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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Iodonium, [4-(2-methylpropyl)phenyl](4-methylphenyl)-, hexafluorophosphate(1-)

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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 9577 8888.
Website:	www.nicnas.gov.au

Director
Chemicals Notification and Assessment

TABLE OF CONTENTS

FULL PUBLIC REPORT

Iodonium, [4-(2-methylpropyl)phenyl](4-methylphenyl)-, hexafluorophosphate(1-)

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Ciba Specialty Chemicals (ABN 97 005 061 469)
235 Settlement Road Thomastown VIC 3082

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

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
None

NOTIFICATION IN OTHER COUNTRIES
USA – PMN, details not provided

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
Iodonium, [4-(2-methylpropyl)phenyl](4-methylphenyl)-, hexafluorophosphate(1-)

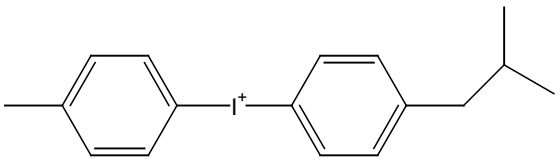
OTHER NAME(S)
TKA 40210

MARKETING NAME(S)
CGI-551

CAS NUMBER
None assigned

MOLECULAR FORMULA
$C_{17}H_{20}F_6IP$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
496.21

SPECTRAL DATA
IR: Peaks at – above 3000, 2958-2870 (three peaks), ~1600, 1483-1386 (three peaks), 844, 558 cm^{-1}
^{1}H nmr: Peaks at – 8.10 (doublet), 8.09 (doublet), 7.322 (doublet), 7.31 (doublet), 2.47 (doublet), 2.33 (singlet), 1.81 (doublet of doublets) and 0.81 (doublet) ppm
^{13}C nmr: Peaks at – 145.8, 142.5, 113.3, 135.0, 134.9, 132.3, 112.8, 43.9, 29.4, 21.9, 20.8 ppm
^{19}F nmr: Peak at –69.7 ppm
^{31}P nmr: Peak at –143.0 ppm
Mass spectrometry: Peaks at m/e – 145 (anion), 351 (cation)

METHOD Infrared (IR) spectroscopy, ^{1}H, ^{13}C, ^{19}F and ^{31}P nmr spectroscopy, mass spectrometry
Remarks Summaries of spectral features were provided in a report; copies of the raw spectra were not provided.
TEST FACILITY Ciba Specialty Chemicals Inc., Structure Elucidation (2000)

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD Spectroscopic identification, as described above.

3. COMPOSITION

DEGREE OF PURITY
typical > 96.5 %, range 90.0 – 99.0 %

HAZARDOUS IMPURITIES
None

NON HAZARDOUS IMPURITIES (> 1% by weight)

Chemical Name	Polyvinyl alcohol		
CAS No.	9002-89-5	*Weight %*	< 1.7 %

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 as a liquid containing 25 % propylene glycol for reformulation in Australia.

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

Year	*1*	*2*	*5*
Kilograms	500 - 1000	500 - 1000	3000

USE
The notified chemical is a photoinitiator for UV curable inks, lacquers and varnishes used in metal coating and printing applications, for example as overprint lacquer for labels on soup cans.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
Ciba Specialty Chemicals

TRANSPORTATION AND PACKAGING
The solution containing the notified chemical at 75 % will be imported by sea in 25 L varnish lined steel drums, and transported to the notifier's site and then to reformulation sites by road transport. Reformulated inks containing the notified chemical will be transported by road in 20 L steel pails.

5.2. Operation Description

The 75 % solution of the notified chemical will be stored at the notifier's site and transported to up to three ink manufacturing sites for reformulation into inks, containing 2 – 4 % notified chemical. The required quantity of the notified chemical will be added to polymer resins in a 200 L stainless steel mixing tank (approximately 2.5-5 kg of the imported solution for each 200 kg batch), and the formulated inks will be pumped to 20 L pails ready for sale to the end users. Reformulated inks will be applied to metal or paper substrates by standard printing techniques, then exposed to UV light. During the curing process the notified chemical is partially consumed and residual traces are bound within the ink matrix. Ink containers and printing components are washed and the aqueous wastes collected by liquid waste disposal contractors.

5.3. Occupational exposure

Number and Category of Workers

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

Exposure Details

Transport and storage workers, including waterside workers, transport drivers and warehouse workers, will handle sealed containers of the 75 % solution of the notified chemical, and also of inks containing up to 4 % notified chemical. No exposure is expected except in the case of an accident involving damage to the packages.

At the ink manufacturing site, the 75 % solution of the notified chemical will be manually weighed and added to a 200 L stainless steel blending vessel and mixed with the other components of the printing ink. Dermal exposure and accidental ocular exposure to the 75 % solution of the notified chemical is possible during this procedure. The blended ink will then be piped to an automated filling system and dispensed into 20 L metal pails. The only point where the notified chemical is handled outside the closed system is at addition to the blending vessel. Extraction ventilation will be used at this point. Workers will wear overalls, PVC coated cotton gloves and protective goggles. Respiratory protection may be used if conditions are dusty or high vapour concentrations are present. Due to the physical state of the notified chemical, little risk of inhalation exposure is likely.

At the printing sites, the inks containing up to 4 % notified chemical will be manually poured from the pails into ink ducts. Residual ink will be scraped into the ink duct prior to the containers being washed. Dermal and accidental ocular exposure could occur during these processes. From this point, the printing process will be highly automated, and the ink will be cured by UV exposure prior to the substrates being manually handled. This will decompose and immobilise the notified chemical, which will no longer be available for exposure. There may also be exposure to the notified chemical as part of residual ink in containers and on printing equipment when they are cleaned in a washing machine. Workers will wear overalls, PVC coated cotton gloves and protective goggles while handling the inks. The inks contain monomers which polymerise under the UV curing conditions, and a number of these are

known skin sensitisers, and a high level of precautions to avoid dermal exposure are required even in the absence of the notified chemical.

