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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Irganox 1726

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Director
Chemicals Notification and Assessment

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Ciba Specialty Chemicals (ABN 97 005 061 469)
235 Settlement Road, Thomastown, Victoria 3074

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, CAS No., molecular weight, molecular and structural formulae, spectral data, import volume and details of customers.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Data for a close chemical analogue, Irganox 1520, have been provided for the majority of toxicological and all environmental fate and ecotoxicological endpoints. No acute inhalation toxicity data was provided.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
Italy, year not stated.

2. IDENTITY OF CHEMICAL

OTHER NAME(S)
TKA 40236
CGX AO 726

MARKETING NAME(S)
Irganox 1726

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	IR, NMR, Mass Spectroscopy, Gas Chromatography, HPLC for impurities determination.
Remarks	Proposed structure was confirmed and various impurities related to the notified chemical were detected. Residual starting materials were determined by GC.

3. COMPOSITION

DEGREE OF PURITY
High

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None are present at concentrations which would result in the notified chemical being classified as a hazardous substance.

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)

Chemical Name Isomer of notified chemical
CAS No. *Weight %* 1.1

ADDITIVES/ADJUVANTS
None.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported in pure form as a raw material for local formulation into end use products.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Less than three tonnes of the notified chemical will be imported per annum for each of the first five years.

USE
Stabiliser in adhesives

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Melbourne.

IDENTITY OF MANUFACTURER/RECIPIENTS
Various formulators of adhesives may be customers for the notified chemical. Currently three likely customers in NSW and Victoria have been identified.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in 25 kg bung hole drums as a solid or liquid (depending on temperature, the notified chemical is a low melting point solid mp = 28°C).

5.2. Operation Description

The notified chemical will be imported in 25 kg bung hole drums and will be melted using drum heating equipment to 40°C prior to pumping. For hot melt glue production, the notified chemical is pumped to mixing vessel with tackifying resins, waxes, plasticisers and thermoplastic components. The mixture is liquefied by heating, extruded, granulated and packed. For water- and solvent-based adhesives the chemical is pumped to a mixing vessel together with other adhesive components such as tackifying resins, pigments and solvents as required. The adhesive is then prepared in a closed system from which it is packed for distribution.

The hot melt granules will be employed by customers is packaging applications such as lamination. The other adhesives will be mainly for consumer use.

5.3. Occupational Exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Production workers	Up to 30	Up to 8 hours/day	5 days per year
QC technician	3	Up to 8 hours/day	5 days per year
Transport and Storage worker	6	2-3 hours per day	5 days per year
Hot melt adhesive users	not stated	Up to 8 hours/day	daily

Exposure Details
Dermal exposure of production workers to drips and spills of the notified chemical may occur while

pumping the imported chemical from drums to mixing vessels. Once in the mixing vessel, the system is essentially enclosed. Local exhaust ventilation is employed at points where hot fumes or solvent vapours are emitted. Packing of the final products is automatic and local exhaust ventilation is provided. The solvent and water based adhesives will be packed in consumer sized containers and the granulated adhesive in large polyethylene sacks. Exposure of production workers to the finished adhesives is only likely in the case of malfunction of the automated equipment.

Quality control involves taking small samples of the adhesive containing up to 1 % notified chemical for small scale testing. All workers will employ protective clothing, gloves and safety goggles. Respirators will be provided where exposure to hazardous vapours or fumes may occur.

During end use of the granules containing up to 1 % notified chemical, the granules are poured into the hopper of a laminating machine which liquefies the adhesive prior to application to the layers of packaging material. Workers will not be in contact with the adhesive while the machine is in operations but may have minimal contact during cleaning operations.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Environmental release is not anticipated at the port, the notifier's storage facility or during distribution and transport to formulation sites, except in the event of an accident. In the event of an accident, the type and size (25 kg drums) of the containers would limit the release of the chemical to the environment. The MSDS provides spill clean-up procedures, which include sending solid wastes containing the notified chemical to landfill.

