File No: STD/1007

April 2002

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

CGL-074

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

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Website:	www.nicnas.gov.au

Director
Chemicals Notification and Assessment

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FULL PUBLIC REPORT

CGL 074

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
CIBA SPECIALTY CHEMICALS
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)
Data items and details claimed exempt from publication:
Chemical name
CAS number
Molecular formula
Structural formula
Molecular weight
Spectral data (UV/vis, IR, NMR) (except as shown in technical bulletin)
Estimated import
Number of sites at which the product will be formulated
Identity of sites at which the product will be formulated
Bibliographic material
References to composition of commercial form (other than 'sterically hindered amine' content: high (>99 %))

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
Italy; Notification Number: 00-05-0376-00 1992

2. IDENTITY OF CHEMICAL

OTHER NAME(S)
CGL-074
TKA 45024
CA37-0074 C18 monomer

MARKETING NAME(S)
CGL-074
METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	1H nmr spectroscopy Infrared (IR) spectroscopy Flow Injection LC/Apcl/Mass Spectroscopy
TEST FACILITY	Ciba Specialty Chemicals Corporation Tarrytown, NY 10591 USA

3. COMPOSITION

DEGREE OF PURITY
> 92 %

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 introduced in a ready to use pelleted (granular) form.

USE
The notified chemical will be incorporated into masterbatch formulations of base polymer at 10-20 % and in end-use polymer products at 0.1 -1.0 %. Masterbatch formulations containing the notified polymer may be converted to articles or films for end use.
The principal function of the notified chemical in the polymer is to impart some resistance against solar ultra-violet radiation to polymers into which it is incorporated.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Not specified.

IDENTITY OF MANUFACTURER
Ciba Specialty Chemicals Corporation
Tarrytown, NY 10591 USA

TRANSPORTATION AND PACKAGING
The notified chemical will be transported in 20 kg polythene bags housed within fireboard boxes (suitable for road/rail transport) or in 50 kg fibre drums designed for international transport. No repackaging operations will be carried out.

5.2. Operation Description

Masterbatch Production
The notified chemical is weighed and charged before being added to base polymer in a blending vessel for mixing with other components. The powdered masterbatch is then transferred to the feed hopper of an extruder from which molten strands are chopped into pellets and allowed to cool before being discharged via a closed transfer system for packaging. During this process, the notified chemical becomes encapsulated in the polymer matrix. Local exhaust ventilation ensures capture of fugitive dust/vapours released during processing. High temperature injection moulding processes are used for production of end-use articles or films containing the notified chemical.

Extrusion and Moulding Operations
At the factories of the final users, the small pellets of masterbatch containing the notified chemical (and possibly other additives) are mixed with polymer in an typical ratio of around 1:10 masterbatch: polymer in the hopper of an injection moulding machine, and again melted and extruded under pressure through dies or moulds of the appropriate shapes so as to produce the final plastic article. Since the notified chemical typically comprises 10-20% of the masterbatch, the final concentration in the finished polymer products is estimated as being typically around 1.0-2.0%, although the notifier indicated that the range could be 0.1-1%.

Initially up to 3 end users might use masterbatch material containing the notified chemical, although this may increase in the future. It was indicated that polymer containing the notified chemical would be used in the manufacture of a diverse range of plastic products where light stability is important. Use in agricultural and horticultural plastic products (presumably articles such as agricultural polyethylene pipe) was indicated as a major end use.

5.3. Release

RELEASE OF CHEMICAL AT SITE OF MASTERBATCH PREPARATION AND EXTRUSION MOULDING OF FINISHED ARTICLES

Masterbatch Preparation

Small quantities of the chemical could be lost during preliminary mixing with polymer and other components prior to extrusion of the masterbatch, and all of this is likely to be placed into landfill. Small spills of chemical would be swept up and either returned to the mix or disposed of with other factory waste to landfill. It is expected that the mixing and extrusion operations would be performed using vacuum extraction/filtration so that any particulate matter released to the air during operations would be captured and retained on the filters, and all solid material retained on the filters would also be placed into landfill.

On occasions the extrusion equipment would be cleaned out and some solid scrap material removed from the equipment and also placed into landfill, as would any of the granulated masterbatch lost during packaging. Emptied bags of the chemical would be shaken into the masterbatch mix to remove residual material and then be placed into landfill.

Extrusion and Moulding Operations

Apart from spills no release of the chemical during dry mixing of the masterbatch compound with polymer, filler and other materials is expected during injection moulding of the final articles although it is possible that some scrap plastic may be produced during finishing of the final products. All such waste would be placed into landfill.

Overall Manufacturing Release

While no details of likely release of the notified chemical were provided, large releases are not expected. If it is assumed that 2% is lost during masterbatch preparation and a further 3 % lost as scrap and waste from injection moulding, then total losses associated with manufacturing activities are 5 %. This equates to a maximum annual release of 500 kg, all of which will be placed into landfill.

RELEASE OF CHEMICAL FROM USE

Once incorporated into plastic/polymer articles the notified chemical will be immobilised in the polymer matrix and little release is expected.

5.4. Disposal

Disposal via incineration in the presence of excess air, is the disposal route of choice. Waste arising from formulation processes is not expected to exceed 10-20 kg per year. Non-recyclable waste arising from article manufacturing sites is expected to be negligible and disposed of to landfill.

6. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20^{o}C AND 101.3 kPa	White to Yellowish Granules.
MELTING POINT	59 – 64 ^{o}C

METHOD	OECD TG 102 Melting Point/Range EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	The melting range was determined using differential scanning calorimetry (Ciba Specialty Chemicals, 2000a). Small endotherms at 30 – 36 and 44 – 54 ^{o}C attributed to crystal

phases.

TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

BOILING POINT Not determined

METHOD OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.

Remarks The substance thermally decomposed before boiling at atmospheric pressure (98.8 kPa) under nitrogen. Degradation was apparent from an exothermic transition above 260 ºC (270 ºC at the reduced pressure of 4 kPa). Accordingly, boiling point could not be determined.

TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

DENSITY 1004 kg/m^3 at 24 ºC

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

Remarks As the instrument used for analysis, a gas comparison pycnometer (Ciba Specialty Chemicals, 2000b), was not temperature controlled, therefore, the relative density was reported at 24 ºC rather than 20 ºC.

TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

VAPOUR PRESSURE Upper Limit (estimated): < 2x10^{-5} Pa at 20 ºC.

METHOD OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure
Handbook of Chemical Property Estimation Methods (Lyman *et al*, 1990).