Laboratory workers will be responsible for quality control measurements on the blended inks and for small scale testing of mixtures using up to 1 kg notified chemical. These workers will handle concentrated solutions of the notified chemical as well as formulated inks. Normal laboratory protective equipment (laboratory coats, safety glasses, protective gloves and fume hoods) would be expected to be used.

5.4. Release

RELEASE OF CHEMICAL AT VARNISH FORMULATION SITE.

Transfer of the notified chemical from the pails in which it is imported to the 200 L steel mixing vessel is a manual operation where the chemical is scooped from the 25 L drums, weighed and added to the mixing vessel. Accordingly there is scope for released through spillage, and although the notifier indicated that < 0.5 % (maximum 15 kg per annum) would be lost in this operation, larger losses are possible and as a worst case it will be assumed that 5 % of the chemical (up to 150 kg per annum) could be lost through spills and leaks and from unused chemical remaining in the emptied drums. Consequently, assuming three factories are involved in formulating the varnish, it is possible that each could release approximately 50 kg of the chemical each year.

While it was indicated that any spilt chemical would be adsorbed to appropriate material (eg. saw dust) and then be incinerated or disposed of to landfill by waste contractors, the possibility that it would enter the metropolitan sewer systems through hosing down the production floor cannot be discounted.

RELEASE OF CHEMICAL FROM USE IN VARNISH AND LACQUER

The formulated varnishes containing between 2 and 4 % of the notified chemical will be used in specialised printing machines designed to apply print information and a cured varnish protecting coat to metal plate – eg. for processed food cans. In the printing machines the varnish is transferred from the reservoir to the metal plate (previously printed with the desired text and pictures) using a special roller, and the coated plate is then subjected to intense UV light which cures the varnish into a crosslinked polymer which then affords protection to the printed material. The notified chemical is intended as a photo-initiating agent in the varnish and initiates the curing of the polymer components under the influence of intense UV light.

The varnish is dispensed to the printing machines by manually pouring the liquid into the ink ducts, and losses through spills and splashes are possible during this procedure. No estimate of this loss was provided by the proponents, but if it is assumed that a maximum of 2 % of the varnish is spilt during the transfer operation, this amounts to a maximum annual release of approximately 60 kg of the notified chemical. Spilt chemical would normally be cleaned up and disposed of through incineration or to landfill, but it could possibly also be hosed from the printing shop floor and then enter metropolitan sewer systems.

It is expected that very little of the varnish containing the chemical would remain unused since the formulated varnish is stable except after exposure to UV light, and unused material can be returned to the reservoir for later use.

5.5. Disposal

The notifier indicated that all spilt or unused chemical should be disposed of to secured landfill or be incinerated. Given that the compound is toxic to aquatic organisms and is not readily biodegradable, incineration appears the better disposal method.

5.6. Public exposure

The notified chemical will be imported into Australia as a solution and will be distributed to manufacturing sites for reformulation, and thence to printing sites. There is potential for public exposure to the notified chemical in the unlikely event of an accidental spillage during transportation. However, the potential for public exposure to the notified chemical during transportation is low.

The UV-curable varnish will be applied to objects as food containers and beverage cans. The public

will frequently consume food or beverages which have been exposed to the packaging, and will handle the packaging. Although the coated and cured articles bind a trace amount of the notified chemical within the ink matrix, it is no longer bioavailable. Hence, the hazard to the general public exposed to the stable coating film containing the notified chemical is considered to be low.

6. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa	White to light beige powder with characteristic odour; imported solution in propylene carbonate is a yellow-brown liquid.
MELTING POINT	92°C

METHOD OECD TG 102 Melting Point/Melting Range.
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Test system: Differential scanning calorimeter (DSC).
TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000a)

BOILING POINT > 264°C at 101.3 kPa in air (decomposes)

METHOD OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks DSC analysis showed an endothermic effect at 264 °C; visual observation confirmed that decomposition rather than boiling occurred.
TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000b)

DENSITY 1617 kg/m^3 at 20°C

METHOD OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Remarks Test system: gas comparison pycnometer
TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000c)

VAPOUR PRESSURE 4.69×10^{-9} kPa at 25°C (or 20°C).

METHOD OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Calculated using Modified Watson Correlation
TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000d)

WATER SOLUBILITY 1.2 g/L at 20°C

METHOD OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Analytical Method: HPLC
The water solubility was determined using the shake flask method. The compound is the PF_6^- salt of an organic cation containing iodine in the (formally) +I oxidation state. Despite the presence of fairly large aromatic hydrocarbon moieties, given the ionic nature of the compound the moderately high the water solubility is not unexpected.
TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000e)

HYDROLYSIS AS A FUNCTION OF PH $t_{1/2}$ > 1 year

METHOD OECD TG 111 Hydrolysis as a Function of pH.
Remarks The test was conducted by incubating solutions of the compound (concentration approximately 105 mg/L) at 50°C for 5 days in buffer solutions of pH 4, 7 and 9. The solutions were analysed for content of the CGI 511 using HPLC at the end of the 5 day

period, and since there was no significant decrease in the content of the chemical in any of the test solutions, it was concluded that the compound is not susceptible to hydrolysis in the pH region 4-9.

TEST FACILITY RCC Ltd, Environmental Chemistry and Pharmanalytics Division (2000f)

PARTITION COEFFICIENT (n-octanol/water) log Kow at 20ºC = 1.0 approximately.

METHOD OECD TG 107 Partition Coefficient (n-octanol/water): Shake Flask Method.

Remarks The n-octanol/water partition coefficient was determined from the ratio of the concentration of the compound in water saturated n-octanol to the concentration in n-octanol saturated water after equilibration of the two phases. Six different experiments were conducted at a temperature of around 20ºC, with the concentration of CGI-551 in each phase determined using HPLC. The ratio of concentrations varied between 8.4 and 10.2 (mean 9.3), providing a value of Log Kow of approximately 1.0.
This low value for Log Kow reflects the relatively high water solubility due to the ionic nature of the notified chemical.

