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September 2005

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

AO-282-39

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Carter Holt Harvey Australia Pty Ltd (ABN 77 000 601 892)
Como Office Tower
644 Chapel Street
South Yarra VIC 3141

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
Molecular Weight
Purity
Composition
Identity of Chemical Analogue Accepted for Toxicological Assessment

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

Dissociation constant
Flammability
Acute dermal toxicity
Acute inhalation toxicity
Skin irritation
Eye irritation
Skin sensitisation
Mammalian genotoxicity
Toxicity to fish
Toxicity to Daphnia
Toxicity to algae
Ready biodegradation

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
No.

NOTIFICATION IN OTHER COUNTRIES
USA (1994)
Currently being notified in the EU, China, Korea and the Philippines.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
AO-282-39

SPECTRAL DATA

METHOD	^{1}H Nuclear Magnetic Resonance Spectroscopy UV/visible Spectroscopy Infrared Spectroscopy
Remarks	Reference spectra were provided.
TEST FACILITY	Arizona Chemical BV

METHODS OF DETECTION AND DETERMINATION

METHOD	Gas chromatography.
Remarks	Reference chromatogram was provided.
TEST FACILITY	Arizona Chemical BV

3. COMPOSITION

DEGREE OF PURITY
>80%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
No hazardous impurities at concentrations requiring classification.

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% by weight)
Eight non-hazardous impurities totally <20%.

ADDITIVES/ADJUVANTS
None.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia within formulated inks, at concentrations up to 14%.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	100	100	100	100	100

USE
The notified chemical is an “ink solvent” that plasticises the ink. Imported formulated inks will be used in printing plants to print documents such as magazines, labels and packaging materials.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Not known yet.

IDENTITY OF MANUFACTURER/RECIPIENTS
Not known yet.

TRANSPORTATION AND PACKAGING
Formulated inks will be imported in metal containers ranging from 1 L tubs to 25 kg drums.

5.2. Operation description

Formulated inks in import containers will be transported to printing works.

In small scale works, the ink will be poured or scooped out of 1 L tubs into the ink reservoir of the printing machine. During the printing operation the ink will be replenished in the machine in the same manner as the initial charging.

In larger scale printing works, the ink will be pumped from larger containers directly to the ink reservoir of the printing machine, and automatically replenished as required during operation. The ink container will be changed regularly, often daily. This will involve transferring the dip tube from the empty drum to the full drum.

At the end of each day, or at the end of a printing job, the machine will be cleaned. Typically the ink-contaminated parts of the machine will be wiped with rags, with or without solvents.

5.3. Occupational exposure

Number and Category of Workers per Site (number of sites not yet known)

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency (days/year)*
Transport & warehouse	Not known	4 hours/day	10
Printing (decanting)	2	5 minutes, 8 times/day	230
Printing (cleaning)	2	30 minutes/day	230

Exposure Details

Transport and warehousing

Transport and warehouse workers may come into dermal and ocular contact with the notified chemical through accidental leaks and spillages of the drums and containers.

Printing

Workers involved in printing processes may be dermally exposed to ink containing up to 14% notified chemical when decanting drums of ink into the reservoir of a printing machine, and when replenishing the reservoir of the ink pump. Ocular exposure is possible in the event of accidental splashing. It is usual for the machine operator to wear goggles, rubber gloves and overalls for this operation. The operator may also wear an apron if the risk of ink splashing is greater for a lower viscosity ink formulation. Inhalation exposure is possible during drying of printed material, however this should be minimised by controlled drying. Once dried, the ink will be cured into an inert matrix, and hence unavailable for further exposure. Dermal exposure is possible during cleaning of the printing machine, however goggles, gloves and overalls will be worn during this operation.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Environmental release of the notified chemical is unlikely during importation, storage and transportation. Accidental spills, leaks and catastrophic mechanical failure during a transport accident are the most likely reasons for environmental release. Engineering controls (eg. drum specifications) and emergency clean-up procedures (ie. spill response instructions on the Material Safety Data Sheet and label) will limit the impact on the environment of such incidents. Containers holding the notified chemical will be transported directly from the Port facility to various facilities in Australia for storage prior to use.

RELEASE OF CHEMICAL FROM USE

There is limited potential for environmental release of the notified chemical during printing operations carried out exclusively by industrial users. Releases are associated with the use of the printed paper articles and disposal of wastes to landfill, by incineration or by recycling. After application, the notified chemical will be bound to the paper surface and will not be available for dissolution or leaching to the environment.