During formulation procedures, it is estimated that up to 1 % of the import volume of the notified chemical (10 kg per annum) may potentially be lost in spills, in solid waste products, residues in emptied imported drums and in washwaters from cleaning of blending equipment. Environmental releases are not anticipated during storage and handling of the notified chemical at formulation facilities, except potentially in the event of an unplanned spill or leak, and the type and size of the containers would limit the release of the notified chemical to the environment. The MSDS provides clean-up procedures, which include sending solid wastes containing the notified chemical to landfill. In general, blending vessels and extruders comprise closed systems, which would minimise environmental releases. The disposal route for wastewaters from formulation facilities may include discharge to on-site wastewater treatment plants (WWTPs); if available, and/or sewer. WWTP sludges and other solid wastes containing the notified chemical are expected to be sent to landfill for disposal.

RELEASE OF CHEMICAL FROM USE

The proposed commercial and household use pattern of the adhesive indicates a widespread distribution of use and disposal. End use products are unlikely to be released directly to the environment. Upon application of adhesives, the notified chemical is expected to be immobilised within a polymer matrix. Most wastes generated would be expected to eventually be sent to landfill for disposal or enter paper recycling schemes. Emptied containers and other solid wastes containing the notified chemical are also likely to be sent to landfill for disposal or enter a container recycling scheme.

5.5. Disposal

Both solid and liquid wastes will be generated throughout the lifecycle of the notified chemical. Eventually most of the notified chemical will be sent to landfills for disposal. A fraction of the notified chemical is expected to be discharged to sewage treatment systems. The disposal pattern is likely to occur over a geographically-widespread area.

Solid waste types containing the notified chemical and their sources may include residues from spilt notified chemical potentially from import, handling, storage, formulation and use. In addition, solid wastes containing residues of notified chemical may occur in emptied drums and containers derived during formulation and following use. Furthermore, the notified chemical may occur in WWTP sludges originating from formulation plants, drum recyclers, and potentially paper recycling facilities.

Liquid wastes containing the notified chemical may be generated at formulation facilities (eg. equipment washings), drum recycling facilities (eg. drum washings), and at paper recycling facilities (eg. pulp effluent). In general, these wastes may be discharged to on-site WWTPs, recycled in water re-use schemes and/or discharged to sewer, where they will be treated and degraded. Residues from

sewage treatment systems may potentially arise in effluents discharged to waters (wetlands, containment ponds, rivers, ocean), in effluents used as irrigation water, or in biosolids, which have the potential to be used as a soil conditioner.

5.6. Public exposure

The public may come in contact with the notified chemical when using water or solvent based adhesives. Contact can be extensive and prolonged if the adhesive sticks to the skin. However, the concentration of the notified chemical in the final adhesives is a maximum of 1 % and is likely to be quickly immobilised in the adhesive matrix after release from its container.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Wax-like colourless to yellowish solid.

Melting Point/Freezing Point 28ºC

METHOD	OECD TG 102 Melting Point/Melting Range. EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	Thermal analysis with calorimeter.
TEST FACILITY	RCC, Switzerland (2001a).

Boiling Point > 400ºC at 101.3 kPa

METHOD	OECD TG 103 Boiling Point. EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	Thermal analysis with calorimeter. No boiling was detected up to 400ºC.
TEST FACILITY	RCC, Switzerland (2001b).

Density 934 kg/m^3 at 40ºC

METHOD	OECD TG 109 Density of Liquids and Solids. EC Directive 92/69/EEC A.3 Relative Density.
Remarks	Density was measured at 40ºC where the chemical was in liquid form.
TEST FACILITY	RCC, Switzerland (2001c).

Vapour Pressure 1.8×10^{-22} kPa at 25ºC (estimated).

METHOD	
Remarks	EC Directive 92/69 A4 and OECD TG 104. Due to the estimated low vapour pressure, the vapour pressure was estimated from the boiling point of 654ºC using the Modified Watson Correlation (Lyman et al., 1990).
TEST FACILITY	RCC, Switzerland (2001d).

Water Solubility < 0.1 mg/L at 20ºC

METHOD	OECD TG 105 Water Solubility. EC Directive 92/69/EEC A.6 Water Solubility.
Remarks	Water solubility for the analogue (Irganox 1520) was determined by RCC (2000) using OECD TG 105. The water solubility was determined to be 0.0074 mg/L.
TEST FACILITY	RCC, Switzerland (2001e).

Hydrolysis as a Function of pH Not determined

Remarks	The notified polymer does not contain any groups capable of undergoing hydrolysis in the pH range of 4-9.

