File No: NA/991

January 2002

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

4-(2-hydroxyethoxy)phenyl-(2-hydroxy-2-propyl)ketone (Irgacure 2959)

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act* 1989 (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 & safety assessment. The assessment of environmental hazard is conducted by the Department of the Environment and the assessment of public health is conducted by the Department of Health and Aged Care.

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Director
Chemicals Notification and Assessment

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4-(2-hydroxyethoxy)phenyl-(2-hydroxy-2-propyl)ketone (Irgacure 2959)

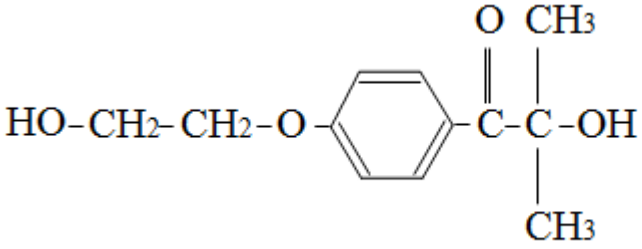
1. APPLICANT

Ciba Specialty Chemicals Pty Ltd of 235 Settlement Rd Thomastown Victoria 3074 has submitted a standard notification statement in support of their application for an assessment certificate for 4-(2-hydroxyethoxy)phenyl-(2-hydroxy-2-propyl)ketone (Irgacure 2959).

Ciba Specialty Chemicals Pty Ltd has not applied for any information relating to '4-(2-hydroxyethoxy)phenyl-(2-hydroxy-2-propyl)ketone (Irgacure 2959)' to be exempt from publication in the Full Public Report and Summary Report.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-methyl-1-propanone.
Chemical Abstracts Service (CAS) Registry No.:	106797-53-9
Other Names:	4-(2-hydroxyethoxy)phenyl-(2-hydroxy-2-propyl)ketone Darocur 2925. ZLI 2959. TKA 40053.
Marketing Name:	Irgacure 2959
Molecular Formula:	$C_{12}H_{16}O_4$
Structural Formula:	



Molecular Weight:	224
Method of Detection and Determination:	UV/Visual (UV/Vis) and Infrared (IR) spectroscopy.
Spectral Data:	3330, 3270, 3000-2850, 1660, 1595, 1560, 1500, 1452, 1370, 1310, 1255, 1160, 1085, 1050, 985, 955, 920, 890, 850, 775, 660 and 635 cm^{-1}.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Colourless solid
Boiling Point:	331°C
Melting Point:	89-90ºC
Density:	1284 kg/m^3
Vapour Pressure:	7.0×10^{-5} Pa at 25°C
Water Solubility:	7.6 g/L at 25°C
Partition Co-efficient (n-octanol/water):	log P_{ow} = 0.84
Hydrolysis as a Function of pH:	$T_{1/2}$ at pH 4.0 > 1 year $T_{1/2}$ at pH 7.0 > 1 year $T_{1/2}$ at pH 9.0 > 1 year
Adsorption/Desorption:	Log K_{oc} = 1.05
Dissociation Constant:	Not determined
Flash Point:	Not applicable (solid at room temperature)
Particle size:	84 % of particles are below 10 μm (Respirable)
Flammability:	Combustible. Not highly flammable (EC method A.10)
Autoignition Temperature:	No autoignition occurs up to the melting point (EC method A.16)
Explosive Properties:	Not explosive (EC method A.14)
Reactivity/Stability:	Not oxidising (EC method A.17)

3.1 Comments on Physico-Chemical Properties

The water solubility was determined using a modified flask method described in OECD TG 105 (Ciba 1988a). To each of three glass ampoules was added the notified chemical (0.4 g) and water (10 mL) and the resulting suspensions were vibrated at 30°C for 24 h. After a further 24, 48 and 72 h at 25°C, the suspensions were centrifuged, filtered and the extinction coefficient determined at 275 nm. This method indicated that the solubility of the notified chemical is 7.6 g/L.

The abiotic degradation of the notified chemical was investigated over five days at 50°C at pH 4, 7 and 9 using OECD TG 111 (Ciba 1988b). A quantity of the notified chemical (100 mg) was added to the each of the buffered solutions (50 mL). The resulting solutions were incubated at 50°C and sampled at 2, 4 h and 5 d. At these times an aliquot was removed for analysis by HPLC. The report indicates that there was no evidence of hydrolytic loss of the notified chemical. Therefore, in the environmental pH range of 4 to 9, significant hydrolysis is unlikely to occur.