5.5. Disposal

A small amount of ink is wasted during start-up of presses and this is applied to paper that is discarded as waste paper for recycling. Cleaning of printing presses and other equipment results in a limited amount of solvent-based waste, which is collected by a licensed contractor for solvent recovery and incineration of residue. Emptied containers will be discarded with the containers to container/metal recycling facilities or washed and sent to landfill with the washings collected for solvent recovery.

Eventually, most of the notified chemical will be either landfilled or sent for recycling in paper products. Recycling may take place in a number of centres throughout Australia. During the paper recycling process, waste paper is repulped using a variety of alkaline, dispersing and wetting agents, water emulsifiable organic solvents and bleaches. Trade sources estimate the washing process will recover 30-60% of the total amount of ink and therefore, at least 30% of the notified chemical in the recycled paper will be disposed of with sludge in landfill or incinerated. However, in this case a greater proportion can be expected to partition to the sludge compartment due to the very low water solubility of the notified chemical.

5.6. Public exposure

Imported formulated inks containing up to 14% notified chemical will not be available to the general public. The public will come into contact with documents printed with ink containing the notified chemical; however this will be cured into an inert matrix. Thus overall exposure to the notified chemical is expected to be low.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Yellow liquid.

Melting Point <-20ºC

METHOD	EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	Method for the determination of crystallising point.
TEST FACILITY	SafePharm (2005a)

Boiling Point 349ºC at 101.7 kPa

METHOD	EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	Differential scanning calorimetry method.
TEST FACILITY	SafePharm (2005a)

Density 897 kg/m^3 at 20ºC

METHOD	EC Directive 92/69/EEC A.3 Relative Density.
Remarks	Pycnometer method.
TEST FACILITY	SafePharm (2005a)

Vapour Pressure 8.3 x 10^{-6} kPa at 25ºC

METHOD	EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks	Vapour pressure balance method. The test substance is classified as slightly volatile (Mensink *et al.* 1995).
TEST FACILITY	SafePharm (2005b)

Water Solubility 1.6 x 10^{-3} g/L at 20ºC

METHOD	Flask/visual estimation method/GC analysis.
Remarks	This result is likely to be an overestimation due to emulsification. A calculated estimate using an atom-fragment contribution method gave a result of 3.81 x 10^{-6} g/L.
TEST FACILITY	SafePharm (2005a)

Hydrolysis as a Function of pH

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

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

Remarks Samples were analysed by gas chromatography. Less than 10% hydrolysis was observed at pH 4, 7 and 9 after 5 days at 50°C. This is likely to result from the low water solubility.

TEST FACILITY SafePharm (2005a)

Partition Coefficient (n-octanol/water) log P_{ow} > 6.5

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

Remarks HPLC Method.
A calibration curve was prepared using standard chemicals with Log P_{ow} ranging from 2.1-6.5. The test material eluted from the column after all the standard chemicals.

TEST FACILITY SafePharm (2005a)

Adsorption/Desorption log K_{oc} > 5.63

METHOD EC Directive 92/69/EEC C.19 Adsorption Coefficient.

Remarks HPLC Screening Method.
A calibration curve was prepared using standard chemicals with log K_{oc} ranging from 1.25-5.63. The test material eluted from the column after all the standard chemicals.

TEST FACILITY SafePharm (2005a)

Dissociation Constant Not determined.

Remarks The notified chemical is a mixture of components that will have a range of dissociation constants, while the OECD and EU test guidelines are applicable to pure substances only.

Particle Size Not applicable to a liquid.

Flash Point 125ºC at 101.3 kPa

METHOD EC Directive 92/69/EEC A.9 Flash Point.

Remarks Closed cup method.

TEST FACILITY SafePharm (2005b)

Flammability Limits Not determined.

Remarks Based on the flash point result, the notified chemical is not classified as flammable according to ADG criteria.

Based on the known properties of the notified chemical and its chemical structure, negative results are predicted for flammability in contact with water or with an oxidising substance. Negative results are also predicted for pyrophoric properties.

Based on the high auto-ignition temperature, the notified chemical is not liable to spontaneous combustion.

Autoignition Temperature 316ºC

METHOD	92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	None.
TEST FACILITY	SafePharm (2005b)

Explosive Properties

Remarks	There are no chemical groups that would imply explosive properties. Hence the result is predicted negative.