Remarks Attempts to measure the vapour pressure of the notified chemical using the "dynamic method" were unsuccessful due to thermal decomposition. The vapour pressure limit was estimated (Ciba Specialty Chemicals, 2000c) Ciba Specialty Chemicals, 2000c)(Ciba Specialty Chemicals, 2000c) at 20ºC using the modified Watson correlation (Organisation for Economic Cooperation and Development 1993)and in the Handbook of Chemical Property Estimation Methods (Lyman *et al*, 1990).

TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

WATER SOLUBILITY < 50 ppb (0.05 mg/L) at 20ºC

METHOD OECD TG 105 Water Solubility.
EC Directive 84/449 A.6 Water Solubility.

Remarks Analytical Method: HPLC/evaporative light scattering detection. The water solubility was determined (Ciba Specialty Chemicals, 2000d) by stirring the compound in water at 30ºC for three days and then allowed to equilibrate at 20ºC for another day following which the filtered samples were analysed for contained test compound using HPLC after extraction with dichloromethane. The concentration of the test material in the water was found to be less than the detection limit of the method employed which was 50 µg/L.

TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

HYDROLYSIS AS A FUNCTION OF pH

Remarks No experimental data was provided due to the very low water solubility. However, the compound contains no functional groups which are susceptible to hydrolysis in the environmental pH region where 4<pH<9.

PARTITION COEFFICIENT (n-octanol/water) Log Kow at 20ºC =10.15 (estimated)

METHOD OECD TG 117 Partition Coefficient (n-octanol/water): HPLC Method.
Remarks The value of Log Kow was estimated (Ciba Specialty Chemicals, 2000e) using methods based on the molecular structure of the compound described by Lyman *et al*, 1990. These authors state that values of Log Pow greater than 6 estimated by these methods are questionable, but nevertheless a high value for Log Pow is expected for the present compound due to the high content of aliphatic hydrocarbon.
TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

ADSORPTION/DESORPTION

Remarks No experimental data was provided, but the low water solubility and high estimated value of Log Kow indicate that the chemical would have a high affinity for organic matter in soils and sediments and would not be mobile in these media.

DISSOCIATION CONSTANT

Remarks No data provided. However, the notified chemical contains no groups expected to be either acidic or basic under environmental conditions so this property is not relevant for this chemical.

PARTICLE SIZE

METHOD OECD TG 110 Particle Size Distribution Using the Dry Sieve Method.

Range (μm)	*Particle Size Distribution (%)*
< 45	< 0.22 (n.b. Base = 0.185 %)
retained on 45	0.23
63	0.01
75	0.61
125	3.95
250	8.48
500	14.7
1000	30.2
2000	41.6

Remarks A millimetre rule was used to determine the general shape and size of (25) notified chemical particles. The Dry Sieve Method (2.0 mm – 0.045 μm) determined a more accurate particle size distribution from 97.065 g of starting material, however, 0.185 % of the notified chemical was collected at test termination. The particle size distribution of the notified chemical indicated that a small percentage of particles were below the classifiable limits for inspirable and respirable mass fractions as set out in National Occupational Health and Safety Commission Guidance Note on the Interpretation of Exposure Standards for Atmospheric Contaminants in the Occupational Environment [NOHSC:3008(1995)].
TEST FACILITY Springborn Laboratories, Inc (2000)

FLASH POINT 218 °C at 101.351 kPa (closed cup)

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks
TEST FACILITY Ciba Specialty Chemicals Corporation (2000)

FLAMMABILITY Not flammable

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks During the application of the flame, the notified chemical melted, creating a waxy coating over the burn plate surface, but did not ignite. The notified chemical was determined to be

non-flammable as it did not burn or propagate along the powder train.

TEST FACILITY Springborn Laboratories, Inc (2000)

AUTOIGNITION TEMPERATURE

METHOD 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.

Remarks Not conducted.

TEST FACILITY

EXPLOSIVE PROPERTIES None with respect to shock, friction or heat

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.

Remarks Explosive properties of the notified chemical were examined in relation to mechanical sensitivity with respect to shock, friction and thermal sensitivity.

TEST FACILITY Springborn Laboratories, Inc (2000)

REACTIVITY Non-oxidizing

METHOD EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).

Remarks The notified chemical is considered to be a non-oxidizing substance as no signs of a vigorous oxidation or combustion were evident during preliminary testing. No further testing (train test) was necessary.
Protocol deviation: The notified chemical was not dried during testing as its melting temperature (50 ºC) precluded achieving an effective drying temperature. The deviation did not negatively impact the study results.

TEST FACILITY Springborn Laboratories, Inc (2000)

STABILITY TESTING Stable, no significant changes

METHOD OECD TG 113 Screening Test for Thermal Stability and Stability in Air.

Remarks The notified chemical is considered to be thermally stable at 55 ºC $\pm$ 2 ºC in a water saturated air environment.
Protocol deviation: No protocol deviations were reported.

TEST FACILITY Springborn Laboratories, Inc (2000)

7. TOXICOLOGICAL INVESTIGATIONS

7.1. Acute toxicity – oral

TEST SUBSTANCE CGL-074

METHOD OECD TG 401 Acute Oral Toxicity – Limit Test.
Species/Strain rat/Hsd:Sprague Dawley (SD)
Vehicle PEG400
Remarks - Method No protocol deviations were reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
	5/sex	2000	1/5 (male only)

LD50 > 2000 mg/kg bw

Signs of Toxicity Clinical abnormalities observed were faecal/urine stains, mucoid/soft stools, diarrhoea, congested breathing and dark material around the nose and eyes. Combinations of these effects were observed at treatment Day 0 in 2/5 and 5/5 males and females, respectively. These effects abrogated within 24 to 48 h after treatment and may be indicative of an

	adaptive response to exposure to the compound. A slight decrease (not statistically significant) in food consumption was noted in males (-9.7 %) and females (-9.6 %) during the period Day 7-14 period, however this had no biologically relevant effect on body weight variation.
Effects in Organs	No gross internal findings were noted in scheduled euthanased animals that survived the study. One male animal died by study day 9 and on necropsy presented with abnormal small intestinal contents, mottled lungs, enlarged spleen, distended urinary bladder and fluid contents in the thoracic cavity.
Remarks - Results	The absence of vehicle controls in the limit test provides no indication toxic effects arising from the vehicle control (PEG 400). The evident toxicity effects and single mortality observed in the limit study suggest an increased incidence in mortality would be expected at doses greater than 2000 mg/kg bw.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Springborn Laboratories, Inc (2000)