The partition coefficient was determined according to OECD TG 107 (Ciba 1988c). The notified chemical (~2 g) was dissolved in n-octanol (200 mL). To each of four ampoules was added 36, 24, 18 and 12 mL of the chemical solution. An appropriate volume of water saturated with n-octanol was then added to each ampoule such that the final volume was 36 mL. Each ampoule was then inverted around its lateral axis for 1 h. The concentration of the notified chemical in the organic and aqueous phases was then determined using the extinction coefficient. This method indicated that the partition coefficient of the notified chemical is 6.93, which is indicative of partitioning into the aqueous phase.

The adsorption coefficient, K_{OC} was obtained by a HPLC screening method using a set of reference compounds with adsorption coefficients determined using OECD TG 106 (Fraunhofer 1996). The capacity factor of the notified chemical was determined based on comparison of its HPLC retention time with those of known substances. Using the relationship $\log K_{OC} = 2.239 \times \log k' + 2.874$, the log adsorption coefficient for the notified chemical is 1.05, classifying it as highly mobile in soil.

Although no dissociation tests were conducted, the notified chemical contains alcohol functional groups that are expected to have pK_as of approximately 16.

4. PURITY OF THE CHEMICAL

Degree of Purity: 97.0 – 99.5 %

Hazardous Impurities: None

Non-hazardous Impurities (> 1% by weight): None

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical is a photoinitiator used for UV-hardening. It is mixed into UV-curable systems, such as lacquers, printing inks and varnishes, which will be applied onto various objects, particularly paper, used in the packaging of beverages, pharmaceuticals and cosmetics and prefabricated medium density woods used for housing construction.

1 500 kg of the notified chemical, in the powder form, will be imported for each of the first five years.

The notified chemical will be imported in 20 kg fibre drums as Irgacure 2959 and transported by road to Thomastown Victoria for storage. The notified chemical is then transported to customer sites for ink manufacture.

The notified chemical is added into a 200 L stainless steel mixing vessel by scooping into a small receptacle used for weighing and then mixed with a resin system consisting of monomers and oligomers. The overprint lacquer, which has the appearance of a metallic liquid, is then piped from the blending vessel into 20 L metal pails. The overprint lacquer is then transported by road to printers. The final concentration of the notified chemical in the overprint lacquer is 2-5 %.

The notifier has indicated that in the future they intend to produce an ink in the form of a powder coating. The notified chemical is added into the mixing vessel manually and dry blended with other powdered ingredients and then put through an extruder, which mixes the powders and melts into a homogeneous solid resin granule. The granule is then ground into a powder, by cryogenic grinding. The powder coating will be pumped into polyethylene sacks using a gravity fed system. The polyethylene sacks are sealed and stored in boxes before shipping to the end user. The final concentration of the notified chemical in the powder coating is 2 %. The notifier estimates that only 10 % of imported Irgacure 2959 will be used in the formulation of the dry powder coat.

At the printer the 20 L overprint lacquer is manually poured into the ink duct. The ink is then transferred by an alinox roll to the printing plate cylinder, which in turn transfers the ink image onto the substrate being printed. The printing substrate then travels 600 mm before being exposed to protected UV light, which solidifies and cures the ink. Alternatively, if the ink is in the form of a powder coating, it will be sprayed via a gun onto an electrically charged substrate. Spraying takes place in specially designed spray booths with powerful backward vacuums that suck the powder away from the applicator and back into the gun reserve. The substrate is then cured under exposure to UV light.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
Transport and storage workers (6-8 workers, 2-3 hours per day, 10-15 days per year).
Waterside, warehouse and transport workers are unlikely to be exposed to the notified chemical unless the packaging is breached.

Formulation of overprint lacquer

Blending process workers- overprint lacquer (4 workers, 8 hours per day, 50 days per year).
Blending process workers may experience dermal and inhalation exposure to dusts containing up to 99.5 % notified chemical when it is weighed out and added to the mixing vessel. Dermal exposure to drips and spills of lacquer containing the notified chemical at up to 5 % may occur when connecting pumping equipment prior to the filling of the 20 L metal pails.

The area immediately above the mixing vessels will be ventilated through an extractor. The entire blending process in undertaken within closed loop systems with local and general ventilation. Workers will wear overalls, PVC coated cotton gloves, protective goggles and respirators. In the event of high vapour concentrations or inadequate ventilation, self-contained breathing apparatus (half face mask with cartridge) will be worn. Given the presence of engineering controls and the use of personal protective equipment, the exposure of blending process workers to the notified chemical is likely to be low.