Reactivity

Remarks	The chemical does not have oxidising properties based on known chemical and physical properties and its chemical structure. There is no known incompatibility with other substances. There are no known conditions contributing to instability. The notified chemical is considered to be stable. However, the chemical will burn if involved in a fire, evolving noxious fumes (e.g. carbon oxides).

7. TOXICOLOGICAL INVESTIGATIONS

Acute oral toxicity and bacterial mutagenicity were tested for the notified chemical. All other toxicity end points were assessed using data from studies using a close chemical analogue that was previously notified as STD/1136 by the current notifier.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral	LD50 >2500 mg/kg bw low toxicity
Rat, acute dermal	low toxicity
Rat, acute inhalation LC50	not performed
Rabbit, skin and eye irritation	slightly irritating
Guinea pig, skin sensitisation – non-adjuvant test.	no evidence of sensitisation
Rat, repeat dose oral toxicity – 90 days.	NOEL 50 mg/kg bw/day
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	non genotoxic

7.1. Acute toxicity – oral

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
EC Directive 2004/73/EEC B.1tris Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain Rat/Sprague-Dawley (CD)
Vehicle None.
Remarks - Method None.

RESULTS

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

LD50 >2500 mg/kg bw
Signs of Toxicity None observed.
Effects in Organs None observed.
Remarks - Results None.

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

TEST FACILITY SafePharm (2005c)

7.2. Acute toxicity – dermal

TEST SUBSTANCE A close analogue of the 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/Crl: CD (SD) IGS BR
Vehicle None.
Type of dressing Semi-occlusive.
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	0

LD50	>2000 mg/kg bw
Signs of Toxicity - Local	There were no signs of local toxicity.
Signs of Toxicity - Systemic	There were no signs of systemic toxicity. One female showed a bodyweight decrease in the first week of the study but expected body weight gain during the second week. All other animals showed expected bodyweight gains throughout the study.
Effects in Organs	No abnormalities were noted at necroscopy.
Remarks - Results	None.

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

TEST FACILITY SafePharm (2004a)

7.3. Acute toxicity – inhalation

The test was not conducted. The notified chemical is a non-volatile liquid hence is not expected to be an inhalation hazard when imported as a component of a liquid formulation.

7.4. Irritation – skin

TEST SUBSTANCE A close analogue of the notified chemical.

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None.
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.3	0.7	0.7	2	48 hours	0
Oedema	0.3	0.3	0.3	2	24 hours	0

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

Remarks - Results Area of test site: dorsal/flank region. Well-defined erythema and slight oedema was observed in all test animals at the 1-hour observation period, which resolved over 24 to 48 hours.

CONCLUSION The analogue chemical is slightly irritating to the skin.

TEST FACILITY SafePharm (2002a)

7.5. Irritation – eye

TEST SUBSTANCE A close analogue of the notified chemical.

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

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	0.3	0.3	2	24 hours	0
Conjunctiva: chemosis	0	0	0	1	1 hour	0
Conjunctiva: discharge	0	0.3	0	2	24 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks – Results Minimal to moderate conjunctival irritation was noted in all animals one hour after treatment with minimal conjunctival irritation in 2 animals at the 24-hour observation period. No signs of irritation were observed in one animal at 24 hours. No signs of irritation were observed in any animal at the 48-hour observation period.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY SafePharm (2002b)

7.6. Skin sensitisation

TEST SUBSTANCE A close analogue of the notified chemical.

METHOD Magnusson and Kligman maximisation method
OECD TG 406 Skin Sensitisation
EC Directive 96/54/EC B.6 Skin Sensitisation
Species/Strain Guinea pig/Dunkin Hartley
PRELIMINARY STUDY Maximum Non-irritating Concentration:

Intradermal: Not determined. At 1% (v/v) in arachis oil BP, moderate and confluent erythema was seen at injection sites, persisting for >72 hours.

Topical: Not determined. At 25% (v/v) in arachis oil BP, discrete or patchy erythema was seen up to 24 hours.