TEST FACILITY RCC Ltd, Environmental Chemistry and Pharmanalytics Division (2000g)

ADSORPTION DESORPTION Not determined.

Remarks No adsorption/desorption study was submitted, but the positive charge on the iodonium moiety suggests that this would have a high affinity for the colloidal material in soils and sediments which usually carry negative electrical charge. However, the relatively high water solubility indicates that the compound may also be mobile in soils and sediments.

DISSOCIATION CONSTANT Not applicable

Remarks The compound contains no acidic or basic functional groups.

PARTICLE SIZE Mass median Aerodynamic Diameter = 99.4 μm

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

Range (μm)	*Mass (%)*
< 10	4.21
10 – 40	12.26
40 – 100	31.65
100 – 200	36.55
> 200	13.13

Remarks Method: Laser diffraction; particles suspended in water

TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2001a)

FLASH POINT

Remarks Test not applicable for solid

FLAMMABILITY LIMITS Not flammable

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).

Remarks The test substance could not be ignited with a flame.

TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000h)

AUTOIGNITION TEMPERATURE

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.

Remarks No autoignition observed up to the melting point of the test substance.

TEST FACILITY RCC Ltd, Environmental Chemistry & Pharmanalytics Division (2000i)

EXPLOSIVE PROPERTIES Not explosive

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks No explosion observed in tests on thermal sensitivity, mechanical sensitivity to shock and mechanical sensitivity to friction.
TEST FACILITY Institute of Safety and Security (2001)

REACTIVITY

Remarks The notified chemical is not an oxidising agent. It is stable under normal environmental conditions.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 = 380 mg/kg bw	harmful
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rat, acute inhalation	test not conducted
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	severely irritating
Guinea pig, skin sensitisation - adjuvant test.	evidence of sensitisation.
Rat, oral repeat dose toxicity - 28 days.	NOEL = 5 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosome aberration test	non genotoxic
Genotoxicity – in vivo	test not conducted

7.1. Acute toxicity – oral

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
EC Directive 92/69/EEC B.1 tris Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain Rat/HanIbm: WIST (SPF)
Vehicle Polyethylene glycol PEG 300 (dose volume 10 mL/kg bw)
Remarks - Method A stepwise procedure was used in relation to the deaths.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	3 female	2000	3/3
II	3 female	400	3/3
III	3 male	400	2/3
IV	3 female	250	0/3
V	3 male	250	0/3
VI	3 female	150	0/3
VII	3 male	150	1/3

LD50 380 mg/kg bw
Signs of Toxicity Animals treated at 2000 mg/kg bw were found dead 90 minutes after treatment. Ventrolateral recumbency and respiratory distress preceded death. Five of six animals treated at 400 mg/kg bw died on day 2. Hunched posture and ruffled fur was seen in most treated animals, persisting up to test day 3.
Effects in Organs A distended stomach with or without gas was observed in all animals which died during the test.
Remarks - Results Body weights of the surviving animals were within normal ranges for the age and strain.

CONCLUSION	The notified chemical is harmful via the oral route.
TEST FACILITY	RCC Ltd, Toxicology Division (2000j)

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/HanIbm: WIST (SPF)
Vehicle	PEG 300 (dose volume 4 mL/kg bw)
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5/sex	2000	0/10

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	No signs of dermal irritation were observed.
Signs of Toxicity - Systemic	No clinical signs of systemic toxicity were observed.
Effects in Organs	No gross abnormalities were seen at necropsy.
Remarks - Results	Three females showed weight loss of up to 5 % one week after treatment.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	RCC Ltd, Toxicology Division (2000k)

7.3. Acute toxicity - inhalation

No study reports on the inhalation toxicity of the notified chemical were provided by the notifier.

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
Number of Animals	3
Vehicle	Moistened with water.
Observation Period	3 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

Remarks - Results	No oedema or erythema was recorded at any observation time. Slight weight loss was recorded in two animals during the study.
CONCLUSION	The notified chemical is non-irritating to skin.
TEST FACILITY	RCC Ltd, Toxicology Division (2000l)

7.5. Irritation - eye

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain: Rabbit/New Zealand White
Number of Animals: 3
Observation Period: 1 day
Remarks - Method: The test was terminated after 1 day due to the severity of the effects.

RESULTS

Lesion	*24 hour Score* *Animal No.*		
	1	2	3
Conjunctiva: redness	3	3	3
Conjunctiva: chemosis	4	4	4

Remarks - Results: Assessment of the cornea, iris and sclera could not be undertaken due to swelling of the conjunctiva which resulted in closure of the treated eye. All animals showed conjunctival discharge at 1 (slight watery discharge) and 24 hours (marked mucous discharge) after instillation.

CONCLUSION: The notified chemical is severely irritating to the eye.

TEST FACILITY: RCC Ltd, Toxicology Division (2000m)

7.6. Skin sensitisation

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 406 Skin Sensitisation – Maximisation Test.
EC Directive 96/54/EC B.6 Skin Sensitization - Maximisation Test.

Species/Strain: Guinea pig/Ibm: GOHI; SPF
PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal: 3 %
topical: 50 %
MAIN STUDY
Number of Animals: Test Group: 10 male Control Group: 5 male
induction phase: Induction Concentration:
intradermal injection 3 %
topical application 50 %
Signs of Irritation: All animals including controls showed irritation scores of 1 at 24 and 48 hours following topical induction; assumed due to treatment with SLS.
CHALLENGE PHASE
1st challenge: topical application: 50 %
Remarks - Method: Vehicle: PEG 300. One day prior to topical induction, irritation was induced by application of 10 % sodium lauryl sulphate (SLS) in *paraffinum perliquidum*.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		24 h	*48 h*
Test Group	Vehicle	0/10	0/10
	50 %	8/10	10/10

Control Group	Vehicle	0/5	0/5
	50 %	0/5	0/5

Remarks - Results: After 24 hours, the test group responses to the challenge application of notified chemical were three animals with an irritation score of 2, five with a score of 1 and two with no reaction; after 48 hours nine animals showed scores of 2 and the remaining animal a score of 1.