Blending process workers-ink powder coating (2 workers, 8 hours per shift, 1 batch per week, 48 weeks per year).
Blending process workers may experience inhalation exposure to dusts containing up to 99.5 % notified chemical when manually adding the notified chemical to the mixing vessel. The ink powder coating is produced in a closed system in an area where local and general ventilation is in operation. The mixing area will be in a positive pressure room to limit exposure to dust particles. Workers will wear overalls, gloves, safety glasses and respirators. Given the presence of engineering controls and the use of personal protective equipment, the exposure of blending process workers to the notified chemical is likely to be low.

Laboratory QC and R & D workers (2 workers, 12 hours per day, 50 days per year).
Laboratory workers may receive dermal and inhalation exposure to dusts and vapours containing up to 99.5 % notified chemical and dermal exposure to drips and spills of lacquer containing the notified chemical at up to 5 % when conducting scale ups of mixtures using 1 kg of notified chemical.

As laboratory workers will wear overalls, PVC coated cotton gloves, protective goggles and respirators and conduct all laboratory work within fume cupboards, exposure to the notified chemical is expected to be low.

Printing
Printer workers- overprint lacquer (6-8 workers, 4 hours per day, 200 days per year).
Printer workers may receive dermal exposure to drips and spills when manually pouring the overprint lacquer containing the notified chemical at 2-5 % into the ink duct of the printing machine.

The notifier has indicated that the printing and curing process using the liquid ink occurs within a closed system. Furthermore, workers will wear overalls, PVC coated cotton gloves, protective goggles and respirators. In the event of high vapour concentrations or inadequate ventilation, a self-contained breathing apparatus (half face mask with cartridge) will be worn.

Given the low concentration of notified chemical in the lacquer and the engineering controls and personal protective equipment indicated by the notifier, exposure of printer workers to the notified chemical is expected to be low.

Printer workers-ink powder coating (1-2 workers, 8 hour shift per day, 5 days per year, 48

weeks per year).
Spraying takes place in specially designed spray booths with powerful backward vacuums that suck the powder away from the applicator and back into the gun reserve. The spray gun is fed through a pipe that is connected to the holding tank of the powder coating. The holding tank is sealed to prevent contamination. Spray gun operators may receive dermal and respiratory exposure to powder particles containing the notified chemical at up to 2 % during application of the powder coatings. Applicators will wear full face masks and have a separate air supply during application.

Given the low concentration of notified chemical in the powder coating and the high level of control, exposure to the notified chemical is expected to be low.

Washing operations (0.5 hours per day, 50 days per year).
Washing operations workers may receive dermal exposure to drips and spills containing the notified chemical at less than 5 % when scraping out the remaining ink from the 20 L metal pails into the printing equipment and loading used containers and the anilox rollers and ink ducts into a water based washing machine. The wearing of overalls, PVC coated cotton gloves, and protective goggles are expected to limit the exposure of washing operations workers to the notified chemical.

7. PUBLIC EXPOSURE

The public may be exposed to the notified chemical either as a pure powder or as a component of an ink lacquer following transport accidents involving the breakage of the containers in which they are carried. Such accidents are unlikely. Members of the public may also be exposed to the notified chemical as an environmental contaminant. This is also unlikely. The notified chemical will be used for industrial applications and will not be sold to the public. Public contact with the notified chemical is expected to be by means of contact with it as a component of cured varnish on packaging. However it will be present in the varnish at a low concentration and in a state inaccessible to human contact. The potential for human exposure to the notified chemical is therefore minimal.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

The notifier estimates that up to 0.5% of the notifier chemical's yearly import volume will be lost during reformulation and the cleaning of equipment. The residues remaining in the empty import containers will be disposed of in landfill by licensed waste disposal contractors while liquid wastes from the cleaning of equipment will be incinerated. It is estimated that up to 15 kg of the notified chemical will be lost in this manner. There will be no release to the sewer.

Waste ink from the printing process will be passed on to a licensed waste disposal contractors for disposal in landfill while liquid wastes from the cleaning of printing machines will be incinerated. The empty plastic ink containers and any residual ink they contain will also be disposed of in landfill. The notifier estimates that up to 11 kg per annum of the notified chemical will be disposed of from the printing process in each of the first five years.

The ultimate fate of the printed material will be disposal in landfill. However, after the ink has been exposed to UV light, the notified chemical is consumed in the polymerisation process.

8.2 Fate

The majority of the notified chemical will be incorporated in printed packaging material. However, prior to leaving the printers, the printed material is irradiated with UV light which promotes homolysis of the ether bond linkage in the notifier chemical which then initiates a free radical polymerisation process to form a high molecular weight, crosslinked compound. Therefore, once incorporated into the printed material, the notified chemical is consumed and poses little risk to the environment.