MAIN STUDY
Number of Animals Test Group: 10 Control Group: 5
INDUCTION PHASE Induction Concentration:
intradermal: 1% (v/v) in arachis oil BP
topical: undiluted

Signs of Irritation	Intradermal injection: Moderate and confluent erythema was seen at 24 hours and 48 hours in all treated animals. Discrete and patchy erythema was seen at 24 hours and 48 hours in all control animals receiving 100% arachis oil BP Topical: Staining was noted at the topical induction site of all test group animals, lasting for 2 hours, but did not affect the evaluation of skin responses. Moderate and confluent erythema, with slight oedema, was seen in every test group animal at 2 hours. Bleeding was noted in three test group animals at the 2-hour observation. Discrete or patchy to moderate and confluent erythema, without oedema, was seen in every test group animal after 24 hours. Small superficial scattered scabs were noted in one test group animal. No reactions were seen for any animals receiving the control dose.
CHALLENGE PHASE	
1st challenge	intradermal: not conducted topical: 75% *v/v* in arachis oil BP – right flank 50% *v/v* in arachis oil BP – right flank
Remarks - Method	Erythema and oedema were assessed 2 hours after topical induction, in addition to the usual assessment after 24 hours. Both 75% and 50% concentrations of the notified chemical were used in the topical challenge phase to ensure that the maximum non-irritant concentration was used in the study. Test sites were not pre-treated with sodium lauryl sulfate before topical induction.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		24 h	*48 h*
Test Group	75% (right flank)	1	0
	50% (left flank	0	0
Control Group	0	0	0

Remarks - Results	The slight erythema observed in one animal receiving a challenge dose of 75% at the 24-hour observation period, but not the 48-hour observation period, was most likely residual erythema caused by irritation.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the analogue chemical under the conditions of the test.
TEST FACILITY	SafePharm (2002c)

7.7. Repeat dose toxicity

TEST SUBSTANCE	A close analogue of the notified chemical.
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Crl:CD (SD) IGS BR
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	Arachis oil BP
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	10/sex	0	0
II (low dose)	10/sex	5	0
III (mid dose)	10/sex	50	0
IV (high dose)	10/sex	1000	0

Mortality and Time to Death

All animals survived until the end of the study.

Clinical Observations

Increased salivation was detected up to one hour after dosing for animals of either sex treated with 1000 mg/kg bw/day from day 14 onwards. This is commonly observed following oral gavage administration of a slightly irritant or unpalatable test material. Males treated with 50 or 1000 mg/kg bw/day showed a statistically significant increase in sensory reactivity parameters. These were attributed to abdominal discomfort associated with the gavage procedure.

Males treated with 5 and 50 mg/kg bw/day showed a statistically significant ($p<0.05$) increase in bodyweight gain during week 2 compared to controls (15% and 19% respectively) with all other weekly bodyweight gains not significantly different from controls. In the absence of a dose-related response, or findings in other weeks, this is considered not to be of toxicological significance.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Blood chemistry analysis revealed that males treated with 1000 mg/kg bw/day showed statistically significant increases ($p<0.05$) in cholesterol (17%) and creatinine (8%) levels. In the absence of a dose-related response this is considered not to be of toxicological significance.

Males treated with 1000 mg/kg bw/day showed a statistically significant decrease in erythrocyte count ($p<0.05$, 4%). In the absence of any other haematological changes, and given the marginal nature of the decrease, this is considered not to be of toxicological significance.

Effects in Organs

The following effects were observed in the 1000 mg/kg bw/day group:

- increased absolute spleen weight ($p<0.05$, 20%) in males.
- increased relative kidney weight ($p<0.01$, 9%) in females
- increased absolute ($p<0.01$, 22%) and relative adrenal weight ($p<0.01$, 20%) in females.

The toxicological significance of these findings is uncertain as there were no supporting histopathology findings.

In the liver, the following effects were observed:

- increased absolute liver weights in males ($p<0.001$, 36%) and females ($p<0.001$, 24%), and
- increased relative liver weights in males ($p<0.001$, 28%) and females ($p<0.001$, 22%).

A marginal effect on hepatocyte size was observed in females treated with 1000 mg/kg bw/day ($p<0.05$) with a few animals from this group exhibiting centrilobular hepatocyte enlargement.

Remarks – Results

The most marked changes occurred in the liver of animals in the 1000 mg/kg bw/day group. The elevated relative and absolute liver weights in male and female rats are suggestive of an adaptive response in the liver to the notified chemical in the high dose treatment group. Animals in the 1000 mg/kg bw/day also showed increases in spleen, kidney and adrenal weight. None of these changes were observed in the 50 mg/kg bw/day group.

CONCLUSION
The No Observed Effect Level (NOEL) of the analogue chemical in male and female rats was established as 50 mg/kg bw/day in this study on the basis of both relative and absolute weight changes in the liver at 1000 mg/kg bw/day.

