reference material was tested simultaneously under the same conditions as the test item, and functioned as a procedure control.
The notified chemical was tested at concentration of 25 mg/L (15 mg TOC/L).
The reference material was tested at concentration of 25.7 mg/L (15 mg TOC/L).

RESULTS

Test substance		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	0.9	2	38.8
5	1.8	5	59.9
9	2.9	9	67.5
14	4.5	14	76.1
19	3.9	19	80.7
23	5.0	23	85.4
28	5.7	28	89.1

- Remarks - Results: In the abiotic control containing the notified chemical and poisoned test medium, no degradation was noted at the end of the 28 day period.
In the toxicity control containing both the notified chemical and reference item no inhibitory effect on activated sludge microorganism was observed.
In the procedure controls, the reference item was degraded to an average extent of 76% by exposure day 14, thus confirming the suitability of the activated sludge (> 60% degradation by Day 14).
The notified chemical was found to be not biodegradable under the test conditions.

CONCLUSION: The notified chemical cannot be classed as readily biodegradable.

TEST FACILITY: RCC Ltd (2004u)

8.1.2. Bioaccumulation

REMARKS: Test not conducted.
Based on the physicochemical properties:
- moderate fat solubility,
- low water solubility,
- no dissociation,
- high values for sorption and partitioning coefficient,

A moderate to high bioconcentration potential cannot be excluded.

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	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 Hours
Auxiliary Solvent	
Water Hardness	175 - 200 mg $CaCO_3$/L
Analytical Monitoring	HPLC-UV-Vis
Remarks – Method	Local tap water (non chlorinated well water of drinking water quality) was used as test water, reduced for total hardness by ion exchange. The test medium was freshly prepared before the start of the test and before each test renewal. Due to low water solubility of the notified chemical, a dispersion of the notified chemical with a loading rate of 100 mg/L was ultrasonicated for 15 minutes and intense stirring by a magnetic stirrer for 96 hours at room temperature in the dark to dissolve the maximum concentration of the notified chemical in dispersion. The dispersion was filtered (0.45 μm) before use. To determine the actual concentration of the notified chemical, duplicate samples from freshly prepared solutions of notified chemical and control were collected at day 0 at 0 hours, day 1 at 24 hours, day 3 at 0 hours and at day 4 at 24 hours. The biological results are related to the mean measured concentration. The test medium was clear throughout.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
100	0.009	7	0	0	0	0	0
Control		7	0	0	0	0	0

LC50	> 0.009 mg/L at 96 hours.
LOEC	> 0.009 mg/L at 96 hours.
Remarks – Results	In the control and in the undiluted filtrate with mean concentration of 0.009 mg/L, no mortality of test fish or other visible abnormalities were determined during the test period of 96 hours. The LC50 and LOEC were clearly higher than the mean measured concentration of 0.009 mg/L.
CONCLUSION	The notified chemical has no acute toxicity effect on Zebra fish up to the solubility limit in the test water under the test conditions.
TEST FACILITY	RCC (2004v)

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 non-renewal test. EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	
Water Hardness	Not determined
Analytical Monitoring	HPLC-UV-Vis

Remarks - Method	Due to low water solubility of the notified chemical, a dispersion of the notified chemical with a loading rate of 100 mg/L was ultrasonicated for 15 minutes and intense stirring by a magnetic stirrer for 96 hours at room temperature in the dark to dissolve the maximum concentration of the notified chemical in dispersion. The dispersion was filtered (0.45 µm) before use. To determine the actual concentration of the notified chemical, duplicate samples from freshly prepared solutions of notified chemical and control were collected at day 0 at 0 hours and at day 4 at 48 hours. The biological results are related to the mean measured concentration.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
100	0.049	20	0	0
Control		20	0	0

LC50	> 0.049 mg/L at 48 hours
NOEC	0.049 mg/L at 48 hours
Remarks - Results	The test medium was a clear solution throughout the whole test duration. The range finding test and the pre-experiment to determine the selection of suitable methods for the preparation of the stock dispersion and the test media were not performed in compliance with the GLP-Regulation. In the control and in the undiluted filtrate with mean concentration of 0.049 mg/L no immobilized test organisms were observed during the test period of 48 hours. The NOEC was determined to be 0.049 mg/L. The LC50 was clearly higher than 0.049 mg/L.