Partition Coefficient (n-octanol/water) log Pow at 20ºC = 14.1 (estimated)

METHOD EEC Directive 92/69/EEC. Guideline A.8. Partition Co-efficient Shake Flask Method and OECD TG 107 & 117.

Remarks Due to high solubility in octanol, the partition coefficient was estimated using a calculation method. The Log Kow of the notified chemical was estimated by the calculation method based on the theoretical fragmentation of the molecule into substructures for which reliable log Kow increments were known using PC program KOWWIN version 1.6 (Syracuse, 1998). The Log Kow was obtained by summing the fragment values and the correction terms for intramolecular interactions.

TEST FACILITY RCC Ltd (2001f).

Adsorption/Desorption log K_{oc} = 1.99 at 20°C.

METHOD OECD TG 106 Adsorption - Desorption Using a Batch Equilibrium Method.

Remarks OECD TG 106 – Preliminary and screening tests were performed with 5 soils to determine the adsorption behaviour of the test chemical. The test chemical was dissolved in 0.01 M $CaCl_2$-solution and shaken together with the soil to be tested. (ratio soil/solution = 1/5 w/w). After 16 h (equilibrium state), the concentrations of the test chemical in the aqueous phase was determined using HPLC after enrichment by solid phase extraction. The adsorption of the test chemical could only be determined for one of the soils (Koc = 99; Sand 3.3 %, Silt 21.9 %, clay 75 %, C organic 1.3 %, pH 5.9, CEC 29.9 meq/100 g) as others were below the detection limit. The concentration of the test solution was 0.00043 mg/L. The test was performed on a structurally similar chemical.

TEST FACILITY Fraunhofer-Institut Fur Umweltchemie und Okotoxikologie (1995).

Dissociation Constant Not determined

Remarks The test could not be conducted due to low water solubility; a pK_a of the order of 10 may be expected based on the functional groups present in the notified chemical.

Surface Tension 67.9 mN/m at 20ºC

METHOD EEC Directive 92/69 A.5 Surface Tension and OECD TG 115. The determination was carried out using a tensiometer using the Ring Method.

Remarks The test solution was prepared by adding 204.1 mg of notified chemical to double distilled water. The mixture was ultrasonicated and stirred for 24 hours, centrifuged (10 mins at 1630 g), filtered (0.45 μm) and diluted to the required concentration. A platinum-iridium ring was lowered into the test solution and then raised until the ring was attached to the liquid surface. The tensiometer measured the torque exerted by the ring as the ring was extracted from the solution surface (ie. as the lamina was broken). As the surface tension of a solution varies over time, the surface tension of the test solution was measured at intervals until a constant reading was recorded.

TEST FACILITY RCC, Switzerland (2001g).

Particle Size not determined

Remarks Not measurable due to the waxy low melting nature of the notified chemical.

Flash Point 232ºC at 101.3kPa

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

Remarks Closed cup.

TEST FACILITY RCC, Switzerland (2001h).

Flammability Limits Not highly flammable.

Remarks It is known through use and the chemical structure that the chemical is not pyrophoric and does not evolve flammable gases when in contact with an aqueous environment.

Autoignition Temperature > 28ºC

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks No autoignition was observed below the melting point of the notified chemical.
TEST FACILITY RCC, Switzerland (2001i).

Explosive Properties Not explosive.

METHOD Expert statement.
Remarks No groups suggesting explosiveness and no exothermic peak detected in differential scanning calorimetry.
TEST FACILITY RCC, Switzerland (2001j).

Oxidizing Properties Not oxidising.

METHOD Expert statement.
Remarks Chemical fulfils the second criterion in the UN Recommendations on the Transport of Dangerous Goods (Orange Book, 3rd edition, 1999) in that the chemical contains oxygen but it is chemically bonded only to carbon.
TEST FACILITY RCC, Switzerland (2001j).

Thermal Stability in Air Thermally stable in air up to 150ºC.

METHOD OECD Guideline for Testing of Chemicals No. 113, "Screening test for thermal stability and stability in air".
Remarks No decomposition or chemical transformation occurred in the temperature range 25ºC - 150ºC.
TEST FACILITY RCC, Switzerland (2001k).