The notifier provided the results of a ready biodegradation test in an aerobic aqueous media following OECD TG 301D Closed Bottle Test (Ciba 1988d). The biodegradation was determined by the measurement of chemical oxygen demand (COD) after the medium was inoculated with a mixed population of aquatic microorganisms and stored in the dark at 22ºC for 28 days. Sodium-*n*-dodecylsulfate was used as the standard material. The results indicated that 24.3% of the notified chemical had degraded over this time, while approximately 62% of the standard degraded in 28 days. The results indicate that the notified chemical is not readily biodegradable as less than 70% degraded within 10 days of 10% having been reached. However, a reasonable degree of biodegradation may be expected over time.

The wastes containing the notified chemical generated during the reformulation process will be disposed of in landfill. The notified chemical has a log K_{OC} of 1.05 and a relatively high water solubility. Therefore it will be mobile in both the terrestrial and aquatic compartments. Analysis of the notified chemical's physico-chemical properties using the Mackay Level 1 Fugacity Model indicates that 99.34% of releases will remain in the aquatic compartment. However, in water the notified chemical is expected to degrade photochemically (see algal study in Section 10 of this report).

Liquid wastes containing the notified chemical will be incinerated by licensed waste disposal contractors and are expected to produce water vapour and oxides of carbon.

The notified chemical's high water solubility and log P value indicate it has a low bioaccumulation potential (Connell, 1990).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Summary of Toxicological Investigations

Endpoint & Result	*Assessment Conclusion*
Rat, acute oral LD50 = 4082-3108 mg/kg bw	low toxicity
Rat, acute dermal LD50 > 5000 mg/kg bw	low toxicity

Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	non-irritating
Guinea pig, skin sensitisation - adjuvant test 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	Non genotoxic

9.2 Acute Toxicity

9.2.1 Acute Oral Toxicity (Merck 1987)

TEST SUBSTANCE Darocur 2959

METHOD OECD 401 Acute Oral Toxicity.
Species/Strain Rat/Emd: Wi-AF/HAN
Vehicle 0.25 % aqueous Methocel K4M Premium solution
Remarks - Method 10 rats from another study were used as controls for bodyweight development.

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw*	*Mortality*	
			Males	*Females*
1	5 rats per sex	0	Not presented	
2	5 rats per sex	1500	0/5	1/5
3	5 rats per sex	2000	0/5	1/5
4	5 female rats	2500		4/5
5	5 rats per sex	3000	1/5	5/5
6	5 male rats	3500	1/5	

LD50 DAY 1 Male & female: 4082 mg/kg bw
Male: 4986 mg/kg bw
Female: 2502 mg/kg bw
LD50 DAYS 8 + 15 Male & female: 3108 mg/kg bw
Male: 4032 mg/kg bw
Female: 2098 mg/kg bw
Signs of Toxicity Intoxication symptoms started within 0-15 minutes after treatment and subsided after 5 days. Symptoms included dyspnea, locomotor disturbances, tremor, piloerection, salivation, abdominal position, increased lacrimation, tonic-clonic convulsions, retention of faeces, blood crusted snout, abnormal tail posture and wet anal region. A transient reduction in body weight was observed on days 2 and 4.
Effects in Organs 6/13 rats that died had haemorrhages and/or erosions in the

	glandular stomach. In 4/13 rats that died dark red contents were seen in parts of the small intestine. In one rat the small intestine was completely empty, while in the colon and rectum smaller amounts of grossly inspissated and moulded faeces were observed. The liver of three female rats treated with 3000 mg/kg bw showed yellow-brownish colour. Peripheral fatty degeneration of liver cells (fine droplets) was observed histologically in these rats. Two rats had yellow-tinged, partly reddish mucuous contents in parts of the small intestine.
Remarks - Results	All deaths occurred on days 1 and 2 of the study.
CONCLUSION	The notified chemical is of very low toxicity via the oral route.
TEST FACILITY	E. Merck, Darmstadt.

9.2.2 Acute Dermal Toxicity (Merck 1987a)

TEST SUBSTANCE	Darocur 2959
METHOD	OECD 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/ Emd: Wi-AF/HAN
Vehicle	Aqua pro injectione
Type of dressing	Occlusive
Remarks - Method	24 hour exposure time.

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	0	0/10
2	5 per sex	5000	0/10

LD50	> 5000 mg/kg bw
Signs of Toxicity	
- Local	None
- Systemic	None
Effects in Organs	None
Remarks - Results	On the day of administration the general condition and motility of the rats were obviously affected. As it was difficult to distinguish between reactions due to the fixation of the rubber sleeve and symptoms possible due to the test material, certain reactions may have been masked.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	E. Merck, Darmstadt.