7.2. Acute toxicity - dermal

TEST SUBSTANCE	CGL-074
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	rat/Hsd:Sprague Dawley (SD)
Vehicle	Deionised water
Type of dressing	Occlusive
Remarks - Method	

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
CGL-074	5/sex	2000	1/5 (male only)

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	No dermal irritation was observed at the site of test article application. Noticeable dermal irritation outside the test site was observed in four females and 1 male at study day 1 and persisting in 1 of the females until study day 3. No macroscopic dermal lesions (erythema or oedema) were reported in either sex.
Signs of Toxicity - Systemic	Body weight loss was noted for one female during study day interval 0-7 and for two females during study day 7-14 however food consumption was considered to be comparable between these intervals. Clinical abnormalities observed in both sexes were dark material around the facial area, urine stain and ocular discharge. One male animal died by study day 9 and on necropsy presented with abnormal small intestinal contents, mottled lungs, enlarged spleen, distended urinary bladder and fluid contents in the thoracic cavity.
Effects in Organs	No gross internal findings were observed in scheduled euthanased animals that survived the study period.
Remarks - Results	The study also examined the incidence of erythema and oedema using a Macroscopic Dermal Grading System based on the Draize Testing System however quantitative data were not provided. No protocol deviations occurred during this study.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.

TEST FACILITY Springborn Laboratories, Inc (2000)

7.3. Acute toxicity – inhalation not provided.

7.4. Irritation – skin

TEST SUBSTANCE CGL-074

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 (male)
Vehicle	Deionized water
Observation Period	1 h, 24 h, 48 h and 72 h post treatment
Type of Dressing	Occlusive
Remarks - Method	*Protocol deviation:* The temperature of the animal room (19 – 24 °C) exceeded the preferred range (17 – 23 °C) during the study. This occurrence was considered to have no adverse effect on the outcome of the study. The study examined for the incidence of erythema and oedema using a Macroscopic Dermal Grading System based on the Draize Testing System (Draize, 1959).

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema	0.33	0.00	0.33	1	24 h (two animals)	0
Oedema	0	0	0	0	0	0

*Calculated on the basis of the scores at 24, 48, and 72 h for EACH animal using the EEC Dermal Evaluation Criteria of each animal for erythema and oedema. Scores are summed and each total divided by 3.

Remarks - Results Using the EEC Dermal Evaluation Criteria, exposure to the test article produced very slight erythema (grade 1) on 3/3 test sites at the 1 h scoring interval, persisting until the 24 h scoring interval in two out of the three animals. The dermal irritation resolved completely on all test sites by the 48 h scoring interval.

In a second evaluation (FIFRA) study, the test article was considered to be a slight irritant to the skin. The Primary Irritation Index was calculated as 0.42.

CONCLUSION The notified chemical is slightly irritating to skin of rabbits.

TEST FACILITY Springborn Laboratories, Inc (2000)

7.5. Irritation - eye

TEST SUBSTANCE	CGL-074
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 (male)
Observation Period	1 h, 24 h, 48 h, 72 h and up to 7 days post treatment.
Remarks - Method	*Test article preparation* The test article was ground and filtered through a 40-mesh sieve. Dose administered was predicated on the weight (0.0510 g), which occupied a 0.1 mL volume. *Protocol deviation:* The temperature of the animal room (18 – 24 °C) exceeded the preferred range (17 – 23 °C) during the study. This occurrence was considered to have no adverse effect on the outcome of the study.
RESULTS	CGL-074 produced iritis in 1/3 test eyes at the 1 h scoring interval, resolving completely by the 48 h scoring interval. Conjunctivitis was noted in all treated test animals (3/3 test eyes) at the 1 h scoring interval, resolving completely by study Day 7. Positive secondary ocular findings revealed presence of the test article on the eyes of all treated animals. No fluorescein dye retention associated with corneal opacity was noted in any of the treated animals throughout the study period.

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Effect*	*Maximum Value at End of Observation Period (72 h)*
	1	2	3			
Conjunctiva: redness	0.67	0.67	0.33	2.0	48 h	0
Conjunctiva: chemosis	1.0	0.33	0.67	1.0	72 h	0
Conjunctiva: discharge	0.5	0.25	0.25	1.0	24 h	0
Corneal opacity	0.0	0.0	0.0	0.0	0.0 h	0
Iridial inflammation	0.33	0.0	0.0	0.0	24 h	0

*Calculated on the basis of the scores at 1, 24, 48, and 72 h for EACH animal using EEC Criteria grading. Scores for *Conjunctiva Discharge* were based on a revised Draize Testing System (Ocular Grading System: Kay and Calandra, 1962).

Remarks - Results	The notified chemical produced iritis in 1/3 test eyes at the 1 h scoring interval, however the iridal irritation resolved completely by the 48 h scoring interval. Although conjunctivitis (redness, swelling and discharge was noted in 3/3 test animals at the 1 h scoring interval, the conjunctival irritation resolved completely in all test eyes by study Day 7.
CONCLUSION	Taken together, the data suggest that the notified chemical is slightly irritating to the eye.
TEST FACILITY	Springborn Laboratories, Inc (2000)

7.6. Skin sensitisation

TEST SUBSTANCE	CGL-074
METHOD	OECD TG 406 Skin Sensitisation – Guinea Pig Maximization Test. EC Directive 96/54/EC B.6 Skin Sensitisation.
Species/Strain	Guinea pig/ Dunkin Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration (range-finding studies): intradermal: 1.0 % w/v (see *protocol deviation*)

topical: 100 % (undiluted)

MAIN STUDY

Number of Animals induction phase: Test Group: 20 Control Group: 10
Induction Concentration:
intradermal injection 1.0 % w/v (CGL-074 in PEG 400 or FCA)
topical application 100 %

Signs of Irritation

CHALLENGE PHASE

1st challenge: topical application (100 %): no irritation detected[1, 2, 3]

2nd challenge: topical application: not conducted.

Notes

[1]Noticeable dermal irritation was noted outside the test site in all CGL-074- treated and challenge control animals at both dosing time points (24 h and 48 h), the effect being attributable to binding of the tape material.

[2]Slightly patchy erythema (grade=0.5) was noted in 7 out of 20 CGL-074-treated animals at the 24 h time point and persisting in 4 out of 20 animals at the 48 h time point, the effect being absent in challenge controls.

[3]Positive clinical observations (Day 8 and to a limited extent Days 9 and 10) were noted in 2 challenge control animals. Effects noted were laboured breathing, apparent grinding of teeth and piloerection. Individual observations were pale eyes in one animal, and ocular discharge, dilated pupils, decreased food consumption and decreased faeces in the other.