TEST FACILITY SafePharm (2004b)

7.8. Genotoxicity – bacteria

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.
USA, EPA (TSCA) OPPTS harmonised guidelines
Plate incorporation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	β-naphthoflavone and phenobarbitone-induced rat liver S9 fraction.
Concentration Range in Main Test	a) With metabolic activation: 50-5000 µg/plate b) Without metabolic activation: 50-5000 µg/plate
Vehicle	Acetone.
Remarks - Method	None.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	None observed up to 5000.	None observed.	5000	None observed.
Test 2		None observed.	5000	None observed.
Present				
Test 1	None observed up to 5000.	None observed.	5000	None observed.
Test 2		None observed.	5000	None observed.

Remarks - Results Positive control chemicals induced marked increases in the frequency of revertant colonies. Negative controls prepared on the same day as the main test were within historical ranges.

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

TEST FACILITY SafePharm (2005d)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE A close analogue of the notified chemical.

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

Cell Type/Cell Line	Lymphocytes cultured from the blood of a suitable volunteer
Metabolic Activation System	S9
Vehicle	Acetone
Remarks – Method	2500 µg/ml was used as the maximum dose due to precipitation at 5000 µg/ml.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 39, 78.1, 156.25, 312.5*, 468.75*, 625*	24 hours	24 hours
Test 2	0*, 78.1, 156.25, 312.5, 625*, 1250*, 2500*	4 hours	24 hours
Present			
Test 1	0*, 78.1, 156.25, 312.5, 625*, 1250*, 2500*	24 hours	24 hours
Test 2	0*, 78.1, 156.25, 312.5, 625*, 1250*, 2500*	4 hours	24 hours

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	Not performed	Up to 39% mitotic inhibition	>2500 µg/plate	negative
Test 2	Not performed	Up to 14% mitotic inhibition	>2500 µg/plate	negative
Present				
Test 1	Not performed	Negligible mitotic inhibition	>2500 µg/plate	negative
Test 2	Not performed	Up to 22% mitotic inhibition	>2500 µg/plate	negative

Remarks - Results

The notified chemical did not induce a statistically significant increase in the frequency of cells with chromosomal aberrations in either the absence or the presence of a liver enzyme metabolic system in either of two separate experiments.

Treatment with positive control substances induced distinct increases in cells with structural chromosomal aberrations.

CONCLUSION

The analogue chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.

TEST FACILITY

SafePharm (2004c)

8. ENVIRONMENT

No environmental fate or toxicity data are available for the notified chemical. The following data were presented for an analogue chemical AO-119-144 which was notified as STD/1136. Similar results for other ethers have also been provided but have not been included. Results for the acid salts have also not been included as they are less relevant.

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE: AO-119-144

METHOD
- Inoculum: Mixed culture of activated sewage sludge micro-organisms (Severn Trent Water plc sewage treatment works); tripled rinsed; suspended solids 3.0 g/L prior to use.
- Exposure Period: 28 d
- Auxiliary Solvent: None
- Analytical Monitoring: CO_2 in produced gas and dissolved organic carbon in solution
- Remarks - Method: Test material (38.4 g) was dispersed directly in the culture medium (200 mL) and subjected to ultrasonication (30 mins) prior to dispersal in inoculated culture medium made up to 3 L and added to 5 L glass bottles. Bottles were sealed and CO_2-free air bubbled into the stirred solutions (40 mL/min) and maintained in the dark. Initial test material concentration was 12.8 mg/L (10 mg C/L). The CO_2 produced was captured and analysed approximately daily. Test temperature 21°C. Each test vessel was inoculated to give a final concentration of 30 mg suspended solids/L. Test solutions pH range: 7.4-7.5.

RESULTS

Test substance (12.8 mg/L)		*Sodium benzoate (17.1 mg/L; 10 mg C/L)*	
Day	*% Degradation*	*Day*	*% Degradation*
1	0	1	13
2	19	2	38
6	37	6	45
12	40	12	55
16	58	16	73
28	60	28	92

- Remarks - Results: All test validation criteria were met. The reference substance (sodium benzoate) degraded by 92% after 28 d confirming the suitability of the inoculum and test conditions. In the toxicity control, the test material attained 79% degradation by day 28 confirming that the test substance was not toxic to the sewage micro-organisms used in the study.