9.2.3 Acute Inhalation Toxicity

The notifier did not provide an acute inhalation study.

9.2.4 Skin Irritation (Merck 1987b)

TEST SUBSTANCE	Darocur 2959
METHOD	OECD 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	Three
Observation Period	8 days
Vehicle	Aqua pro injectione
Type of Dressing	Occlusive
Remarks - Method	0.5 g of Darocur 2959 was applied for 4 hours.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.125	0.125	0	1	2 days	0
Oedema	0	0	0	0	NA	0

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

Remarks - Results	No signs of systemic toxicity were observed.
CONCLUSION	The notified chemical is slightly irritating to skin.
TEST FACILITY	E. Merck, Darmstadt.

9.2.5 Eye Irritation (Merck 1987b)

TEST SUBSTANCE	Darocur 2959
METHOD	OECD 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	Three
Observation Period	8 days
Remarks - Method	0.1 g of Darocur 2959 was applied to the conjunctival sac of the left eye. The eyes were not flushed afterwards.

RESULTS

Remarks - Results	All Draize scores were zero. No signs of systemic toxicity were observed. Individual animal data was not presented.
CONCLUSION	The notified chemical is non-irritating to the eye.
TEST FACILITY	E. Merck, Darmstadt.

9.2.6 Skin Sensitisation (Merck 1988)

TEST SUBSTANCE	Darocur 2959
METHOD	OECD 406 Skin Sensitisation – Maximisation test.
Species/Strain	Guinea pig/Iva: PDH
MAIN STUDY	
Number of Animals	Test Group: 10/sex Control Group: 10/sex
INDUCTION PHASE	Induction Concentration *intradermal:* Pairs of intradermal injections (0.1 mL) to the scapular region as follows: • 1:1 Freund's Complete Adjuvant (FCA) and Aqua pro injectione; • 5% Darocur 2959 in Aqua pro injectione; 5% Darocur 2959 in 1:1 FCA and Aqua pro injectione. *topical:* 20 % Darocur 2959 in Aqua pro injectione under occlusive dressing for 48 hours.
Signs of Irritation	During the induction phase, all injection sites were swollen and red up to day 2 of the study. Thereafter, open wounds, formation of scab and epithelization of tissue at the injection sites were observed in the guinea pigs of the test and control groups.
CHALLENGE PHASE	
1st challenge	*topical application:* 5 % Darocur 2959 in Aqua pro injectione under occlusive dressing for 24 hours.
Remarks - Method	A preliminary study was not described in this report.

RESULTS

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

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	E. Merck, Darmstadt.

9.3 Repeat Dose Toxicity (Merck 1988a)

TEST SUBSTANCE	Darocur 2959
METHOD	OECD 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week; Post-exposure observation period: Not stated.
Vehicle	Methocel K4M Premium
Remarks - Method	5 rats/sex/group

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	5 rats/sex	0	0/10
2	5 rats/sex	64	0/10
3	5 rats/sex	160	0/10
4	5 rats/sex	400	0/10
5	5 rats/sex	1000	0/10

Mortality & Time to Death

No animals died during the study.

Clinical Observations

Rats in groups 3-5 showed a dose dependent increase in the incidence of non-specific symptoms, such as pushing through the bedding or salivation, immediately after treatment. Some animals in group 5 showed a brown discoloration of the saliva. These effects may have been caused by the catheter during dosing or the bitter taste of the test material.

One animal in the control group and one from group 2 displayed limited hair loss from the third week of treatment.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No remarkable peripheral haematological changes were observed. Isolated significant differences in mean values relative to controls were within in-house laboratory biological variation limits.

A significant increase in serum alanine aminotransferase (ALAT) activity was observed in group 5. This increase was within the upper limit of the normal range.

Effects in Organs
Signs of increased liver metabolism, such as a slightly increased incidence of eosinophilic degenerated hepatocytes and single cell necrosis, were observed in 4/5 male rats in group 5. These effects are typically reversible.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was the top dose of 1000 mg/kg bw/day.

TEST FACILITY E. Merck, Darmstadt.

9.4 Genotoxicity

9.4.1.1 Genotoxicity-Bacteria (Merck 1987c)

TEST SUBSTANCE Darocur 2959

METHOD OECD 471 and 472 Bacterial Reverse Mutation Test.
and
EC Directive 2000/322/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.