CONCLUSION The notified chemical had not acute toxicity on *Daphnia magna* up to its solubility limit in the test water under the present conditions of the test.

TEST FACILITY RCC (2004w)

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: 0.127 mg/L
Auxiliary Solvent	
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC-UV-Vis
Remarks - Method	

RESULTS Due to low water solubility of the notified chemical, a dispersion of the notified chemical with a loading rate of 100 mg/L was ultrasonicated for 15 minutes and intensely stirred by a magnetic stirrer for 96 hours at room temperature in the dark to dissolve the maximum concentration of the notified chemical in dispersion. The dispersion was filtered (0.45 µm) before use.
To determine the actual concentration of the notified chemical, duplicate samples from freshly prepared solutions of notified chemical and control were collected at day 0 at 0 hours and at day 3 at 72 hours. The biological

results are related to the mean measured concentration. Additionally, volumes of filtrate were diluted with test water 1:2.2, 1:4.6, 1:10 and 1:22.

Biomass Experiment A		*Growth Experiment A*	
E_bC50 (95% CL) mg/L (0-72 h)	*NOEC* mg/L	*E_bC50 (95% CL)* mg/L (0-72 h)	*NOEC* mg/L
> 0.127	0.127	> 0.127	0.127

Remarks - Results

The algal cell densities in the test media on all counting dates were identical with or even slightly higher than those in the parallel control.
The microscopic examination of the algal cell after 72 hours test period showed no difference between the algae growing in the highest test concentration and the algal in the control. The shape and size of the algal cells growing in the test media containing the test item at up to this test concentration were not affected. In the control the cell density was sufficiently high under the conditions of the test, so the validity criterion of increase cell density by at least a factor of 16 over the duration of the study was fulfilled.
All test media were clear solutions throughout the test period. At the start of the test and after 24 hours, the undiluted filtrate and the test medium diluted by a factor of 2.2 were slightly yellowish coloured. At later times the colour could not be determined due to algal growth. The slight coloration had no impact on algal growth.
The 72 hours EC50 for both algal biomass and the mean growth rate were clearly higher than 0.127 mg/L. The notified chemical concentration of 0.127 mg/L was determined as the 72 hours NOEC.

CONCLUSION

The notified chemical has not toxic effect on *Scenedesmus subspicatus* up to it solubility limit in the test water under the present conditions of the test.

TEST FACILITY

RCC (2004x)

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: Activated sludge (ARA Ergolz II, Fullinsdorf, Switzerland)
Exposure Period: 3 hours
Concentration Range: Nominal: 100 mg/L
Actual: not determined

Remarks – Method

The notified chemical was mixed into tap water using ultrasonication over 15 minutes and intense stirring over 24 hours at room temperature in the dark to dissolve a maximum amount of the notified chemical and/or disperse it as homogenously as possible. After the stirring period, 16 mL of synthetic wastewater and 200 mL of activated sludge inoculum were added.
At the start of the test 200 mL activated sludge inoculum with a sludge concentration of 3.7 g dry weight/L (corresponding to about 1.5 g dry material per litre test medium) was added.
The concentration of dissolved oxygen did not drop below 2.5 mg/L during incubation period, and just before the measurements of the respiration rates the dissolved oxygen concentration were at least 8.4 mg/L.

RESULTS	
IC50	> 100 mg/L
NOEC	≥ 100 mg/L
Remarks – Results	At the notified chemical concentration of 100 mg/L a part of the chemical was suspended in the test media. Thus, the test concentration was clearly above the water solubility limit of notified chemical under the conditions of the test. The notified chemical had no significant inhibitory effect (< 15%) on the respiration rate of activated sludge after the incubation period of 3 hours based on the solubility limit of the test concentration of 100 mg/L. The 3 hours EC50 of reference item 3,5-dichlorophenol (positive control) was calculated to be 23 mg/L, which is within the guideline recommended range of 5 – 30 mg/L, confirming the suitability of the activated sludge used.
CONCLUSION	The notified chemical had no significant inhibitory effect (< 15%) on the respiration rate of activated sludge up to it solubility limit in the test water under the conditions of the test.
TEST FACILITY	RCC (2004y)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

No release of the notified is expected during shipping and transport. During formulation of the printing ink preparation, < 100 kg/year of notified chemical waste, which are mainly from washing of mixing vessel and pump lines, will be generated. Less than 10 kg/year will remain as waste residues in import container (paper sacks). It is expected these import sacks containing residual notified chemical will be collected by licensed hazardous waste contractor and disposed to licensed waste landfill site.