Reactivity Stable under normal conditions of use.

Remarks Not oxidising, flammable or explosive.

7. TOXICOLOGICAL INVESTIGATIONS

The bacterial reverse mutation test was conducted with the notified chemical. The other toxicological data were obtained using the close analogue, Irganox 1520.

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 > 5000 mg/kg bw	low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rat, acute inhalation LC50	test not conducted
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation - adjuvant test.	limited evidence of sensitisation.
Rat, oral repeat dose toxicity - 28 days.	NOEL = 50 mg/kg/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberrations in CHO cells	non genotoxic
Developmental and reproductive effects	non teratogenic, not reprotoxic; maternal NOAEL 200 mg/kg bw/day

7.1. Acute toxicity – oral

TEST SUBSTANCE	Irganox 1520
METHOD	OECD TG 401 Acute Oral Toxicity – Limit Test.
Species/Strain	Rat/Tif: RAIf(SPF).
Vehicle	Distilled water containing 0.5% carboxymethylcellulose and 0.1% polysorbate 80.
Remarks – Method	Dose volume 10 mL/kg bw

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	5000	None.

LD50	> 5000 mg/kg bw
Signs of Toxicity	Dyspnea, exophthalmos, ruffled fur and curved body position which resolved by day 11.
Effects in Organs	None.
Remarks – Results	

CONCLUSION Irganox 1520 is of low toxicity via the oral route.

TEST FACILITY Ciba-Geigy Limited, Switzerland (1986a).

7.2. Acute toxicity – dermal

TEST SUBSTANCE	Irganox 1520
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/Tif: RAIf(SPF).
Vehicle	None.
Type of dressing	Semi-occlusive.
Remarks – Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	None.

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	None.
Signs of Toxicity - Systemic	Dyspnea, exophthalmos, ruffled fur and abnormal body positions which resolved by day 10. Also sedation was seen from 3 hours after application up to day 1.
Effects in Organs	None.
Remarks – Results	

CONCLUSION Irganox 1520 is of low toxicity via the dermal route.

TEST FACILITY Ciba-Geigy Limited, Switzerland (1987a).

7.3. Acute toxicity – inhalation

Test not conducted.

7.4. Irritation – skin

TEST SUBSTANCE Irganox 1520.

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Vehicle None
Observation Period 7 days.
Type of Dressing Semi-occlusive.
Remarks – Method The observation period was extended to 7 days as effects were still present at 72 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	1	0	1	1	72 hours	0
Oedema	0	0	0	0		0

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

Remarks – Results Scaling at the application area was seen in all animals at the 7 day observation. No erythema or oedema was observed at this time.

CONCLUSION Irganox 1520 is slightly irritating to skin.

TEST FACILITY Ciba-Geigy Limited, Switzerland (1986b).

7.5. Irritation – eye

TEST SUBSTANCE Irganox 1520

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Observation Period 7 days.
Remarks – Method The observation period was extended to 7 days although effects were not present at 72 hours.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.66	0.66	0.66	1	48 hours	0
Conjunctiva: chemosis	0	0	0	1	1 hour	0
Corneal opacity	0	0	0	0		0
Iridial inflammation	0	0	0	0		0

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

Remarks – Results Chemosis was seen in two animals at the 1 hour observation.

CONCLUSION Irganox 1520 is slightly irritating to the eye.

TEST FACILITY Ciba-Geigy Limited, Switzerland (1986c).

7.6. Skin sensitisation

TEST SUBSTANCE	Irganox 1520.
METHOD	OECD TG 406 Skin Sensitisation – maximisation test.
Species/Strain	Guinea pig/Pirbright White.
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: Not determined topical: 3 %
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 20
induction phase	Induction Concentration: intradermal injection: 1 % topical application: 30 %
Signs of Irritation	Not reported
CHALLENGE PHASE	
1st challenge	topical application: 3 %
2nd challenge	topical application: 3 %
Remarks – Method	The second challenge was performed after a 7 day rest period.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	0 %	0/20	0/20		
	3 %	7/20	6/20	1/20	1/20
Control Group	0 %	0/20	0/20		
	3 %	0/10	0/10		

Remarks – Results	The responses at the first challenge consisted of erythema and/or oedema, both of Draize score 1 in all cases. The second challenge was intended to confirm whether these were true sensitisation responses or a manifestation of adjuvant induced hypersensitivity.
CONCLUSION	There was limited evidence of reactions indicative of skin sensitisation to Irganox 1520 under the conditions of the test.
TEST FACILITY	Ciba-Geigy Limited, Switzerland (1987b).