CONCLUSION: There was evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY: RCC Ltd, Toxicology Division (2000n)

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/HanIbm: WIST (SPF)
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week; Post-exposure observation period: 14 days.
Vehicle	PEG 300
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
Control	5/sex	0	0/10
Control (recovery)	5/sex	0	0/10
I (low dose)	5/sex	5	0/10
II (mid dose)	5/sex	20	0/10
III (high dose)	5/sex	80	2/10
III (recovery)	5/sex	80	5/10

Mortality and Time to Death

Two males and five females of the high dose groups (one male and one female of the high dose group and one male and four females of the high dose recovery group) were found dead between study days 10 and 15.

Clinical Observations

Soft faeces persisting up to 2 days into the recovery period was noted in animals of all groups including controls. One high dose male was noted to be emaciated at day 22, and one high dose female on day 13. These animals survived to the study termination. Three other high dose females were observed to be emaciated on days 10 and 13, prior to death. Piloerection was observed on at least one occasion in five males and six females of the high dose groups, while hunched posture was seen in one male and five females of the high dose groups. These clinical signs were seen immediately prior to death in a number of cases.

Forelimb and hindlimb grip strength was reduced in the high dose males and females, and there was a decrease in total mean locomotor activity in the high dose males. Reflexes and gait observations were normal, and no functional observation battery changes were seen in the low and mid dose groups.

Body weights and body weight gains for the high dose males were significantly lower than controls during the latter part of the treatment period. Lower food consumption was seen in the high dose groups during the treatment phase, with a compensatory increase during the recovery phase.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

A number of statistically significant changes in clinical chemistry parameters were seen in the high dose group. These included decreases in glucose, chloride, globulin and total protein levels, and increases in alanine aminotransferase activity, triglycerides and calcium and phosphorus levels in both sexes. In the males, urea levels, aspartate aminotransferase activity and albumin to globulin ratio were increased. In the females, gamma glutamyltransferase activity and sodium levels were increased, while total bilirubin and albumin levels were decreased. After the 14 day recovery period, the high dose males showed statistically significant differences from controls, while no differences were observed for the females. The changes in the males included lower glucose and globulin levels, and increased creatinine, calcium, phosphorus and sodium levels and aspartate aminotransferase activity. Differences observed in the mid dose group were restricted to lower total protein in the females, while no statistically significant differences from controls were observed in the low dose group.

Statistically significant differences from controls were seen in a number of haematological parameters in the high dose group, including higher erythrocyte count, mean haemoglobin levels and haemocrit in both sexes. Lower mean cell volume and shorter partial thromboplastin times were seen in the males, along with changes in absolute and relative reticulocyte counts. Changes in reticulocyte counts in females were generally not statistically significant, but the trends appeared similar to the males. Reticulocyte ratios appeared to be shifted from high fluorescence to low fluorescence cells, particularly in the males. Following the recovery period, the majority of the changes, with the exception of the erythrocyte count in the males, were reversed. In the mid dose group, the erythrocyte counts and haemoglobin levels were increased. While the changes from controls were not statistically significant, they appeared to follow a similar trend to the changes seen in the high dose group.

The males and females of the high dose group showed increased urine output and lower urine specific gravity. The pH of the urine was significantly lower in the males, and ketone was present in the urine of both sexes. After the recovery period, no significant differences from controls were noted. Females in the low dose group had increased urine output, and lower specific gravity and osmolality; similar changes were not seen in the males or the mid dose group. Males in the mid dose group showed an increase in urine pH, contrary to the observation for the high dose group.

Effects in Organs

In the high dose animals at the end of the treatment period, dilation of the small intestinal segments and caecum was observed in all animals that survived to necropsy. Dilation of the colon was also observed in two animals. Reddish foci on the stomach mucosa, dark red discolouration of thymus and lungs, and reduction in thymus size (in males) were also seen. In the mid dose group, dilation of the caecum was seen in two males. In the high dose recovery group, intestinal dilation was seen in one female. Some cases of organ discolouration and reduction in thymus size were reported. All other macroscopic findings were either scattered or occurred with similar frequency in all groups.

Organ weight differences included increase in absolute liver and kidney weights in both sexes, and reduction in thymus weights in males. Relative liver and kidney weights were also increased. Other changes in relative organ weights in males were related to the reduced body weight for the high dose group. Similar changes were not observed in the mid dose group. After the recovery period, absolute thymus weights were found to be reduced in both sexes, and absolute and relative adrenal weights were increased in females.

Histopathological examination showed effects in the stomach, liver, kidney, spleen, bone marrow and mesenteric lymph nodes. Superficial erosion of the glandular mucosa of the stomach was observed in one animal at the end of the treatment period and in three after the recovery period. This finding was also recorded for one animal in the mid dose group. Slight hypertrophy of the liver cells was seen in all of the high dose animals examined during the main study, and also in the recovery animals which died during the study, but not in the animals sacrificed at the end of the recovery period. Vesicular fatty changes in the liver were more prevalent in the high dose animals than in the controls, and showed a different distribution, corresponding to the localisation of hepatocellular hypertrophy.

Discrete swelling of the tubular epithelial cells in the inner stripe of the outer medulla of the kidney was observed in all but one of the high dose group at the end of the main study, also in all the high dose recovery animals that died during the study, but not in the animals sacrificed at the end of the recovery period. Decreased severity and incidence of haemopoiesis was seen in the spleen of all high dose animals at the end of the main study, and no haemopoiesis was seen in the high dose animals which died during the study.

Increased haemopoiesis was seen in the high dose recovery males. Reduction in haemopoiesis in the bone marrow was also seen in the main study high dose animals and also in the prematurely deceased high dose recovery animals.

Lymphoid atrophy in the spleen was seen in four out of five examined high dose animals which died during the study; in three cases it was accompanied by lymphoid hyperplasia of the periarteriolar sheath. Atrophy of the thymus was a common finding in the high dose animals, including those sacrificed at the end of the recovery period. Decreased lymphoid hyperplasia of the mesenteric lymph node accompanied by increased numbers of mastocytes in the sinusoidal spaces was seen in high dose animals sacrificed at the end of the main study and also in the prematurely deceased high dose recovery animals.