Release from the use of printing ink is estimated at < 1000 kg/year notified chemical.
Printers are cleaned periodically with a blend of ethanol, isopropanol and ethyl acetate solvent and waste from this process will be collected for solvent reclamation. The resulting solid will be disposed of to landfill. It is expected that formulation equipment will be cleaned in similar manner with the resulting waste disposed as described above.

The reminder of the notified chemical will be incorporated into ink and applied to packaging substances (e.g. fibreboard, plastics).

The dye containing the notified chemical will be formulated in one city warehouse and distributed to two different states, it major environmental exposure would come from warehouse discharge and from the use of printing ink.

Worst-Case Predicted Environmental Concentration (PEC) Values

Based on the typical use of the dye expected per day, assuming that the whole 100 kg/year waste from formulation is released in either of two STPs (one discharging into a large sewage treatment works, other into a smaller sewage treatment works).

Scenario 1: No Partitioning to sludge
Assuming minimum or no partitioning to sludge within the sewage treatment works as the discharge levels are below the solubility limit.

Process or Dilution Factor	Small STP	Large STP
Typical notified chemical use expected per year	100 kg	100 kg
Number of day per year	260	260
STP daily Volume	139 ML	470 ML
Concentration in effluent from sewage treatment plant	2.71 µg/L	0.8 µg/L
Predicted environmental concentrations (PECs) in receiving waters		
Ocean (Dilution Factor 1:10)		
PEC	0.27 µg/L	0.08 µg/L
River (Dilution Factor 1:1)		
PEC	2.71 µg/L	0.82 µg/L

Scenario 2: Assuming partitioning to sludge
Using the SIMPLETREAT model (European Commission, 2003) to Predicted Environmental Concentration (PEC) Values
Based on the typical use of the dye expected per day, assuming that the whole 100 kg/year waste is released to the two STPs (one discharging into a large sewage treatment works, other into a small sewage treatment works).
Assuming 85% partitioning to sludge within the sewage treatment works as the discharge levels are below the solubility limit and that:

- Henry's Law Constant for the notified chemical is log H = -5,
- log Kow between 6.3 to 6.9,
- No readily biodegradability.

Then, the notified chemical % in the different environmental compartments is as follows:

- 0 % to air
- 15% to water
- 85% to sludge
- 0% degraded
- 85% removal by treatment

Process or Dilution Factor	Small STP	Large STP
Typical notified chemical use expected per year	100 kg	100 kg
Number of day per year	260	260
STP daily Volume	139 ML	470 ML
Concentration in effluent from sewage treatment plant	0.42 µg/L	0.12 µg/L
Predicted environmental concentrations (PECs) in receiving waters		
Ocean (Dilution Factor 1:10)		
PEC	0.04 µg/L	0.01 µg/L
River (Dilution Factor 1:1)		
PEC	0.42 µg/L	0.12 µg/L

Conclusion
The notified chemical physicochemical characteristics strongly suggest that the notified chemical will sorb to the biosolid during treatment (especially in the case of secondary treatment). If the notified chemical does not sorb to the biosolid during treatment (especially in the case of primary treatment), it will leave the STP in the water column but it is expected to sorb to solid and/or sediment components in the aquatic environment.

A moderate to high bioconcentration potential cannot be excluded based on the physicochemical properties (moderate fat solubility, low water solubility, no dissociation, high values for sorption and partitioning coefficient).

9.1.2. Environment – effects assessment

The results of the aquatic toxicity tests are listed below.

Organism	*Duration*	*End Point*	*mg/L*
Fish	96 h	LC_{50}	>0.009
Daphnia	48 h	LC_{50}	>0.049
Algae	0-72 h	EbC_{50}	>0.127
		EuC_{50}	>0.127

Using the most sensitive results of 9 µg/L and a safety factor of 100 (base on 3 experimental results) for fish/*Daphnia*/algal acute toxicity endpoints, a Predicted No Effect Concentration (PNEC) for aquatic ecosystems of > 0.09 µg/L is estimated.