7.7. Repeat dose toxicity

TEST SUBSTANCE	Irganox 1520
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Tif: RAIf(SPF).
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week;
Vehicle	Distilled water containing 0.5% carboxymethylcellulose and 0.1% polysorbate 80.
Remarks – Method	Four dose levels (10, 50, 250, 1000 mg/kg bw/day) were used in this study.

RESULTS

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

IV	5/sex	250	0/10
V	5/sex	1000	0/10

Mortality and Time to Death

No unscheduled mortalities occurred.

Clinical Observations

No clinical signs of toxicity were observed. There was no effect on food consumption, water consumption, body weight or body weight gain throughout the study.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No treatment related effects on haematology parameters were observed in any group.

A slight elevation in alkaline phosphatase levels in Group IV males and Group V animals was observed.

Effects in Organs

Slightly increased liver/body weight ratios were observed in Group IV and Group V males and Group V females. There were no macroscopic or microscopic findings.

Remarks – Results

Slight effects on the liver were thought by the study authors to be an adaptive response and of no toxicological significance. A number of macroscopic necropsy findings were observed but the incidence did not indicate that these were treatment related.

CONCLUSION

The No Observed Effect Level (NOEL) was established as 50 mg/kg bw/day in this study, based on slightly increased alkaline phosphatase and liver weights at the higher doses.

TEST FACILITY Ciba-Geigy Limited, Switzerland (1988).

7.8. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure/Pre incubation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100. *E. coli*: WP2 uvrA.
Metabolic Activation System	S9 fraction from livers of phenobarbital/β-naphthoflavone-induced rats.
Concentration Range in Main Test	a) With metabolic activation: 33 - 5000 µg/plate. b) Without metabolic activation: 33 - 5000 µg/plate.
Vehicle	DMSO
Remarks – Method	Two independent assays were performed in triplicate, the first by the plate incorporation method and the second by the pre-incubation method.

RESULTS

Remarks – Results

No precipitation was observed at any concentration; cytotoxicity was only seen for TA 98 in the second experiment at the maximum dose used.

No significant increases in the numbers of revertants were seen for any strain either in the presence or absence of metabolic activation. Appropriate positive controls were used and indicated that the test system responded appropriately.

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

of the test.

TEST FACILITY RCC (2001l)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE Irganox 1520

METHOD OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.
EC Directive 84/449 B.10

Cell Type/Cell Line: Chinese Hamster Ovary (CHO) cells.
Metabolic Activation System: S9 fraction from livers of Aroclor 1254-induced rats.
Vehicle: DMSO
Remarks – Method: The dose range used was determined from a pre-experiment where toxicity was indicated by the plating efficiency assay.

Metabolic Activation	*Test Substance Concentration (µg/mL)**	*Exposure Period*	*Harvest Time*
Present			
Test 1	50	4 h	8 h
Test 2	5, 20, 50	4 h	24 h
Test 3	50	4 h	30 h
Absent			
Test 1	50	4 h	8 h
Test 2	5, 20, 50	4 h	24 h
Test 3	50	4 h	30 h

*All cultures selected for metaphase analysis.

RESULTS

Remarks – Results: Only slight reductions in plating efficiency and mitotic index (always greater than 70 % of controls) were observed even at the highest concentration used; higher concentrations precipitated and could not be used.

No significant increases in the numbers of cells containing structural chromosome aberrations were seen for any strain either in the presence or absence of metabolic activation. Appropriate positive controls were used and indicated that the test system responded appropriately.

CONCLUSION Irganox 1520 was not clastogenic to CHO cells treated in vitro under the conditions of the test.