Species/Strain	*S. typhimurium* strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100; *Escherichia coli* strains WP2 and WP2*uvrA*.
Metabolic Activation System	Induced rat liver microsomal fraction (S9).
Concentration Range in Main Test	a) With metabolic activation: 0 – 10000 µg/plate. b) Without metabolic activation: 0 – 10000µg/plate.
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks - Method	

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	> 10000 µg/plate	> 10000 µg/plate	Not stated	Negative
Absent				
Test 1	> 10000 µg/plate	> 10000 µg/plate	Not stated	Negative

Remarks - Results The negative controls were within normal limits and the positive controls (1-ethyl-2-nitro-3-nitrosoguanidine, methyl methanesulfonate, 2-nitrofluorene, 4-nitro-1,2-phenylene diamine, sodium azide and 9-aminoacridine (-S9); 2-aminoanthracene (+S9) demonstrated the sensitivity of the test.

CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	E. Merck, Darmstadt.

9.4.1.2 Genotoxicity-Bacteria (Merck 1991)

TEST SUBSTANCE	Darocur 2959
METHOD	OECD 472 Bacterial Reverse Mutation Test. *and* EC Directive 2000/322/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Species/Strain	*Escherichia coli* strains WP2 and WP2*uvrA*.
Metabolic Activation System	Induced rat liver microsomal fraction (S9).
Concentration Range in Main Test	a) With metabolic activation: 0 – 10000 µg/plate. b) Without metabolic activation: 0 – 10000µg/plate.
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks - Method	

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	> 10000 µg/plate	> 10000 µg/plate	Not stated	Negative
Absent				
Test 1	> 10000 µg/plate	> 10000 µg/plate	Not stated	Negative

Remarks - Results	The negative controls were within normal limits and the positive controls (1-ethyl-2-nitro-3-nitrosoguanidine (-S9); 2-aminoanthracene (+S9) demonstrated the sensitivity of the test.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	E. Merck, Darmstadt.

9.4.2 Genotoxicity-In Vitro (Merck 1988b)

TEST SUBSTANCE	Darocur 2959

METHOD	OECD 473 In vitro Mammalian Chromosomal Aberration Test.
Cell Type/Cell Line	V79 Chinese hamster cells
Metabolic Activation System	Induced rat liver microsomal fraction.
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks - Method	

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Present			
Test 1	150, 300, 600, 1200 and 2400	5 hours	18 hours
Test 2	1200 and 2400	5 hours	7 hours
Test 3	1200 and 2400	5 hours	28 hours
Absent			
Test 1	150, 300, 600, and 1200	5 hours	18 hours
Test 2	1200	5 hours	7 hours
Test 3	1200	5 hours	28 hours

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*		
	Cytotoxicity in Main test	*Precipitation*	*Genotoxic Effect*
Present			
Test 1	2400	> 2400	Negative
Test 2	2400	> 2400	Negative
Test 3	> 2400	> 2400	Negative
Absent			
Test 1	> 1200	> 1200	Negative
Test 2	1200	> 1200	Negative
Test 3	> 1200	> 1200	Negative

Remarks - Results	In a preliminary range finding study it was determined that concentrations of Darocur 2959 at 2400 mg/mL without metabolic activator and 4800 mg/ml with metabolic activator resulted in a significant inhibition of cell growth. Positive controls demonstrated the sensitivity of the test.
CONCLUSION	The notified chemical was not clastogenic under the conditions of the test.
TEST FACILITY	E. Merck, Darmstadt.

9.4.3 Genotoxicity-In Vivo

The notifier did not submit a toxicological study for this endpoint.

9.5 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity and low acute dermal toxicity in rats (each LD50 > 3000 mg/kg). It was a slight skin irritant in rabbits, was not an eye irritant in rabbits and was not a skin sensitiser in guinea pigs.

Reversible signs of increased liver metabolism, such as a slightly increased incidence of eosinophilic degenerated hepatocytes and single cell necrosis, were observed in a 28-day oral repeated dose study in rats (NOAEL = 1000 mg/kg bw/day). The notified chemical was neither mutagenic in bacteria nor clastogenic in Chinese hamster cells in vitro.

The notified chemical is not determined to be a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Full test reports on the following ecotoxicity studies for Irgacure 2959 were provided by the notifier.