9.1.3. Environment – risk characterisation

Scenario 1

	Location	PEC* µg/L	PNEC µg/L	Risk Quotient (RQ)*
Large STP	Ocean outfall	0.08	>0.09	<0.89
	Inland River	0.8	>0.09	<8.92
Small STP	Ocean outfall	0.27	>0.09	<3.02
	Inland River	2.71	>0.09	<30.16

* The worst-case PEC and the RQ values calculated assuming the notified chemical is not removed during the wastewater treatment during STP process.

The resulting risk quotient (RQ = PEC/PNEC) values for the aquatic environment, assuming that the chemical is not removed during STP processes, are all greater than 1 for freshwater for both STPs and for marine environment for a small STP indicating a concern to these aquatic compartments.

Scenario 2

	Location	PEC* µg/L	PNEC µg/L	Risk Quotient (RQ)*
Large STP	Ocean outfall	0.01	>0.09	<0.14
	Inland River	0.12	>0.09	<1.36
Small STP	Ocean outfall	0.04	>0.09	<0.46
	Inland River	0.42	>0.09	<4.61

* The SIMPLETREAT model PEC and the RQ values calculated assuming the notified chemical is removed during the wastewater treatment during STP process.

The resulting risk quotient (RQ = PEC/PNEC) values less than 1 for ocean waters and greater than 1 for freshwaters for both STPs, indicating a concern to freshwater compartments. However, city plants are not expected to release to fresh water.

The notified chemical is expected to sorb to solid/sediment components in the aquatic environment and decant to ocean and river floor over time.

As toxicology data indicates, the notified chemical is not toxic to fish or aquatic invertebrate up to its water solubility limit. However, the potential problem for this chemical could be it bioaccumulation potential. It is a small and uncharged molecule that has high Pow/Koc values, moderate fat solubility and low water solubility, characteristic that suggest potential to bioaccumulate.

This would not be a problem for the small amounts discharged from formulation, but if uses are proposed that lead to greater amounts being released to water, the risk would have to be reassessed.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Transport and Storage

Exposure to transport and warehouse workers is expected to be negligible, except in the event of an accidental spill.

Ink Formulation

Dermal and possibly ocular and inhalation exposure to the notified chemical may occur during the transfer from the paper sacks to the blending vessel. The estimated typical case dermal exposure is 3000 mg and 900 mg respectively using measured data for the exposure scenario 'dumping of powders in a formulation facility' (European Commission, 2003). Therefore, for a 70 kg worker and a 100% dermal absorption factor, reasonable worst-case and typical case dermal exposure is estimated to be 43 mg/kg bw/day and 13 mg/kg bw/day, respectively.

The estimated atmospheric concentration of notified chemical due to dust is 5-50 mg/m^3, based on EASE model (EASE) using reasonable worst-case defaults (European Commission, 2003). Therefore for a 70 kg worker, assuming an inhalation rate of 1.3 m^3/hour, 8 hour exposure time and 49% Inhalable fraction, inhalation exposure is estimated to be 0.4-3.6 mg/kg bw/day

Exposure would be limited by the use of personal protective equipment (PPE). Due to the automated nature of the blending and filling process, exposure to the notified polymer is expected to be negligible except in the case of a machine malfunction.

Exposure to quality control chemists during sampling and analysis is expected to be low due to low concentration (up to 5%) and the expected small samples involved. Exposure would also be limited by the use of PPE.

Exposure during cleaning processes is expected to be low due to the low concentration (up to 5%) and the expected use of PPE.

Ink Application

The greatest potential for dermal exposure is during introduction of the ink to the print machine especially in the case of small flexographic operations where this process is expected to be completed manually. However, the notified polymer is only present at a maximum concentration of 5% in the printing ink and exposure would be further limited by the wearing of gloves.

9.2.2. Public health – exposure assessment

Public exposure to the notified chemical is only likely after the ink has been applied to the articles such as decorative foil, wrapping or metallised films. The notified chemical is bound within the coating after hardening and is unavailable for exposure. As such, public exposure is expected to be negligible.

9.2.3. Human health - effects assessment

Toxicokinetics, metabolism and distribution

The colouration observed in the oral repeat dose study indicates that the notified chemical and/or its coloured metabolites are both absorbed from the gastrointestinal tract and excreted via the faeces.