CONCLUSION: The test material achieved 60% degradation after 28 days; however, it was not readily biodegradable under the conditions as it did not pass the 10 day window criterion for this test.

TEST FACILITY: SafePharm (2002d)

8.1.2. Bioaccumulation

- Remarks - Results: Not determined. The notified chemical has an affinity for lipids and may potentially be capable of passing biological membranes; however, the limited potential for release to water indicates a low potential for accumulation in aquatic organisms.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE AO-119-144

METHOD OECD TG 203 Fish, Acute Toxicity Test - Freshwater/semi-static.

Species Rainbow trout *Onchorhynchus mykiss.* Juvenile 3.6 cm long, 0.57 g. Loading rate 0.29 g bodyweight/L

Exposure Period 96 h

Auxiliary Solvent Acetone

Water Hardness 100 mg/L as $CaCO_3$

Analytical Monitoring GC (Limit Of Quantitation 0.0035 mg/L). Test solution samples were analysed at 0, 24, 48, 72 and 96 h.

Remarks – Method At concentrations greater than 0.2 mg/L, the test substance formed a dispersion in the test solution. Stock solution (200 mg/10 mL solvent) was dispersed in dechlorinated tap water to give the nominal test concentration made up to 22 L. Test temperature: 14°C. DO range: >9.8 mgO_2/L. pH: 7.5-8.0. Photoperiod: 16 h light and 8 hours dark. Effects were monitored at 3, 6, 24, 48, 72 and 96 h.

In a preliminary stability test, the test material was unstable in water and acetone after storage in sealed glass vessels at ambient temperature in light and dark conditions for 24 h. Under these conditions, stability was also assessed without mixing (sonication) and analytical testing of the unsonicated stability vessel solution showed no evidence of insolubility or adherence to glass. Stability was found to be directly proportional to storage temperature. The analytical method gave low recoveries (~50%) but was considered by the laboratory to be sufficiently precise for the purposes of the test. All test sample results were corrected for mean procedural recovery applicable to each test sample period. Centrifuged test solutions showed much lower concentrations than uncentrifuged samples, indicating that the test substance was in a dispersion, separate phase (eg. fine globules) or settled form (undissolved). The test substance concentration was stable for the test period of renewal only in the centrifuged samples but reduced over time in the untreated solutions.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Solvent control	<LOQ	20 (2 replicates of 10)	0	0	0	0	0
0.20	0.29	20 (2 replicates of 10)	0	0	0	0	0

LC50 >0.045 mg/L at 96 hours (time-weighted mean)

NOEC 0.045 mg/L at 96 hours (time-weighted mean)

Remarks – Results An estimate of the LC50 value was made based on the inspection of the mortality data.

The test material was unstable during the test, with marked reduction in test material concentration after the period of media renewal (24 h) and the reason for this was not determined.

Bioconcentration of the test substance into test organisms may also have occurred during the test. Exposure concentrations were calculated using mean measured values of the centrifuged samples.

CONCLUSION The test material was not toxic to fish up to the mean measured test concentration of ≤0.045 mg/L, or conversely up to the limit of its solubility.

TEST FACILITY SafePharm (2004d)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE AO-119-144

METHOD OECD TG 202 *Daphnia* sp. Acute Immobilisation Test and Reproduction Test – freshwater/semi-static.

Species	*Daphnia magna* (<24 h old)
Exposure Period	48 hours
Auxiliary Solvent	Acetone
Water Hardness	250 mg/L as $CaCO_3$
Analytical Monitoring	GC (0, 24 and 48 h)
Remarks - Method	Preliminary and definitive tests were conducted. Test temperature: 21°C. pH: Photoperiod: 16 h light and 8 h dark. Effects were monitored at 24 and 48 h. Test aquaria: 250 mL glass beakers.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Solvent control	<LOQ	40 (4 replicates of 10)	0	0
0.20	0.20	"	0	0

EC50	>0.044 mg/L (time-weighted mean) at 48 hours
NOEC	0.044 mg/L (time-weighted mean) at 48 hours
Remarks - Results	As above for the fish toxicity test, the test material was unstable and there was a marked decline in concentration over a 24 h period when test solutions were replaced. Unlike in the fish test, the centrifuged samples were not stable for the duration of the test solution renewal period. Test values are presented on a time-weighted average basis of centrifuged samples.

CONCLUSION The test material was not toxic to *Daphnia magna* at the time-weighted mean concentration tested (0.045 mg/L), or conversely up to the limit of its solubility.