Test	***Species***	***Results***
Acute Toxicity OECD TG 203	Zebra Fish *Brachydanio rerio*	LC_{50} (96 h) = 340 mg/L
Acute Immobilisation OECD TG 202	Water Flea *Daphnia magna*	EC_{50} (48 h) = 615 mg/L
Growth Inhibition OECD 201	Algae *Scenedesmus subspicatus*	E_bC_{50} (72 h) = 9.1 mg/L E_rC_{50} (72 h) = 97.6 mg/L Pre-illumination E_bC_{50} (72 h) = 34.9 mg/L Pre-illumination E_rC_{50} (72 h) > 100 mg/L
Growth Inhibition	Algae *Scenedesmus subspicatus*	EC_{50} (72 h) = 2.6 mg/L NOEC < 1.0 mg/L

* NOEC - no observable effect concentration

The tests on fish (Ciba 1987a) were performed using a static methodology and observations were performed at 3, 6, 24, 48, 72 and 96 hours. The test was performed using ten specimen fish per loading rate at a temperature range of 21-25 ºC. The tests were conducted using the test substance at nominal concentrations of 1, 10, 100, 198, 296, 444, 667 and 1000 mg/L. The results of the definitive study showed that no mortalities were observed in the test vessels with less than 198 mg/L of the notified chemical. After 96 h, 20% mortality was observed at a test concentration of 296 mg/L while 100% was observed at test substance concentrations above 444 mg/L. The 96-hour LC_{50} for the notified chemical to *Brachydanio rerio* is 340 mg/L.

The immobilisation tests with *Daphnia* (Ciba 1987b) were also performed under static conditions with observations performed at 24 and 48 hours. The test was performed using 20 daphnids per flask at a temperature of 20 ºC. The tests were conducted using the test substance made up at nominal concentrations of 50, 100, 250, 300, 400, 500, 600, 800, 900,

1000 and 1200 mg/L. No immobilised daphnids were observed in the test vessels with less than 250 mg/L. After 48 h, 15, 25, 30, 35, 50, 70, 95 and 100 % mortality was observed after at test substance concentrations of 300, 400, 500, 600, 800, 900, 1000 and 1200 mg/L, respectively. The 48-hour EC_{50} for the notified chemical to *Daphnia magna* is 615 mg/L as determined by probit analysis. Analysis of the raw data using the Toxcal program gave an EC_{50} of 642 mg/L.

Algae were exposed to the test substance at nominal concentrations of 1, 3.2, 10, 32 and 100 mg/L for 72 h without pre-illumination and for 72 h with 24 h pre-illumination under static test conditions and constant illumination (RCC 1998). The test substance at a concentration of 10 mg/L was also tested without pre-illumination for 120 h and constant illumination (RCC 1998). Analysis of the test media indicated that approximately 80% of the test substance had degraded in the 24 h pre-illumination period and was completely degraded after 72 h of constant illumination. The results (based on nominal concentrations) indicate that both biomass and the growth rate of *Scenedesmus subspicatus* are adversely affected by the test substance and its photolysis degradation products. The notifier indicates that in the 120 h without pre-illumination test the algal cell densities reached those of the control after approximately 96 h and cell growth was inhibited by nutrient limitation in the static test.

In the second test, algae were exposed to the test substance at nominal concentrations of 1.0, 10 and 100 mg/L for 72 h at 24˚C under constant illumination and shaking (ABC 1993). Three replicate test flasks were prepared for the test substance and three controls. No abnormalities were detected in any of the replicate test samples. Both biomass and growth rate of *Scenedesmus subspicatus* was adversely affected by the test substance, giving a 72 h EC_{50} of 2.6 mg/L and NOEC of < 1.0 mg/L.

It should be noted that while there is no apparent difference between the two 72 h (without pre-illumination) algal toxicity tests conducted above, the results obtained differ considerably for unclear reasons.

The ecotoxicity data indicates the notified chemical is moderately toxic to algae, but appears to be practically non-toxic to fish and daphnia.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The majority of the notified chemical will be incorporated in printed packaging material. However, prior to leaving the printers, the printed material is irradiated with UV light which promotes homolysis of the ether bond linkage in the notifier chemical which then initiates a free radical polymerisation process to form a high molecular weight, crosslinked compound. Therefore, once incorporated into the printed material, the notified chemical is consumed and poses little risk to the environment.

The ecotoxicity data indicate the notified chemical is moderately toxic to algae, but appears to be practically non-toxic to fish and daphnia. The notified chemical is not readily biodegradable, however, in water the notified chemical is expected to degrade photochemically.

The wastes containing the notified chemical generated during the formulation process will be disposed of in landfill. The notified chemical has a log K_{OC} of 1.05 and a relatively high water solubility. Therefore it will be mobile in both the terrestrial and aquatic compartments.

Analysis of the notified chemical's physico-chemical properties using the Mackay Level 1 Fugacity Model indicates that 99.34% of releases will remain in the aquatic compartment.

Liquid wastes containing the notified chemical will be incinerated by licensed waste disposal contractors and are expected to produce water vapour and oxides of carbon.