Remarks – Method: Mortality and body weight (but not gross necropsy examinations) were monitored for all sensitisation study animals at 1 day prior to intradermal induction and for test and challenge control animals.

Protocol deviation: The temperature of the animal room (18 – 23 °C) exceeded the preferred range (17 – 23 °C) during the study. This occurrence was considered to have no adverse effect on the outcome of the study.

As viscosity limitations of CGL-074 at 3.0 % and 5.0 % resulted in insufficient dose delivery, 1.0 % w/v in PEG 400 was considered appropriate for intradermal induction.

RESULTS: All irritation scores in both test and challenge control animals were zero during the challenge phase.

Animal	*Challenge Concentration (%)*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	100	0/20	0/20	n.d	n.d
Control Group	100	0/20	0/20	n.d	n.d

Remarks - Results: The slightly patchy erythema (grade=0.5) noted in the challenge group (see note 2 above) was also present at the 24 h time point in 3 out of 4 range-finding animals following a topical exposure at the lowest dose tested (10 %), the effect increasing to 4 out of 4 in animals exposed to a 25 % topical concentration. Accordingly, OECD guideline 406 describes

the challenge exposure as being the highest non-irritant dose. Moreover, the chosen intradermal induction dose of 1.0 % (predicated on viscosity limitations in the range-finding study) reveals less incidence of 'Grade-4 Blanching' (> 50 % test site) than at the lowest dose tested (0.1 %) for both the 24 h and 48 h time point. Whilst, OECD guideline 406 describes the induction concentration as being the highest dose to cause mild-moderate skin irritation, the present study does not provide data distinguishing local irritation responses (seen at the 0.1 % dose in the intradermal induction study) as a consequence of immune response to the diluent or the test article.

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Springborn Laboratories, Inc (2000)

7.7. 28-day Repeat dose oral toxicity

TEST SUBSTANCE	CGL-074
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/Sprague-Dawley Crl:CDBR
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28; Dose regimen: single daily dose; individual doses were adjusted based on most recent body weight data. Group I (0 mg/kg/d); Group II (100 mg/kg/d); Group III (500 mg/kg/d) and Group IV (1000 mg/kg/d); and Group IV_{rec} (1000 mg/kg/d). Pre-study analytical evaluations indicted homogeneity of CGL-074 within 11.9 % of nominal concentrations and within 9.4 % of the Day 0 concentration. Analysis of dosing mixtures revealed average CGL-074 recoveries within 12.1 % of the nominal concentrations. No CGL-074 was noted in the control samples. Post-exposure observation period: five animals (both sexes) from each treatment group euthanised on Day 29 except for remaining controls and high dosed 14-day recovery group (Group IV_{rec}) animals (5 per sex) euthanised at Day 42.
Vehicle	10 % w/v Tween 80: PEG 400
Remarks - Method	Evaluation parameters: • Functional Observation Battery (FOB) (home cage, removal from cage and open field): body posture, clonic involuntary motor movements, tonic involuntary motor movements, vocalisation, reactivity to handling, ocular discharge, eyelid closure, salivation, piloerection, gait score, gait abnormalities, mobility score, arousal, stereotypy, bizarre behaviour, urination, defecation, rearing, • Manipulative Testing: approach response, touch response, startle response, tail pinch, pupil response, righting ability, forelimb grip strength, hind limb grip strength, landing foot splay, body temperature. • Motor activity testing. • Clinical pathology: i. Haematology, including but not limited to; mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular volume (MCV), platelet count, and

reticulocyte count.

ii. Biochemistry, including but not limited to; albumin/globulin ratio, alkaline phosphatase, calcium, cholesterol[1], blood creatinine, globin and triglycerides[1].

iii. Urinalysis: overnight volume, colour and appearance, pH, specific gravity, protein, glucose, ketones, urobilinogen, nitrites, bilirubin, occult blood, leukocytes and microscopy of spun deposit.

- Ophthalmology.
- Organ weights including but not limited to; testes with epididymides, ovaries, spleen, thymus, thyroids, brain and heart. These and other organs were also preserved in 10 % neutral buffered formalin.
- Macroscopic and Microscopic Findings

v. Histopathology was performed on all tissues and organs collected at necropsy from all animals in the control and high-dose (1000 mg/kg/d) groups (Day 29) including 14-day control and high-dosed animals in the recovery Group IV_{rec} (Day 42). Macroscopic examinations in 28-Day Group 2 and 3 animals (100 mg/kg/d and 500 mg/kg/d) were limited to the caecum, colon, diaphragm, epididymides, haircoat, ileum, liver, lung, ovary, stomach, thymus and thyroid gland.

Statistical analysis

Parametric data was analysed by one-way analysis of variance (ANOVA); group comparisons determined by the Tukey-Kramer method. Two tailed pared t-tests were determined at the 5 % (0.05) significance level with group-to-group comparisons performed using Kruskal-Wallis Nonparametric ANOVA.

Descriptive and quantal data were analysed by Fischer's Exact test with group-to-group comparisons were determined by the Fischer's Exact Test.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I	10 per sex	0	1
II	5 per sex	100	0
III	5 per sex	500	0
IV (incl. IV_{rec})	10 per sex	1000	0

Mortality and Time to Death

No treatment related mortalities were noted during the course of the study. One control male died on Day 23. Clinical changes preceding the death of this animal were observed at Day 22 and included diarrhoea, salivation, urine stained hair coat and dark material around the nose. Gross necropsy revealed a distended and thickened bladder/urethra with the bladder calculi (not uncommon in this species/sex) resulting in renal failure and death. Histopathological examination confirmed gross bladder and urethral change and supported pyelonephritis as the most likely cause of death.

Clinical Observations

No clinical signs of systemic toxicity were observed in treated animals. Similarly, no treatment related change in: body weight, food consumption, FOB parameters, or neurotoxicological parameters were observed compared with controls. No statistically, or toxicologically significant changes in mean food consumption among treatment or recovery phase groups were noted. Mean body weight gain in males of Group II (100 mg/kg bw/d) were statistically lower (-30 %) for the period Day 8-15 ($P<0.05$) compared to controls, however the conspicuous absence of statistically significant dose-dependent change at later time periods preclude the effect from being toxicologically meaningful.
Biochemistry: No toxicologically significant differences were noted in any treatment or recovery group animal.