Remarks – Results

Changes in adrenal weights in recovery females were considered to not be treatment related, as no similar changes were seen prior to the recovery period, or in the males. Intestinal dilation, erosion of the stomach glandular mucosa and changes in erythrocyte count and haemoglobin levels were major findings in the high dose group which were also observed to a lesser effect in the mid dose group. Other major findings in the high doses group, such as changes in clinical chemistry and organ weights, were not echoed in the mid dose group. The majority of the changes were found to be reversible after the 14 day recovery period.

CONCLUSION

The No Observed Effect Level (NOEL) was established as 5 mg/kg bw/day in this study, based on findings in the digestive system and haematological parameters in the 20 mg/kg bw/day group which showed a dose-related trend.

TEST FACILITY RCC Ltd, Toxicology Division (2001b)

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. Plate incorporation procedure/Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100. *E. coli*: WP2 uvrA.
Metabolic Activation System	15 % S9 fraction from male rats pretreated with phenobarbital and β-naphthoflavone.
Concentration Range in Main Test	a) With metabolic activation: 0.3 - 1000 µg/plate. b) Without metabolic activation: 0.3 - 1000 µg/plate.
Vehicle	Dimethyl sulphoxide (DMSO).
Remarks - Method	Three independent experiments were performed in the absence of metabolic activation and four in the presence of metabolic activation; both the plate incorporation and pre-incubation procedures were used. Tests 3 and 4 each used only a single strain. The preliminary cytotoxicity test met the criteria for validity as a main experiment and is reported as test 1 below.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Present			
Test 1	10	-	-
Test 2	33	-	-
Test 3	-	-	-
Test 4	32	-	-
Absent			

Test 1	100	-	-
Test 2	100	-	-
Test 3	64	-	-

Remarks - Results

In test 2 (pre-incubation procedure) using WP2 *uvr*A in the presence of metabolic activation, an approximate doubling of the number of revertant colonies was seen at 33 µg/plate; the experiment was carried out a second time with only a marginal increase in revertant colonies seen. No other significant increases in numbers of revertant colonies were seen in any test. Cytotoxicity at higher doses was manifest in reduction of revertant colony numbers; in all cases the background lawn appeared normal.

Appropriate positive controls were used and resulted in large increases in the numbers of revertant colonies in all cases, confirming the sensitivity of the test system.

CONCLUSION

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

TEST FACILITY

Cytotest Cell Research Gmbh (2000)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE

Notified chemical.

METHOD

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

Cell Type/Cell Line: Chinese Hamster Ovary (CHO)
Metabolic Activation System: S9 fraction from male rats pretreated with phenobarbital and β-naphthoflavone (total protein content 0.75 mg/mL).
Vehicle: Dimethyl sulphoxide (DMSO).
Remarks - Method: No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Present			
Test 1	5*, 10*, 20*, 40, 80, 160	4 hr	18 hr
Test 2	7.5, 15*, 22.5*, 30, 45*, 60	4 hr	18 hr
Test 3	22.5, 30*, 45, 60	4 hr	28 hr
Absent			
Test 1	5, 10, 20, 40, 80, 160	4 hr	18 hr
Test 2	0.3, 0.6, 1.3, 2.5*, 5*, 10*	4 hr	18 hr
Test 3	0.3*, 0.6*, 1.3, 2.5*, 5, 10	18 hr	18 hr
Test 4	1.3*, 2.5, 5, 10	28 hr	28 hr

*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	156.3			
Test 1		80.0	-	
Test 2		-	-	
Test 3		30.0	-	
Absent	156.3			
Test 1		not stated	-	

Test 2	10	-
Test 3	10	-
Test 4	2.5	-

Remarks - Results

In the table above, cytotoxicity is reported where the survival of cells was significantly less than 50 % of solvent control. The mitotic index in cultures analyses was generally close to solvent control except in the cases of long exposures in the absence of metabolic activation. Test 1 in the absence of metabolic activation was stated to not be further analysed due to strong toxicity at all doses used.

No significant increases in the number of cells with structural chromosomal aberrations or in the incidence of polyploidy were observed under any treatment conditions.

Appropriate positive controls were used and resulted in large increases in the numbers of cells with structural chromosomal aberrations in all cases, confirming the sensitivity of the test system.

CONCLUSION

The notified chemical was not clastogenic to CHO cells treated in vitro under the conditions of the test.

TEST FACILITY

Cytotest Cell Research Gmbh (2001)

7.10. Genotoxicity – in vivo

No study reports on the in vivo genotoxicity of the notified chemical were provided by the notifier.

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: Sewage bacteria from activated sludge.

Exposure Period: 28 days

Auxiliary Solvent: None

Remarks - Method

The test material (CGI 551) was added to the inoculum at concentration of approximately 37 mg/L which corresponds to a total organic carbon (TOC) content of around 15 mg/L. The test was performed in duplicate with both the test material (CGI 551) and the reference material sodium benzoate which was present in the media at concentration corresponding to approximately 15 mg/L TOC. A toxicity control experiment containing 37 mg/L of CGI 551 as well as 26.3 mg/L of the reference chemical was also conducted.

RESULTS

Test substance		*Sodium benzoate reference*	
Day	*% degradation*	*Day*	*% degradation*
14	low	14	77
28	< 10	28	82.4

Remarks - Results

CONCLUSION

The test material was found to be not readily biodegradable. Further, the presence of the test

material in media containing the biodegradable reference chemical indicated no significant inhibition of biodegradation of the sodium benzozate, and consequently it was concluded that the new chemical is not toxic to sewage bacteria at exposure levels up to around 37 mg/L.

TEST FACILITY

RCC Ltd, Environmental Chemistry and Pharmanalytics Division (2000o)

8.1.2. Bioaccumulation

No test on this property was provided in the notification dossier, but the ionic nature and relatively high water solubility indicates low potential for bioaccumulation (Connell, 1990).