The notified chemical's high water solubility and log P value indicate it has a low bioaccumulation potential (Connell, 1990).

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment

Based on the toxicological data provided, the notified chemical would not be acutely toxic via the oral or dermal routes. It is not likely to be a skin sensitiser, genotoxic, or clastogenic. It is not likely to be an eye irritant but could be a slight skin irritant. Based on the results of a 28-day oral study in rats (NOAEL 1000 mg/kg bw/day- the top dose), organ or systemic effects are not expected. The particle size distribution of the notified chemical indicates it contains a high respirable fraction (84 % of particles are below 10 μm). The notified chemical would not be classified as a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) in terms of the toxicological data provided.

Occupational Health and Safety

There is little potential for occupational exposure to the notified chemical during transport and storage.

The greatest exposure to the notified chemical is expected to occur during the formulation of the overprint lacquer, in particular while weighing and manually adding the 99.5 % notified chemical powder to the mixing vessel. Due to the high percentage of particles in the respirable range and the possibility of skin irritation, weighing and manually adding the 99.5 % notified chemical powder to the mixing vessel must take place in a well ventilated area. Blending process workers should wear overalls, PVC coated cotton gloves, protective goggles and respirators. In the event of inadequate ventilation, self-contained breathing apparatus (half face mask with cartridge) should be worn.

The engineering controls and personal protective equipment indicated by the notifier should control the exposure of washing operators, laboratory QC and R & D workers as well as printer workers using the overprint lacquer to the notified chemical.

Stringent engineering controls, such as a correctly constructed and maintained spray booth, and a high level of personal protective equipment, such as impermeable overalls and gloves and a full face mask with a separate air supply should provide adequate protection from the notified chemical during spray gun application of the powder coating.

The notified chemical becomes biologically unavailable for absorption once it is incorporated in the surface coating during UV-curing. The health risk for workers handling products coated with paint containing the notified polymer is considered to be negligible.

Employers should ensure that NOHSC exposure standard (NOHSC 1995) for a nuisance dust (10 mg/m^3 TWA) is not exceeded in the workplace. Employers should also note that while NOHSC does not have an exposure standard for the respirable fraction of dust, the American Conference of Governmental Industrial Hygienists have developed an occupational exposure standard of 3 mg/m^3 TWA (ACGIH 1991) for the respirable dust fraction.

Given the risk reduction measures indicated and that the notified chemical is unlikely to be hazardous, Irgacure 2959 is of low concern to human health and safety in the workplace.

Public health

The public may be exposed to the notified chemical either as a pure powder or as a component of an ink lacquer following transport accidents involving the breakage of the containers in which they are carried. Such accidents are unlikely. Where they do occur, contact with the powder form is likely to be dermal and minimal and transient. Contact with spilled varnish containing the notified chemical may be hazardous because of the presence of other chemicals. Members of the public may also be exposed to the notified chemical as an environmental contaminant. This is also unlikely as any waste is chemically and physically reduced to inert material and disposed of as land-fill.

Public contact with the notified chemical is expected to be by means of contact with it as a component of cured varnish on packaging. However it will be present in the varnish at a low concentration and in a state inaccessible to human contact. The low likelihood of exposure to the notified chemical and the toxicological profile of the notified chemical suggest that the notified polymer will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

Control Measures

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  - Ensure adequate ventilation and local exhaust

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced and in the powder coating product:
  - NOHSC exposure standard for nuisance dust should not be exceeded in the workplace

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced and in the powder coating product:
  - Overalls, PVC coated cotton gloves, protective goggles and respirators should be worn; where engineering controls do not reduce particulate exposure to safe levels a self-contained breathing apparatus (half face mask with cartridge) should be worn

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.

Secondary notification

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

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

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

14. 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* (NOHSC 1994).

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.

15. REFERENCES

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Merck (1987c) In vitro assessment for mutagenic potential in bacteria with and without addition of a metabolising system (Ames-Test). Report number T13015.

Merck (1988) Skin sensitisation study in guinea pigs using the maximization test according to Magnusson. Report number T13092.

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Merck (1988b) In vitro cytogenetic assay in V79 chinese hamster cells, with and without metabolic activation. Report number T13082.

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NOHSC (1999) Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(1999)]. Canberra, Australian Government Publishing Service.

RCC Ltd (1998) Study Project Number 666674: Acute Immobilisation Test in Daphnia magna, Itingen, Switzerland, (unpublished report submitted by Ciba Specialty Chemicals Inc.).

Attachment 1

The Draize Scale (Draize, 1959) for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale (Draize *et al*., 1944) for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
		Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe

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