Laboratory Findings – Clinical Chemistry, Haematology and Urinalysis

- *Clinical Chemistry*: No treatment-related differences in clinical chemistry parameters were observed in any treatment group compared to controls. Day 42 Group IV_{rec} high-dosed males (1000 mg/kg/bw/d) showed a slight, but statistically significant increase ($p<0.05$) in chloride (+ 3.8 %), by contrast, females in this group revealed a statistically significant decrease ($P<0.01$) in triglycerides (-41.7 %) compared to untreated controls. Whilst these findings were not considered biologically relevant, as they were present at the end of the recovery period and not during the treatment phase and were generally within historical control data, the observation should be dismissed with caution. Apropos, the appearance of toxic effects in the recovery phase may be an indication of late-onset biochemical processes the persistence of which may reasonably lead to a toxic phenotype. Accordingly, further investigation may be warranted at these doses together with a treatment free recovery phase of greater than 14-days to address reversibility or persistence of these effects.
- *Haematology and Coagulation*: No statistically or toxicologically significant differences were noted in any treatment or recovery group animal.
- *Urinalysis*: No statistically or biologically meaningful differences were noted in the urinalysis parameters in any of the treatment or recovery phase animals.

Effects in Organs: No statistically or toxicologically relevant differences in organ weight data as determined by pathological or histopathological criteria were noted in any treatment or recovery group animal. A statistically significant increase in relative testes/epididymides weight and a statistically significant decrease in absolute ovarian weight were noted in the low dosed (100 mg/kg/d) males and high dosed (1000 mg/kg/d) females respectively, on treatment Day 29. However, these differences were not considered toxicologically meaningful in the absence of a dose-dependent response and related histopathological change within the limits of variation.

Macroscopic and Microscopic Findings: No test article associated lesions were observed in any of the Day 29 or Day 42 study animals. All lesions in the study were interpreted to be spontaneous or background lesions commensurate with historical data.

Remarks – Results

[1]The present study uses a peroxidase-chromagen enzymatic method for cholesterol quantification based on a cholesterol esterase-mediated reaction to hydrolyse lipoprotein-cholesterol esters prior to detection. However, esterases used in peroxidase-chromagen systems show varying degrees of specificity toward different cholesterol esters (Derelanko and Hollinger, 1995). It is plausible that the total cholesterol content measured in this study may be underestimated, as rats possess a fivefold higher concentration of cholesteryl arachidonate ester compared with human plasma.

The present study provides no toxicologically relevant data supporting CGL-074-mediated toxicity effects in the rat. Oral administration of CGL-074 did not produce any statistically or biologically relevant treatment-related effects in relation to unscheduled mortalities, clinical abnormalities, body/organ weight, food consumption, ophthalmological, neurotoxicological, clinical, pathological or histopathological criteria during the main or recovery phase of the study. FOB examinations prior to dosing were consistent between control and treated animals and no notable abnormalities were observed in any animal during the recovery phase.

CONCLUSION

The No Observed Effect Level (NOEL) in this study was established as 1000 mg/kg bw/d predicated on the absence of any dose dependent statistically significant effect in clinical or pathological criterion. Taken together, the data suggest a No Observed Adverse Effect Level (NOAEL) at a dose higher then the highest dose tested (> 1000 mg/kg bw/d).

TEST FACILITY Springborn Laboratories, Inc (2000)

7.8. Genotoxicity - bacteria

TEST SUBSTANCE CGL-074

METHOD OECD TG 471 Bacterial Reverse Mutation Test.

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA100, TA98. *E. coli*: WP2 uvrA
Metabolic Activation System	10 % rat liver S9 fraction from animals pre-treated with 500 mg/kg bw Aroclor 1254
Concentration Range in Main Test	With and Without metabolic activation: 33.3, 100, 333, 1000, 3330 and 5000 µg/plate[1].
Vehicle	[2]Ethanol (59.6 mg/mL)[3]

Remarks - Method

[1]doses tested in the mutagenicity assay were selected on the basis of a dose range-finding assay using strains TA100 and WP2*uvr*A in the presence and absence of metabolic activation. Doses tested were: 6.67, 10.0, 33.3, 66.6, 100, 333, 667, 1000, 3330 and 5000 ug/plate. No toxicity was observed in the dose range-finding assay and therefore the highest dose (5000 ug/plate) of GL-074 tested was also used in the mutagenicity assay.
[2]various vehicle solutions were tested for homogeneity with GL-074, however the resultant suspensions were non-homogeneous and therefore unworkable. These included: water, dimethylsulfoxide and dimethylformamide.
[3]GL-074 mixed with ethanol at concentrations of 656, 187 and 109 mg per ml formed unworkable suspensions.

Two separate experiments were performed in triplicate.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	1	1	1[sp,mp]	1
Test 2	1	1	1[sp,mp]	1
Absent				
Test 1	1	1	1[sp,mp]	1
Test 2	1	1	1[sp,mp]	1

Remarks - Results

No significant dose dependent increases in the numbers of revertants were recorded for any strain, either in the presence or absence of metabolic activation. A normal background lawn (evaluation code 1) and a lack of decreased revertant numbers indicated no observable cytotoxicity in either the absence or presence of metabolic activation (S9 mix)
[sp,mp]slight precipitation was noted in the background lawn of the 333 µg-

dosed plates with and without S9 mix.
[mp]moderate precipitation was noted in the background lawn of the 3330, and 5000 μg dosed plates without S9 mix and in the 1000 μg dosed plates in the presence of the S9 mix..

Positive control values in the absence or presence of metabolic activation (S9 mix) were also increased at least 3-fold over the mean values of their vehicle controls, demonstrating positive mutagen identification and promutagen metabolism by the tester strains and S9 mix, respectively.

Confirmatory assays for TA98 (+ S9) and TA100, TA1535, TA1537 and WP2*uvr*A (± S9) validated earlier test results supporting no positive increases in mean number of revertants. Mean positive control values for strain TA98 (-S9) were retested a number of times.

CONCLUSION — CGL-074 was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY — Covance Laboratories, Inc.(2000)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE — CGL-074

METHOD — OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.