TEST FACILITY CCR (1991)

7.10. Developmental toxicity

TEST SUBSTANCE Irganox 1520

METHOD Proprietary method

Species/Strain: Rat/Sprague-Dawley.
Route of Administration: Oral – gavage.
Exposure Information: Exposure period: days 6 – 15 post coitum.
Vehicle: Arachis oil.
Remarks – Method: GLP guidelines were not used for this study. The dosing and timing are as reported above and below. Sacrifice was on day 20 post coitum. Dams were examined macroscopically for abnormalities, and the uteri and

ovaries excised and examined for resorptions and dead foetuses; foetuses were examined macroscopically and half examined for skeletal abnormalities, the other half for visceral abnormalities.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	31	0	0/31
2	25	50	0/25
3	30	150	0/30
4	30	300	0/30

Mortality and Time to Death

No unscheduled mortalities occurred.

Effects on Dams

No clinical signs, effects on bodyweight gain, food consumption or pregnancy were observed. No macroscopic effects were noted.

Effects on Foetus

There was no effect on weight or sex of foetuses or pre-implantation loss. At the high dose the number of foetuses was slightly reduced and the mean number of total intra-uterine deaths calculated from animals with live foetuses in utero at necropsy was increased.

There was no effect of treatment on the incidence of foetuses showing external, visceral or skeletal effects.

Remarks – Results

A number of macroscopic necropsy findings in the parental animals and variations or defects among the foetuses were observed but the incidence did not indicate that these were treatment related.

CONCLUSION

Irganox 1520 did not induce maternal toxicity or teratogenicity in rats at doses up to 300 mg/kg/day during the period of organogenesis. A NOEL of 150 mg/kg bw/day was established, with embryotoxicity seen at 300 mg/kg bw/day

TEST FACILITY Hazleton Laboratories (1987).

7.11. Toxicity to reproduction – one to two generation study

TEST SUBSTANCE Irganox 1520

METHOD OECD TG 415 and 416

Species/Strain	Rat (strain not stated)
Route of Administration	Oral – gavage.
Exposure Information	Exposure period – F0 female: 2 weeks prior to pairing, during gestation and lactation and up to the day before sacrifice, on or shortly after day 21 post-partum. Exposure period – F0 male: 10 weeks prior to pairing until the day before sacrifice (upon the birth of the majority of litters; approximately day 113 of exposure).
Vehicle	Peanut oil.
Remarks – Method	Litters were culled to eight pups. Among the F1 generation, 24 pups per sex in each group were treated with the test substance but the further study was stopped at the sponsor's request due to the results for the first generation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	24/sex	0	2/48
2	24/sex	15	0/48
3	24/sex	50	0/48
4	24/sex	200	0/48

Mortality and Time to Death

Two control males died during the study.

Effects on Parental (P) animals:

There were no treatment-related clinical signs, effects on bodyweight, bodyweight gain or food consumption. There were no macroscopic effects in males (pancreas, liver, duodenum, jejunum, preputial gland, thoracic cavity, thymus, head, tail, whole animal, skin) or females (pituitary, uterus, head, tail, whole animal, skin). No effects were observed on sperm motility or concentration between the control and high dose groups or for the mid-dose male which failed to induce pregnancy.

There were no treatment-related effects on reproductive parameters (oestrus cycle, mating performance and pregnancy rate), implantation, pre-birth loss or gestation length.

Effects on 1st Filial Generation (F1)

There were no treatment-related effects on total and live litter size, litter and mean pup weights and pup loss. There were no clinical signs during the post-partum period related to maternal treatment, no effect on sex ratios or lactation index and no effects on pre-weaning development.

Necropsy of F1 pups did not reveal any toxicologically relevant findings.

Remarks – Results

Three females, one in each of the control, mid dose and high dose groups, were found to not be pregnant. One low dose female gave birth prematurely (day 18 of gestation).

CONCLUSION

Irganox 1520 did not show any effects on reproductive function or F1 pups when administered prior to pairing and throughout gestation and lactation periods at doses of 0, 15, 50 and 200 mg/kg/day. The NOAEL was considered to be 200 mg/kg bw/day.

TEST FACILITY RTC (2000)

8. ENVIRONMENT

8.1. Environmental fate

All environmental fate data were obtained using the close analogue, Irganox 1520.