TEST FACILITY SafePharm (2004e)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE AO-119-144

METHOD OECD TG 201 Alga, Growth Inhibition Test.

Species	Freshwater green algae (*Scenedesmus subspicatus*)
Exposure Period	72 hours
Concentration Range	Nominal: 0.20 mg/L Actual: 0 h = 0.2 mg/L, 72 h = 0.01 mg/L.
Auxiliary Solvent	Acetone
Water Hardness	Not reported
Analytical Monitoring	GC (0 and 72 h; samples with and without centrifugation).
Remarks – Method	Preliminary and definitive tests were performed. Test material (200 mg) was dissolved in acetone and the volume adjusted to 10 mL to give a 200 mg/10 mL solvent stock solution from which a dilution was made (20 mg/10 mL). An aliquot (2 mL) was dispersed in 20 L of algal suspension to give the required test concentration of 0.20 mg/L. Tests were conducted in 250 mL glass flasks (6 replicates, sealed). Cell counts were made at 0, 24, 48 and 72 h using a Coulter multisizer particle counter.

Continuous illumination (7000 lux). Initial cell density: ~10^4 cpm. Final cell density: ~5.5 x 10^5 cpm. Test pH: 7.4-7.9. Statistical analyses included Student's-t test incorporating Bartlett's test for homogeneity.

RESULTS

Biomass		*Growth*	
NOEC mg/L at 72 h	*EbC50 mg/L*	*NOEC mg/L at 72 h*	*ErC50 mg/L*
0.054	>0.054	0.054	>0.054

Remarks - Results: As for the fish and *Daphnia* toxicity tests, there was a marked decline in concentration over the duration of the test (ie. 5-6% of nominal after 72 h). Test results are presented as the geometric mean measured test concentration. No inhibition was seen in the tests.

CONCLUSION: The test material was not toxic to freshwater green algae at the concentration tested (geometric mean 0.054 mg/L), or conversely up to the limit of its solubility.

TEST FACILITY: SafePharm (2004f)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE: AO-119-144

METHOD: OECD TG 209 Activated Sludge, Respiration Inhibition Test and EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test

Inoculum: Mixed culture of activated sewage sludge micro-organisms (Severn Trent Water plc sewage treatment works).

Exposure Period: 3 hours

Concentration Range: Nominal: 1000 mg/L

Remarks – Method: Test material (500 mg) was added to 250 mL of water and subjected to ultrasonication (30 mins). Synthetic sewage (16 mL), activated sewage sludge (200 mL) and water were added to a final volume of 500 mL to give the required concentration of 1000 mg/L. Test temperature: 21°C. pH: 8.0. Hardness: ~100 mg/L. The rate of respiration was determined after 30 mins and 3 h contact time and compared to data for the control and reference material (3,5-dichlorophenol). The EC50 values were calculated from a graphed line-of-best fit equation using X1fit3 software package.

RESULTS

EC50: >1000 mg/L (nominal) after 3 hours

NOEC: 1000 mg/L (nominal) after 3 hours

Remarks – Results: At the test concentration, oily globules of the test material were visible on the surface and dispersed throughout the test media. The reference material gave a 3 hour EC50 of 12 mg/L confirming the suitability of the test conditions. Toxicity to sewage micro-organisms was not evident in the ready biodegradability test performed using the notified chemical.

CONCLUSION: The test material was not toxic to the sewage sludge micro-organisms under the conditions of the test.

TEST FACILITY: SafePharm (2003)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Release of the notified chemical during use as ink is likely to result in very limited release of the notified chemical to the environment. The majority will eventually be sent to landfill for disposal or incinerator for destruction. A fraction of the notified chemical may be released as a result of spills/leaks and drips to pavement or ground during application; however, these would likely be cleaned up and no predicted environmental concentration (PEC) of the notified chemical in soil or water could be derived. In landfill or soil, the notified chemical is likely to be degraded over time to water and oxides of carbon. It is expected to be hydrolytically stable and unlikely to be mobile based on its very low water solubility and would have a high affinity to soil organic matter based on its high partition coefficient (Koc). Incineration of the notified chemical will likely reduce the compound to simpler compounds of water and oxides of carbon. The notified chemical has an affinity for lipids and may potentially be capable of passing biological membranes; however, the limited potential for environmental release indicates a low potential for accumulation in aquatic organisms.