8.1.3. Other Degradation Pathways

The chemical is not susceptible to abiotic degradation through hydrolysis. However, under the influence of UV light it is decomposed to free radicals, and these would react with water, gases and natural organic matter producing species which may be more susceptible to abiotic and biological degradation.

8.2. Environmental Effects

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Static conditions
Species	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 h
Auxiliary Solvent	None
Temperature	21 ºC
pH	7.8-8.0
Dissolved oxygen	8.1–8.6 mg/L
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks – Method	Static method, using duplicate systems at each test concentration with 7 fish in each test vessel. All test media were clear with no undissolved test substance.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
0 (control)		14 (7 per duplicate test)	0	0	0	0	0
4.6	ND	14	0	0	0	0	0
10	ND	14	0	0	0	0	0
22	20.5	14	0	0	0	0	0
46	42.9	14	0	0	1	4	6
100	92.8	14	0	7	14	14	14

LC50	42 mg/L at 96 hours (95% confidence interval 29-59 mg/L).
NOEC	22 mg/L at 96 hours.

Remarks – Results

In addition to the dead fish, after 48 hours exposure to the nominally 46 mg/L solution one fish appeared intoxicated, while after 24 hours exposure at nominally 100 mg/L 7 fish appeared to be intoxicated.

CONCLUSION

According to the US EPA scale of toxicity, the compound is described as being slightly toxic to this species.

TEST FACILITY

RCC Ltd, Environmental Chemistry and Pharmanalytics Division (2000p)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE CGI 551

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test – Static test conditions.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Temperature	20-21ºC
Dissolved oxygen	8.6-8.7 mg/L
pH	7.7-8.1
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	The test at each exposure level was conducted in duplicate using ten daphnia in each test vessel. The test was conducted under static conditions, with the test data were analysed statistically using probit analysis.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h [acute]*	*48 h [acute]*
0 (control)		20 (10 in each replicate vessel)	0	0
0.01	ND	20	0	0
0.032	0.031	20	0	0
0.1	0.097	20	0	16
0.32	0.30	20	9	18
1.0	0.89	20	15	20

LC50	0.085 mg/L at 48 hours (95% confidence interval 0.063-0.11 mg/L).
NOEC (or LOEC)	0.032 mg/L at 48 hours

Remarks - Results

No immobilisation or signs of intoxication were observed for 48 hours exposure at 0.032 mg/L, but effects were observed at higher exposure levels. The criteria for immobility were if the organisms were unable to swim 15 seconds after gentle agitation of the test vessel. The test data were analysed statistically using probit analysis.

CONCLUSION

According to the US EPA scale of toxicity, the compound is described as being very highly toxic to this species.

TEST FACILITY

RCC Ltd, Environmental Chemistry and Pharmanalytics Division (2000q)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE CGI 551

METHOD OECD TG 201 Alga, Growth Inhibition Test

Species	*Scenedesmus subspiticas*
Exposure Period	72 hours
Concentration Range Nominal	0 (control) – 0.46 mg/L (5 solutions tested)
Concentration Range Actual	0 (control) – 0.39 mg/L
Auxiliary Solvent	None
Temperature	22.3-23ºC
pH	7.7 (start) – 8.8 (end)
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC

Remarks - Method

Three replicate tests were conducted for each exposure concentration of the chemical, and six replicates for the control. The growth of biomass over the 72 hour test period was periodically monitored through measuring the cell density with a Coulter counter, and the rate of biomass increase was also determined.

RESULTS

Biomass			*Growth*		
E_bC50 mg/L at 72 h	NOEC mg/L at 72 h	LOEC mg/L at 72 h	E_rC50 mg/L at 72 h	NOEC mg/L at 72 h	LOEC mg/L at 72 h
0.10	0.035	0.081	0.17	0.035	0.081

Remarks - Results

The raw data was analysed statistically using probit analysis for the EC50 determinations, while the LOEC and NOEC were estimated from comparison of the biomass and rate of biomass increase with those of the controls (no test substance) using the Dunnett test. The test concentrations in the data analysis used were the measured concentrations rather than the nominal ones.

CONCLUSION

The results of this test demonstrate that the new compound is at least highly toxic to this species of green algae.

TEST FACILITY

RCC Ltd, Environmental Chemistry and Pharmanalytics Division (2000r)

8.2.4. Inhibition of microbial activity

Remarks

No report on the toxicity to sewage bacteria was provided in the submission, but the MSDS supplied indicated that the compound has a 3 hour IC50 of 3.9 mg/L to sewage bacteria. The test was apparently conducted according to the protocols of OECD TG 209.
This result is at odds with that of the toxicity control test conducted as part of the biodegradation test (RCC, 2000o), where the chemical was found to be not toxic to sewage bacteria at exposure levels up to 37 mg/L.

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure and fate assessment

The major routes of release and exposure of the notified chemical to the environment are through spills and accidents during formulation of the chemical into varnishes. It is estimated that up to 150 kg of the chemical could be released in this manner, and relatively small quantities of the chemical (estimated as approximately 60 kg per annum) could also be released at printing facilities where the varnish containing 2 – 4 % of the chemical is transferred manually to the printing machines.

Although spills of the chemical and the formulated varnish should be adsorbed on appropriate material (eg saw dust or vermiculite) and then disposed of to landfill or incinerated, it is possible that these losses would be simply hosed off the production floors and thus enter metropolitan sewage systems. The chemical is not readily biodegradable and nor is it apparently susceptible to abiotic degradation through hydrolysis and consequently is not expected to be chemically degraded during sewage treatment. However, the chemical is cationic and so is expected to become associated with negatively charged particulate and colloidal material in the sewer (eg. humic material) and would very likely become associated with sewer sludge, although due to its high water solubility it may be mobile in water. Periodically sewage sludge is removed from the sewage pipes and sewage treatment works and then either placed into landfill, composted and used as a soil conditioner, or incinerated.

The maximum potential losses to sewer are estimated as 210 kg per annum, or approximately 1 kg per day assuming 200 working days each year.