Cell Type/Cell Line	Chinese hamster ovary (CHO) cells
Metabolic Activation	1.5 % S9 fraction from the liver of rats pre-treated with Aroclor 1254
Vehicle	Ethanol (10 μl/mL)
Remarks - Method	Numerical aberrations were not determined, however, the occurrence of polyploidy or endoreduplication was investigated as a measure of the numerical aberrations potential of CGL-074. Solubility of CGL-074 was not achieved in either dimethylsulfoxide or water. Initial study test concentrations with a dosing volume of 1 % were prepared from a CGL-074/ethanol stock solution (30.0 mg/mL). Test concentrations used in the initial assay (with and without metabolic activation) were: 4.19[a], 5.98[a], 8.54[a], 12.2[a], 17.4[a], 24.8[a], 35.4[a], 50.5[a], 72.1, 103, 147, 210, and 300 μg/mL. The highest dose tested in the assay, 300 μg/mL, was above the solubility limit in the culture medium. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed in treated cultures. [a]no experimental data were provided at these doses. In addition to the initial study, a repeat confirmatory chromosomal aberrations assay (with and without metabolic activation) was conducted at CGL-074 concentrations: of 6.25a, 12.5a, 25.0a, 50.0a, 75.0, 100, 150, and 200 μg/mL over a 17.7 hour treatment period (without metabolic activation) and at 3 h (with metabolic activation). Cultures from 75.0, 100, 150 and 200 μg/mL (with metabolic activation) and 50.0, 75.0, 100, 150 μg/mL (with metabolic activation) were analysed for chromosomal aberrations, percent polyploidy, or endoreduplication. [a]no experimental results were provided at these doses. A statistically significant increase ($p < 0.01$) in the frequency of chromosomal aberration sensitivity was observed in mitomycin C treated cells indicating that the test system responded appropriately.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*

Absent			
Test 1	72.1 - 210	3.0 h	20 h
Test 2	75.0 - 200	17.6 h	20 h
Present			
Test 1	50.5 - 147	3.0 h	20 h
Test 2	50.0 - 150	3.0 h	20 h

CONCLUSION	CGL-074 was not clastogenic to CHO cells treated in vitro under the conditions of the test.
TEST FACILITY	Covance Laboratories, Inc (2000)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE: TKA 45024

METHOD: OECD TG 301 B Ready Biodegradability: CO2 Evolution Test.

Inoculum	Sewage bacteria
Exposure Period	29 days
Auxiliary Solvent	
Analytical Monitoring	
Remarks – Method	The company provided a report (Springborn, 2000) on the ready biodegradation of the notified chemical determined by a CO_2 evolution test (modified Sturm test) performed according to the protocols of OECD TG 301 B.

RESULTS

Test substance		*Sodium benzoate reference*	
Day	*% degradation*	*Day*	*% degradation*
28	10.5	28	>96

Remarks - Results

Two duplicate tests were conducted with the test material (nominal concentration equivalent to approximately 10 mg/L organic carbon based on the molecular formula for TKA 45024 incubated with sewage sludge bacteria over a 29-day test period. The quantity of CO_2 evolved was monitored over this period, and when compared with the theoretical quantity of CO_2 associated with complete degradation of the notified chemical the results indicated a mean of only 10.5 % degradation over the 28-day test period. In contrast to these results, a reference compound (sodium benzoate) was degraded to >96% over the test period, which demonstrated the viability of the bacteria used in the test. While the degradation figures above appear to be small, it is probable that the compound would be ultimately degraded after prolonged residence in landfill.

It should also be noted that in a toxicity control test where both the reference compound and the notified substance were incubated together with the sludge indicated that the presence of the test material had no inhibitory effect on the respiration of the sewage bacteria.

CONCLUSION: The test substance is not readily biodegradable under the conditions of the test.

TEST FACILITY: Springborn Laboratories (2000)

8.1.2. Bioaccumulation

No test report on bioaccumulation of the compound was provided in the notification, but the low water solubility and expected high value for Log Pow indicates high potential for bioaccumulation (Connell, 1990). However, little of the notified chemical is expected to enter the water compartment during either manufacturing activities or use of finished articles containing the chemical.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	TKA 45024
METHOD	OECD TG 203 Fish, Acute Toxicity Test Static conditions.
Species	Rainbow trout (*Oncorhynchus mykiss*)
Remarks – Method	The test was conducted (Springborn, 2000b) at 14 °C over a 96 h period under static conditions using a control (no test material) and one nominal exposure concentration of the test substance of 100 mg/L, which was well in excess of the water solubility (ie. < 0.05 mg/L). However, the test was conducted in triplicate using 10 fish in each test vessel. The pH of the test media was always between 6.6 and 7.2, dissolved oxygen 5.6 and 10.2 mg/L (corresponding to 54-99 % saturation at 14 °C), while the water hardness was 40 mg/L as $CaCO_3$. Measurement of the actual solution concentration of the test substance for one of the three replicate media indicated a concentration of 0.011 mg/L.
RESULTS	None of the fish had died or showed any signs of distress for exposures to the test media up to 72 h, but after 96 h exposure, 1 fish (of the 30 exposed) had died, while the remaining 9 fish in that particular replicate showed signs of distress. In contrast to this 2 fish in the controls had died after 96 h while 20 (of the 30) were distressed.
LC50	> 100 mg/L (nominal) at 96 h.
NOEC (or LOEC)	100 mg/L (nominal) at 96 h.
Remarks – Results	The data were interpreted as showing that the 96 h LC50 is greater than 100 mg/L nominal exposure concentration (0.011 mg/L measured).
CONCLUSION	The notified chemical is not toxic to rainbow trout up to the level of its water solubility.
TEST FACILITY	Springborn Laboratories (2000b)

8.2.2. Acute/chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	
METHOD	OECD TG 202 Fish, Acute Toxicity Test Static conditions.
Species	*Daphnia magna*
Remarks - Method	The test was conducted (Springborn, 2000c) at 20 °C over a 48 h period under static conditions using a control (no test material) and one nominal exposure concentration of the test substance of 100 mg/L, which was well in excess of the water solubility (ie. < 0.05 mg/L). However, the test was conducted in triplicate using 10 animals in each test vessel. The pH of the test media was always between 7.9 and 8.0, dissolved oxygen 8.6 and 9.6 mg/L (corresponding to 96-106% saturation at 20 °C), while the water hardness was around 115 mg/L as $CaCO_3$. Measurement of the actual solution concentration of the test substance for one of the three replicate media indicated a concentration of 0.90 mg/L.
RESULTS	None of the *Daphnia* had died or showed any signs of distress for exposures to the test media over the full 48 h exposure period.