Persistent skin discolouration after dermal exposure was indicative of dermal absorption.

Acute toxicity

The notified chemical is considered to be of low acute toxicity when administered orally or when applied to the skin.

Irritation and Sensitisation

Rabbit studies of eye and skin irritation found that the notified chemical is slightly irritating to both eyes but non-irritating to skin. However staining of the skin was evident in one animal at the 72 hour observation period but this reversed by 7 days.

The notified chemical is not considered to be a sensitiser at up to 10%w/v, based on the mouse

local lymph node assay results. The concentration of notified chemical used in the LLNA was 10%w/v, which is significantly lower than the concentration workers involved in formulation of inks, would be exposed to (up to 100%).

Repeated Dose Toxicity
Based on a 28-day subacute oral toxicity study in rats, the No Observed Adverse Effect Level (NOAEL) was established as 50 mg/kg bw/day based on the effects in the liver observed at 200 mg/kg bw/day.

Mutagenicity
The notified chemical was found to be non-mutagenic in the Ames tests. The notified chemical was clastogenic in an *in vitro* chromosomal aberration tests in cultured CHL cells. However the notified chemical was considered non-clastogenic in the *in vivo* mouse micronucleus assay. It is therefore not considered to be genotoxic *in vivo*.

Based on the available data, the notified chemical is not 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

Formulation
Exposure and hence the risk of adverse effects is most likely during the initial transfer of the notified chemical to the blending vessel. Reasonable worst-case exposure tot eh notified chemical was estimated to be 46.6 mg/kg bw/day. Based on an NOAEL of 50 mg/kg bw/day, derived from a 28-day rat oral study the margin of exposure (MOE) is calculated as 1.07. MOE greater than or equal to 100 are considered acceptable to account for intra and inter- species differences. Whilst this margin of exposure is lower than the acceptable value, actual exposure is expected to be lower than that estimated due to the use of worst-case assumptions (including dermal absorption). The risk to workers would be mitigated by the use of PPE (coveralls, gloves, eye protection and disposable dust mask where necessary) and the presence of adequate exhaust ventilation.

As the notified chemical is a slight eye irritant these control measures would also reduce the risk of adverse effects.

Following formulation, the risk of adverse effects from exposure to inks is expected to be low due to the low concentration of the notified polymer (up to 5%).

Ink Application
Although exposure to the notified polymer could occur when introducing the ink to the print machine or when mixing screen printing inks, the risk to workers is expected to be low due to the low concentration (up to 5%) and the expected low toxicity at this concentration.

9.2.5. Public health – risk characterisation

Public exposure to the notified chemical is expected to be negligible and therefore the risk to public health is also expected to be negligible.

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

10.1. Hazard classification

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

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	*Hazard statement*
Chronic	4*	May cause long lasting harmful effects to aquatic life

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio:

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 Moderate Concern to occupational health and safety under the conditions of the occupational settings described based on potential adverse systemic effects. The use of recommended controls would mitigate the risk.

10.3.2. Public health

There is Negligible Concern to public health when used in the proposed manner.

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.

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

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  - Local exhaust ventilation

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced, and as diluted for use in the ink products:
  - MSDS should be provided to the authorised medical practitioner responsible for health surveillance in the workplace

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced, and as diluted for use in flexographic inks:
  - Protective clothing
  - Chemical resistant gloves
  - Chemical gloves or safety glasses
  - Respirators where local exhaust ventilation is insufficient.

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

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

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

Disposal

- The notified chemical should be disposed of by:

Via incineration in the presence of excess air. Non-recyclable waste arising from article manufacturing sites should be dispose to landfill.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by:

Small or large spills of the notified chemical should be contained and swept up together with a dust binding agent. Dust formation should be avoided. The spilled product should be placed into suitable containers, which must be tightly sealed and properly labelled. Due to the virtually insoluble nature of the notified chemical, it should not be washed to drains, sewer system or waterways. The spill residue should also be prevented from entering drains, sewer system and waterways.

12.1. Secondary notification

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

(1) Under Section 64(1) of the Act; if
  – *Uses/changes are proposed that lead to greater amounts being released to sewer systems or waterways*

or

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

The Director will then decide whether secondary notification is required.