Although it is not readily biodegradable, if placed into landfill or composted the compound is expected to be slowly degraded through biological and abiotic processes and would be mineralised to water and oxides of carbon while the iodine component would eventually be converted to iodide ions. Incineration of the chemical would produce similar degradation products.

At the end of their lives food tins and other metals coated with varnish containing the chemical would be placed into landfill, although some may be recycled for metal recovery. In either case the chemical will be eventually destroyed either through slow degradation processes within landfills or rapidly by incineration in metal recovery furnaces.

9.1.2. Environment – effects assessment

The compound has been shown to be very highly toxic to *Daphnia* (48 h LC50 = 0.085 mg/L), highly toxic to green algae and slightly toxic to fish. There is also evidence that the compound is toxic to sewage bacteria, with an indicated IC50 of 3.9 mg/L, but the PEC in sewage is expected to be several orders of magnitude below this, so no detrimental effects of the compound on the operation of sewage treatment plants is likely.

9.1.3. Environment – risk characterisation

The notified chemical will be used as an initiator for polymerisation of specialised varnishes used in coating printing on metal articles (eg. processed food cans) when subjected to intense UV light. It will be partially consumed during this process, with residues remaining bound in the varnish films.

The notified chemical is slightly toxic to fish, highly toxic to green algae and is very highly toxic to *Daphnia* (the most sensitive species against which it has been tested), with a 48 hour LC 50 of 85 µg/L. The maximum potential losses to sewer are estimated as 210 kg per annum. If, as a worst case, it is assumed that all release occurs in a single large city with a population of 3 million people each contributing an average of 250 L/day (Australian Bureau of Statistics, 2000) to the overall sewage flow, then the Predicted Environmental Concentration (PEC) of the chemical in the sewage is –

$$210\times10^6 \text{ (mg)}/(200\times250\times3\times10^6\text{L})= 1.4 \text{ µg/L}$$

On discharge from the sewer system to the receiving waters the sewage effluent is further diluted (normally by a factor of 10 for discharge to ocean and 2-3 for discharge to inland river systems), and in the case of discharge to the ocean the environmental PEC is consequently reduced to 0.14 µg/L. The PEC estimate assumes that none of the chemical associates with sludge or sediments, and this is expected to be significant because of its cationic nature. When this is considered the PEC is expected to be significantly lower than 0.14 µg/L

The Predicted No Effect Concentration (PNEC) will be taken as 0.85 µg/L, which is calculated as the LC50 for *Daphnia* divided by a safety factor of 100. Since the worst case PEC indicates a maximum environmental concentration of the chemical in discharged sewage of around 0.14 µg/L, the PEC/PNEC is 0.14/0.87 = 0.16, which corresponds to a modest safety margin of approximately 6. In rural areas this safety margin would be reduced to only 1-2 because of lower dilution factors, but as indicated above, adsorption of the compound onto sediments would also reduce exposure to aquatic organisms which will increase this safety margin. However, these low safety margins highlight the necessity for preventing release of the chemical into watercourses.

The notified chemical is not readily biodegradable and is not susceptible to degradation by hydrolysis, but is expected to be slowly decomposed to free radicals through the action of UV light. These radicals would then react with other molecules in the environment producing species which are expected to be susceptible to abiotic and biological degradation. The chemical would eventually be mineralised to water and oxides of carbon, while the iodine

component will be eventually converted to iodide.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

No exposure of waterside workers, transport drivers and warehouse workers is expected except in the case of an accident involving damage to the packages.

At the ink manufacturing site, the 75 % solution of the notified chemical will be manually weighed and added to a 200 L stainless steel blending vessel. Dermal exposure and accidental ocular exposure to the 75 % solution of the notified chemical is possible during this procedure. Extraction ventilation will be used at this point. Workers will wear overalls, PVC coated cotton gloves and protective goggles. Little worker exposure to the inks is expected during the filling process.

At the printing sites, the inks containing up to 4 % notified chemical will be manually poured from the pails into ink ducts. Residual ink will be scraped into the ink duct prior to the containers being washed. Dermal and accidental ocular exposure could occur during these processes. From this point, the printing process will be highly automated, and the ink will be cured by UV exposure prior to the substrates being manually handled. Some exposure may also occur during cleaning of the printing equipment. Workers will wear overalls, PVC coated cotton gloves and protective goggles while handling the inks.

Laboratory workers will handle concentrated solutions of the notified chemical as well as formulated inks. Normal laboratory protective equipment (laboratory coats, safety glasses, protective gloves and fume hoods) would be expected to be used.

9.2.2. Public health – exposure assessment

There is potential for public exposure to the notified chemical in the unlikely event of an accidental spillage during transportation. However, the potential for public exposure to the notified chemical during transportation is low.

The UV-curable varnish will be applied to objects as food containers and beverage cans. The public will frequently consume food or beverages which have been exposed to the packaging, and will handle the packaging. Although the coated and cured articles bind a trace amount of the notified chemical within the ink matrix, it is no longer bioavailable.

9.2.3. Human health - effects assessment

The notified chemical is harmful by acute oral exposure with LD50 in rats of 380 mg/kg bw. All animals treated with 2000 mg/kg bw and five out of six treated with 400 mg/kg bw died by day 2. The cause of death was not fully determined, but distension of the stomach and behavioural changes were seen. The acute dermal toxicity in rats was low, and no test on the acute inhalation toxicity of the notified chemical was performed.

The notified chemical was not irritating to the skin of rabbits, but was found to be a severe irritant to rabbit eyes, with the test being terminated at 24 hours due to animal welfare concerns, with chemosis scores of 4 at this time. It was found to be strongly sensitising to the skin of guinea pigs in an adjuvant test, with a sensitisation rate of 100 % 48 hours after challenge.

In a 28 day oral repeat dose study in rats, effects on the liver, kidney, digestive system, clinical chemistry and haemopoietic system were seen at the highest dose tested of 80 mg/kg bw/day. Digestive system changes and blood composition changes were also seen to a lesser extent at the mid dose of 20 mg/kg bw/day, and the NOEL was established as 5 mg/kg bw/day.