9.1.2. Environment – effects assessment

Analogue aquatic ecotoxicity data are available for 4 taxonomic groups (freshwater spp.). The disperse nature and instability of the notified chemical created difficulties in performing and interpreting the ecotoxicity test results. No toxicity was evident at the concentrations tested (nominally 0.2 mg/L). Test concentrations declined over time and consequently test results were reported as time-weighted average or similar values. The lowest available L(E)C50 value was >0.044 mg/L (NOEC 0.044 mg/L). A predicted no effect concentration of >0.44 μg/L has been derived by dividing the lowest EC50 value by a safety factor of 100; however, this is considered a conservative estimation as this was the highest concentration tested.

9.1.3. Environment – risk characterisation

The use pattern for the notified chemical will result in very limited potential for environmental release to the aquatic environment. In addition, the notified chemical has a very low water solubility and is unlikely to be released to waters but will partition to sludge, sediments and soils. In the sewer or aquatic environments, the notified chemical is likely to degrade over time due to abiotic and biotic processes. Most of the notified chemical will, after use, be sent with waste materials (paper) to landfill or incinerator and eventually forming water and oxides of carbon. Overall, the environmental risk for the notified chemical is low.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Exposure to the notified chemical is not expected during transport and warehousing. However, transport and warehousing workers may come into dermal and ocular contact with the notified chemical through accidental leaks and spillages of the drums and containers.

Printing workers will use PPE such as gloves and overalls to control dermal exposure to the ink (<15% notified chemical) when decanting drums into the reservoir of the printing machine. The printing machines are provided with guards and covers to minimise exposure to solvents. Where this is not sufficient, local exhaust ventilation and/or eye goggles will be provided to limit the exposure. These controls will serve to minimise exposure to the ink. There is potential for dermal exposure when cleaning machine rollers with solvent but the use of gloves together with dilution of ink by the solvent is likely to minimise exposure.

9.2.2. Public health – exposure assessment

The imported printing inks will be used only in large printing houses. Public exposure to printed articles will be widespread, however the notified chemical will be bound to the printed page, and thus will not be bioavailable.

9.2.3. Human health – effects assessment

The notified chemical was tested for acute oral toxicity in rats and mutagenicity in bacteria but data on the other endpoints were accepted for a close analogue previously notified by the same notifier. The notified chemical was of low acute oral toxicity in rats (LD50 > 2500 mg/kg bw) and low acute dermal toxicity in rats (LD50 > 2000 mg/kg bw). It was a slight skin irritant and a slight eye irritant in rabbits. It was not a skin sensitiser in guinea pigs and was not genotoxic in bacteria or human lymphocytes in vitro. The NOEL for oral repeat dose toxicity in rats was 50 mg/kg bw/day in a 28-day oral repeat dose study with effects at 1000 mg/kg bw/day being limited to changes in organ weights without histopathological correlates.

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

The notified chemical was not classified as a hazardous substance on the basis of a full data set and is imported at a maximum concentration of 14%. Exposure to the ink containing the notified chemical should be limited by the use of PPE and work practices designed to limit spillage. In addition, the use of solvents in inks and to clean printing machines presents a greater hazard during machine cleaning and disposal of waste. Engineering controls and work practices used to prevent exposure to solvents would also limit exposure to the notified chemical. Therefore, there is a low risk of adverse health effects to workers involved in transport, storage, use or disposal of the notified chemical.

9.2.5. Public health – risk characterisation

Given the low intrinsic hazard of the notified chemical and the low probability of contact between the public and products containing it, there is a low risk of adverse public health effects from importation the notified chemical in the manner described.

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*.

The classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) on environmental grounds was not possible as aquatic toxicity test results were inconclusive and based on analogue data. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

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.

10.3.2. Public health

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

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the NOHSC

National Code of Practice for the Preparation of Material Safety Data Sheets (NOHSC, 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

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

12. RECOMMENDATIONS

CONTROL MEASURES
Occupational Health and Safety

- A copy of the MSDS should be easily accessible to employees.
- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical [as introduced]:
  - *Avoid contact with eyes and skin*
- 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

Disposal

- The notified chemical should be disposed of by incineration in accordance with waste disposal regulations.

Emergency procedures

- Spills/release of the notified chemical should be handled by applying absorbent material (eg. paper towel, sand, soil) to the spill. Transfer the spillage to labelled waste containers for disposal. Do not allow spilled materials or washings to enter drains, surface water or groundwater.

12.1. Secondary notification

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

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

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

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