13. BIBLIOGRAPHY

Estimation and Assessment of Substance Exposure (EASE). The EASE system was developed by the UK Health and Safety Executive in conjunction with the Artificial Intelligence Applications Institute. For a further description see: Marquart et al., Evaluation of Methods of Exposure Assessment for Premarket Notifications, TNO Report V 94.229 TNO Nutrition and Food Research (Zeist), 1994.

European Commission (2003) Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances and Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market – Part I. Institute for Health and Consumer protection, European Chemicals Bureau, European Communities.

GenPharmTox BioTech AG (2004a) [Notified Chemical]: Bacterial Reverse Mutation Test. Study Number 03092402. GenParmTox BioTech AG, Martinsried, Germany (unpublished report supplied by notifier)

GenPharmTox BioTech AG (2004b) [Notified Chemical]: In vitro mammalian chromosome aberration test. Study Number 03102401. GenParmTox BioTech AG, Martinsried, Germany (unpublished report supplied by notifier)

Institute of Safety & Security (2004) Determination of the Explosive Properties of [Notified Chemical]. Study Number 853909. Institute of Safety & Security, Basel, Switzerland (unpublished report supplied by 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 (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.

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

RCC Ltd (2004a) Determination of the Melting Point / Melting Range and the Boiling Point / Boiling Range of [Notified Chemical]. Study Number 853903. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004b) Determination of the Relative Density of [Notified Chemical]. Study Number 853904. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004c) Calculation of the Vapour Pressure of [Notified Chemical]. Study Number 853905. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004d) Determination of the Surface Tension of an Aqueous Solution of [Notified Chemical]. Study Number 853906. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004e) Determination of the Water Solubility and the Partition Coefficient (N-Octanol/Water) of [Notified Chemical]. Study Number 853907. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004f) Determination of the Fat Solubility of [Notified Chemical]. Study Number 853914. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004g) Hydrolysis Determination of [Notified Chemical] at different pH Values. Study Number 853931. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004h) Estimation of the Adsorption Coefficient of [Notified Chemical] on Soil using High Performance Liquid Chromatography. Study Number 853932. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004i) Expert Statement on the Dissociation Constant of [Notified Chemical]. Study Number 853913. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004j) Determination of the Particle Size Distribution of [Notified Chemical]. Study Number 853912. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004k) Determination of the Flammability of [Notified Chemical]. Study Number 853908. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004l) Determination of the Relative Self-Ignition Temperature of [Notified Chemical]. Study Number 853910. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004m) Expert Statement on the Oxidizing Properties of [Notified Chemical]. Study Number 853911. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004n) [Notified Chemical]: Acute Oral Toxicity Study in Rats. Study Number 853915. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004o) [Notified Chemical]: Acute Dermal Toxicity Study in Rats. Study Number 853916. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004p) [Notified Chemical]: Primary Skin Irritation Study in Rats (4-Hour Semi-Occlusive Application). Study Number 853917. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004q) [Notified Chemical]: Primary Eye Irritation Study in Rabbits. Study Number 853918. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004r) [Notified Chemical]: Local Lymph Node Assay (LLNA) in Mice (Identification of Contact Allergens). Study Number 853919. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004s) [Notified Chemical]: 28-Day Oral Toxicity (Gavage) Study in the Wistar Rat. Study Number 853920. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004t) Micronucleus Assay in Bone Marrow Cells of the Mouse with [Notified Chemical]. Study Number 817500. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004u) Ready Biodegradability of [Notified Chemical] in a CO2 Evolution (Modified Sturm) Test. Study Number 853930. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004v) Acute Toxicity of [Notified Chemical] to Zebra Fish (*Brachydanio rerio*) in a 96-Hour Semi Static Test. Study Number 853923. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004w) Acute Toxicity of [Notified Chemical] to *Daphnia Magna* in a 48-Hour Immobilization Test. Study Number 853925. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004x) Toxicity of [Notified Chemical] to *Scenedesmus Subspicatus* in a 72-Hour Algal Growth Inhibition Test. Study Number 853927. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

RCC Ltd (2004y) Toxicity of [Notified Chemical] to Activated Sludge in a Respiration Inhibition Test. Study Number 853929. RCC Ltd, Itingen, Switzerland (unpublished report supplied by notifier)

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