LC50	> 100 mg/L (nominal) at 96 h.
LOEC	>100 mg/L (nominal) at 96 h.
Remarks - Results	The data were interpreted as showing that the 48 h LC50 is greater than 100mg/L nominal exposure concentration (0.90 mg/L measured).
CONCLUSION	The notified chemical is not toxic to *Daphnia* up to the level of its water solubility.
TEST FACILITY	Springborn Laboratories (2000c)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE	TKA 45024
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Pseudokirchneriella subcapitata*
Remarks – Method	The algal growth test was conducted (Springborn, 2000d) over a 96 hour period at 24ºC using growth media containing nominal concentrations of the test compound of 0 (control), 6.4, 13, 25, 50 and 100 mg/L, and each exposure test was conducted in triplicate. The corresponding measured concentrations in the media were 0 (control), 0.70, 0.37, 0.91, 1.3 and 3.1 mg/L, and it was noted that these measured concentrations actually exceeded the water solubility of the compound (ie. 0.050 mg/L) which was attributed to the presence of some fine undissolved compound in the media. The growth in biomass was monitored through determining the cell density in each test vessel over the 96 h test period.
RESULTS	All test media showed small inhibition in the growth of algal biomass, with the maximum inhibition compared with the control at 96 h being 5.3% for the media containing nominally 50 mg/L of the test chemical.
CONCLUSION	The results of this test indicate that the notified chemical is not toxic to this species of green algae up to the limit of its water solubility.
TEST FACILITY	Springborn Laboratories (2000)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE	TKA 45024
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Remarks – Method	The test was conducted (Springborn, 2000e) according to the protocols of the test by aerating sewage bacteria containing nominally 0 (control), 0.1, 1.0, 10, 100 and 1000 mg/L of the test material, and then monitoring the rate of respiration by measuring the rate oxygen uptake.
RESULTS	
Remarks Results	In no case was the respiration rate of the bacteria in the test media less than 4% of that of the controls, and so the IC50 > 1000 mg/L (nominal concentration).
CONCLUSION	The notified chemical is not inhibitory to the respiration of sewage bacteria up to the limit of its water solubility. This conclusion is in accord with the results of the toxicity control test conducted as part of

the study on biodegradation (Springborn, 2000e).

TEST FACILITY	Springborn Laboratories (2000)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

A maximum of 500 kg of the notified chemical may be placed into landfill each year with waste resulting from formulation and manufacture of polymer masterbatches as well as from end use injection moulding of polymer into final products such as plastic pipe and other articles. At the end of their useful lives old pipe and other articles containing the chemical would most likely be placed into landfill although some may be recycled for recovery of the polymers.

After incorporation into polymer articles the notified chemical is bound into the polymer matrix with little potential for release during the service life of finished articles, and consequently little release of the notified chemical to the environment is expected during the service life of polyethylene pipes and other articles.

However, once placed into landfill it is expected that the polymer matrix would be slowly degraded and broken down through the agency of slow abiotic and biological processes operative in these situations, and this may lead to release of the chemical. It is probable that the liberated chemical would become associated with the soil, and here it would be slowly degraded through biological and abiotic processes. The notified chemical will be mineralised to water and oxides of carbon and nitrogen.

The chemical is assessed to have high potential for bioaccumulation, but since little is expected to enter the water compartment this is not judged to present an environmental problem.

9.1.2. Environment – effects assessment

Very little of the chemical is expected to be released to the water compartment, but the available ecotoxicity information indicates that it is not toxic to aquatic species in any trophic level up to the limit of its water solubility.

9.1.3. Environment – risk characterisation

When used as indicated as an UV/light stabiliser for polymer/plastic products the notified chemical is not expected to present a hazard to the environment.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

During masterbatch production, skin contact with the notified chemical may occur when it is weighed and charged before being added to base polymer in blending vessel for mixing there may also be occasion for low incidence dermal contact with the notified chemical at up to 20 % dry weight in the masterbatch blend. The possibility of dermal contact is lessened further during extrusion and moulding process, with the notified chemical immobilised in the finished product at a concentration less than 1 % w/w. Dermal exposure therefore, is expected to be low, as protective equipment (safety glasses and impervious gloves) will be used to prevent exposure to the notified chemical.

Additionally, respiratory exposure to the notified chemical is expected to be negligible as engineering controls (local exhaust ventilation) ensure capture of fugitive emissions during processing. Moreover, the particle size of the notified chemical is above the inspirable and respirable ranges as set out in National Occupational Health and Safety Commission Guidance Note on the Interpretation of Exposure Standards for Atmospheric Contaminants in the Occupational Environment (NOHSC: 3008, 1995), although an exposure standard of 10 mg/m^3 for dusts in general will apply.

9.2.2. Public health

Exposure of the general public as a result of transport, reformulation and disposal of products containing the notified chemical is assessed as being negligible. Public exposure to the notified chemical may occur as a result of dermal contact with plastic products containing the notified chemical. However the amounts to which people may be exposed is considered to be negligible since the notified chemical is trapped within the plastic polymer matrix. Very small amounts migrate to the surface of plastic products and it is present in end-use plastic products at low concentrations.

9.2.3. Human health - effects assessment

9.2.3.1 SUMMARY OF TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 > 2000 mg/kg bw	low toxicity*
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity*
Rat, acute inhalation LC50 … mg/L/4 hour	test not conducted *
Rabbit, skin irritation	slightly*
Rabbit, eye irritation	slightly*
Guinea pig, skin sensitisation - adjuvant test	no evidence* of sensitisation.
Rat, oral Repeat Dose Toxicity - 28 Days	NOAEL = 1000 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	Non mutagenic*
Genotoxicity – in vitro Mammalian Chromosomal Aberration Test in CHO cells	Non genotoxic*

9.2.3.2 DISCUSSION

CGL 074 is a stable high molecular weight non-polymeric compound. It possesses low solubility in water, and is moderately soluble across lipids, although its high molecular weight characteristics lessen the degree to which absorption across biological membranes may occur. In the non-encapsulated form CGL-074 is strongly adsorbed onto solids. A preliminary estimation of the partition coefficient revealed a very high log $P_{o/w}$, however the value was outside the quantitation limit for experimental determination by HPLC. These physico-chemical properties support the potential for bioaccumulation of the non-encapsulated but not the encapsulated form compound.

The notified chemical indicated a low acute toxicity profile by both oral and dermal routes, substantiated by an LD50 greater than 2000 mg/kg in rats. CGL 074 is also slightly irritating to the skin of the rabbit for erythema and oedema and slightly irritating to the eye in rabbits. CGL 074 was negative for skin sensitisation in guinea pigs by the Magnussen and Kligman Test (Magnussen and Kligman, 1970) and therefore is not considered to be a contact sensitiser.

In a 28-day repeated dose oral toxicity study, CGL-074 did not produce any statistically or biologically relevant treatment-related effects in relation to unscheduled mortalities, clinical abnormalities, body/organ weight, food consumption, ophthalmological, neurotoxicological, clinical pathological or histopathological criteria during the main or recovery phase of the study. Functional Observation Battery examinations prior to dosing were consistent between control and treated animals and no notable abnormalities were observed in any animal during the recovery phase. Whilst the Mean body weight gain in males of Group II (100 mg/kg bw/d) were statistically lower (-30 %) for the period Day 8-15 ($p<0.05$) compared to controls, the conspicuous absence of statistically significant dose-dependent change at later time periods preclude the effect from being toxicologically meaningful.