No indications of genotoxicity were seen in a bacterial reverse mutation assay or an in vitro mammalian cell cytogenetic assay.

Reports of human sensitisation due to the notified chemical have been received. Four workers handling the solid form of the notified chemical showed reddening of facial skin and swelling of the eyelid, symptoms which disappeared on absence from the workplace. A patch test confirmed

the sensitisation of one of the workers to the notified chemical. It was considered that dust exposure was responsible, and the notified chemical is therefore only traded in solution form. The notified chemical may act as an alkylating agent, which may accordingly be expected to be a sensitiser.

Based on the results of the toxicity testing, the notified chemical should be classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (NOHSC, 1999) and assigned the risk phrases R22: Harmful if swallowed; R41: Risk of serious damage to eyes; R43: May cause sensitisation by skin contact; and R48/22: Harmful: Danger of serious damage to health by prolonged exposure if swallowed. In the absence of toxicity information on products containing the notified chemical at low percentages, the risk phrase R43 should be applied to any product containing the notified chemical at greater than 1 % in accordance with the Approved Criteria. If the notified chemical is introduced into Australia in a form which may be inhaled, such as a respirable powder, additional information on the inhalation toxicity of the notified chemical will be required.

9.2.4. Occupational health and safety – risk characterisation

The primary hazard associated with use of the notified chemical is skin sensitisation, which has been observed in occupational use, as well as being clearly indicated in the guinea pig test. While the notified chemical has moderate oral toxicity and is harmful on repeat oral exposure, the results of the dermal toxicity testing indicate that skin absorption is unlikely to lead to sufficient absorption to produce toxic effects. The notified chemical is also a severe eye irritant, and ocular exposure must be prevented. The notified chemical is only handled in solution form within Australia, as exposure to dusts may result in skin sensitisation and eye irritation, and exposure to the solution may be more easily controlled.

The notified chemical will be handled manually as a 75 % solution in propylene carbonate, and a high level of personal protective equipment will be required to prevent exposure during this procedure. Extraction ventilation will be used at this point. Workers will wear overalls, PVC coated cotton gloves and protective goggles. The Material Safety Data Sheet (MSDS) specifies that the gloves should be PVC, long impervious. Respiratory protection may be used if conditions are dusty or high vapour concentrations are present. High levels of protection would also be required for laboratory workers handling the concentrated solution.

Dermal contact with the inks containing the notified chemical may occur during manual addition of these to the ink ducts of the printing equipment, and during cleaning of the ink containers and the printing equipment. Due to the strongly sensitising properties of the notified chemical, the inks containing 2 – 4 % notified chemical should be classified as skin sensitisers even in the absence of additional sensitising components (which the notifier states may be present in the inks). Accordingly, a high level of personal protective equipment is also required during ink addition and equipment cleaning. The notifier states that long impervious PVC gloves, overalls and safety goggles will be used, along with organic vapour respirators and local exhaust ventilation.

9.2.5. Public health – risk characterisation

The public will frequently consume foods or drinks which have been exposed to the packaging, and also directly contact with the packaging printed using the UV-curable varnish which contains a level of the notified chemical. Although a trace amount of notified chemical binds within the ink matrix after printing and curing, it is not bioavailable from the surface of packaging. Hence, the effect of the notified chemical on public health is considered to be negligible.

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

10.1. Environment

On the basis of the PEC/PNEC ratio the new chemical is not expected to present a hazard to the aquatic environment when used as a photo-initiator for curing polymers in varnish as indicated.

10.2. Health hazard

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (1999). The classification and labelling details are: R22: Harmful if swallowed; R41: Risk of serious damage to eyes; R43: May cause sensitisation by skin contact; and R48/22: Harmful: Danger of serious damage to health by prolonged exposure if swallowed.

10.3. Human health

10.3.1. Human health – Occupational health and safety

There is Moderate Concern to occupational health and safety for workers handling the imported solution and the reformulated inks under the conditions of the occupational settings described, based on the sensitising properties of the notified chemical, particularly as occupational sensitisation has been observed overseas, and on the manual handling procedures used.

10.3.2. Human health – public

There is Negligible Concern to public health when used in UV curable coatings as specified in the notification.

11. RECOMMENDATIONS

REGULATORY CONTROLS

- The NOHSC Chemicals Standards Sub-committee should consider the following [health, environmental and physico-chemical] hazard classification for the notified chemical:
  - R22: Harmful if swallowed;
  - R41: Risk of serious damage to eyes;
  - R43: May cause sensitisation by skin contact;
  - R48/22: Harmful: Danger of serious damage to health by prolonged exposure if swallowed.

- Use the following risk phrases for the inks and varnishes containing the notified chemical:
  - > 1 %: R43: May cause sensitisation by skin contact

- As the notified chemical is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced and in inks:
  - Enclosed automated equipment should be used wherever practicable;
  - Local exhaust ventilation should be used where handling is not enclosed.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced and in inks:
  - Long impervious PVC gloves, safety goggles, overalls and safety boots;
  - Respirators should be available for use as required.

  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.

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

Environment

- The following control measures should be implemented by formulators of varnish and printing facilities using the varnishes to minimise environmental exposure during formulation and end use of the notified chemical:
  - All spills should be soaked up with an adsorbent material and disposed of to landfill, or preferably be incinerated. Every measure should be observed to prevent spilt material entering watercourses or sewer systems.

Disposal

- The notified chemical should be disposed of by incineration.

Emergency procedures

- Spills/release of the notified chemical should be handled by adsorption onto appropriate material and disposal into landfill, or preferably by incineration.

11.1. 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
  - Use of the chemical changes in such a manner as to significantly increase discharge of the compound to the sewer system, the hazard should be reassessed and the full report on the toxicity of the compound to sewage bacteria may be required in order to conduct a more comprehensive environmental assessment.
  - The notified chemical is introduced in powder form, in which case information on the inhalation toxicity and potential of the notified chemical for respiratory sensitisation should be provided.

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.

12. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets*.

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

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