No treatment-related differences in clinical chemistry parameters were observed in any treatment group compared to controls. Day 42 Group IV_{ref} high-dosed males (1000 mg/kg/bw/d) showed a slight, but statistically significant increase ($p<0.05$) in chloride (+ 3.8 %), by contrast, females in this group revealed a statistically significant decrease ($p<0.01$) in triglycerides (-41.7 %) compared to untreated controls. These findings were not considered biologically relevant, as they were present at the end of the recovery period and not during the

treatment phase and were generally within historical control data.

No statistically or biologically meaningful differences were noted in the urinalysis parameters in any of the treatment or recovery phase animals. Similarly, no test article associated lesions were observed in any of the Day 29 or Day 42 study animals. All lesions in the study were interpreted as spontaneous or background lesions commensurate with historical data.

No statistically or toxicologically relevant differences in organ weight data as determined by pathological or histopathological criteria were noted in any treatment or recovery group animal. Whilst a statistically significant increase in relative testes/epididymides weight and a statistically significant decrease in absolute ovarian weight were noted in the low dosed (100 mg/kg/d) males and high dosed (1000 mg/kg/d) females respectively on treatment Day 29, these differences were not considered toxicologically meaningful in the absence of a dose-dependent response and related histopathological change within limits of variation.

Notwithstanding the unscheduled pyelonephritis-induced death of one control male rat on Day 23 of the study, extensive macroscopic and microscopic analysis revealed no statistically relevant or biologically meaningful effects of CGL 074-induced toxicity were observed in the remaining test or recovery animals.

The data suggest a NOAEL at a dose higher then the highest dose tested (> 1000 mg/kg bw/d).

In vitro genotoxicity studies (comprising bacterial reverse mutation assays and mammalian chromosomal aberration tests) examining the mutagenic potential of CGL 074 no indication of genotoxic effects by the notified chemical.

The notifier provided no animal data in relation to the acute inhalation toxicity, developmental and reproductive toxicity, or carcinogenicity potential of the notified chemical. Accordingly, pharmacokinetic (and toxicokinetic) data were not available for assessment. Although the long term effects of repeated exposure in humans to high levels of the notified chemical have yet to be identified; extrapolation of relevant interspecies pharmacokinetic data using physiologically based pharmacokinetic (PBPK) modelling may provide significant insight into predicting the toxic effects of long-term exposure to the notified chemical in humans.

The notified chemical does not meet the criteria for classification as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

9.2.4. Human health – risk characterisation

9.2.4.1 OCCUPATIONAL HEALTH AND SAFETY

The notified chemical will be imported as a commercial free-flowing powder. It will be mixed and extruded with other ingredients to give a masterbatch suitable for use in plastic manufacture. During further processing into finished articles and films, the notified chemical is bound within a polymer matrix.

There is some potential for dermal and eye exposure when handling the notified chemical. The risk of exposure by these routes is greater during masterbatch production. Accordingly, operators opening the bags, weighing and adding the notified chemical to containers in preparation for mixing and extrusion may experience dermal exposure. Therefore, there is a risk of skin and eye irritation during handling. Workers involved in the processes such as extrusion and bagging of plastic pellets would have low exposure since following compounding in the extruder, the notified chemical is encapsulated within the masterbatch pellets. More specifically, the masterbatch formulation, which contains up to 20 % notified chemical, is formulated in pellet form, wherein the concentration of the notified chemical is reduced by more than 10-fold thereby minimising worker exposure to chemical dust and therefore the risk of eye irritation.
Workers involved in the production of the masterbatch pellets should wear gloves, safety glasses and overalls to further minimise the risk of irritant effects.
Local exhaust ventilation is fitted at the weighing, dispensing, blending and packing areas.

The potential for inhalation exposure is low due to limited amounts of the powder being in the inspirable range. Respiratory protection is available when the local exhaust ventilation is inadequate. Considering the low toxicity of the notified chemical, low concentrations in the final finished polymer products, together with engineering controls and personal protective equipment, the occupational health risk to workers considered to be low.

At the customer sites, the masterbatch pellets will be mixed with other ingredients and processed to form plastic articles and films. Since the notified chemical is encapsulated within the polymer matrix in masterbatch, occupational exposure to the notified chemical cannot occur before or after the articles are made. Thus, the health risk to operators of injection moulding or filmmaking machines arising from exposure to the notified chemical is very low.

Under normal working conditions, storage and transport workers will be handling sealed packages of products containing the notified chemical. There are negligible occupational health risks for these workers.

In a 28-day repeated dose oral toxicity study, the notified chemical did not produce any statistically or biologically relevant treatment-related effects. A NOAEL > 1000 mg/kg bw/d suggests a low risk from repeated exposure to the notified chemical.

Notwithstanding, the notified chemical is only slightly irritating to skin and eyes (in animals), it is not a skin sensitiser; and is not considered a hazardous substance.

9.2.4.2 PUBLIC HEALTH

Exposure of the general public as a result of transport and disposal of products containing the notified chemical is assessed as being negligible. Although members of the public may make dermal contact with plastic products containing the notified chemical, the risk to public health is considered to be minimal since the notified chemical is expected to be of low toxicological hazard, it is present at low concentrations and is expected to be largely trapped with the polymeric matrix of the plastic products.

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

10.1. Environment

On the basis of low toxicity to aquatic organisms and the anticipated low environmental exposure due to its intended use as a UV stabiliser in plastics, use of the notified chemical as indicated is not expected to constitute a hazard to the environment.

10.2. Health hazard

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

10.3. Human health

10.3.1. Human health – Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Human health – public

There are No Significant Concerns to public health when the notified chemical is used as prescribed.

11. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical.
  - overalls, safety glasses and PVC or rubber gloves.

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

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

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

Environment
Disposal

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

Emergency procedures

- Spills/release of the notified chemical should be contained as described in the MSDS (ie. Contain with absorbent material and transfer to a sealable waste container) and the resulting waste disposed of in landfill.

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:

Under Section 64(1) of the Act; if
- The use pattern of the compound changes in such a way as to substantially increase its exposure to the environment.

- If the conditions of use are varied from use in plastic products that are not in direct contact with food, greater exposure of the public may occur. In such circumstances, further information may be required to assess the hazards to public health.

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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