8.1.1. Ready biodegradability

TEST SUBSTANCE Irganox 1520

METHOD OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test

Inoculum Bacteria were collected in activated sludge from the sewage treatment plant of Reinach, Switzerland. The tests were performed at concentrations of 10 and 20 mg/L of chemical (7.069-14.14 mg/L of organic C) in sealed

	culture vessels in the dark at 22±2°C.
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Monitoring included titration of CO_2 absorbed in the absorber filters filled with 0.025 N barium hydroxide on the days 7, 10, 14, 17, 20, 24, 27 and 28. The biodegradation was calculated on the basis of the theoretical carbon content of the test substance and the cumulative quantities of carbon dioxide determined on the days of measurements.
Remarks – Method	The chemical did not dissolve in the medium.

RESULTS

Test substance (10 mg/L)		*Test substance (20 mg/L)*		*Sodium Acetate (10 mg/L)*	
Day	*% degradation*	*Day*	*% degradation*	*Day*	*% degradation*
0	0	0	0	0	0
7	1	7	2	7	41
10	1	10	3	10	67
14	1	14	4	14	75
17	1	17	4	17	81
20	3	20	4	20	84
24	3	24	4	24	86
27	3	27	4	27	88
28	3	28	4	28	93

Remarks - Results	The test material attained 3 - 4 % degradation after 28 days for 10 mg/L and 20 mg/L, respectively, and therefore cannot be considered to be readily biodegradable.
CONCLUSION	The test substance is not ready biodegradable.
TEST FACILITY	Ciba-Geigy Ltd, Switzerland (1987c).

8.1.2. Bioaccumulation

REMARKS	No biological study data available. The EU notification provides accumulation factors for the analogue, Irganox 1520, of 24 - 36 at 0.1 ppm and 52 - 89 at 0.01 ppm. These indicate the substance will not bioaccumulate. The study has not been reviewed.

8.2. Ecotoxicological investigations

All ecotoxicological data were obtained using the close analogue, Irganox 1520.

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Irganox 1520
METHOD	OECD Guidelines for Testing of Chemicals 203
Species	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 hours
Auxiliary Solvent	DMF, alkylphenol polyglycolether
Water Hardness	~176 mg $CaCO_3$/L
Analytical Monitoring	Temperature, dissolved oxygen and pH were measured daily. Actual concentrations measured at 0 and 96 hours. Constant concentration of test

substance was achieved during one test during; however, in the duplicate test, the concentration varied from 95 to 150 mg/L.

Remarks – Method: Toxicity Test date November 1986. Static test. Fish mean length 24 (22-25) mm (0.10 (0.07 to 0.12 grams body weight). Dissolved oxygen 95-100% saturation. Water pH 8.0. Temp. 23±1°C. Light:dark 16:8 hours. Reference toxicant substance: none used. Test performed as limit test with one concentration of 100 mg/L. To make the stock solution, 0.5 g of the test substance was dissolved in and made up to 50 mL with DMF. 4 mg/L alkylphenol polyglycolether was added directly to the water in the tank prior to the addition of the stock solution. The test chambers were aerated. The highest vehicle concentration was 950 mg DMF/litre.

RESULTS

Mortality

Concentration mg/L		*Number of Fish*	*Cumulative Mortality (N)*				*Mortality*
Nominal	*Actual*	*N*	*24 h*	*48 h*	*72 h*	*96 h*	*% 96 h*
Control, 0	0	10	0	0	0	0	0
Vehicle	0	10	0	0	0	0	0
100	95-150	10	0	0	0	0	0
100	113	10	0	0	0	0	0

* Values are based on nominal concentrations. Duplicate tests performed.

Sub-lethal Effects

Concentration mg/L		*Number of Fish*	*Cumulative Effects (N)*			
Nominal	*Actual**	*N*	*24 h*	*48 h*	*72 h*	*96 h*
Control, 0	0	10	0	0	0	0
Vehicle	0	10	0	0	0	0
100	95-150	10	0	0	0	0
100	113	10	0	0	0	0

* Values are based on nominal concentrations. Duplicate tests performed. Effects monitored included swimming behaviour, loss of equilibrium, respiratory function, exophthalmos, and pigmentation changes.

LC50: No mortality observed at the concentrations tested (ie. >100 mg/L).

NOAEC (mortality): >100 mg/L

Remarks – Results: Small oily droplets were observed on the water surface after 1 hour of exposure, indicating a water insoluble fraction at the test concentration.

CONCLUSION: Practically non-toxic to fish (LC50 >>100 mg/L).

TEST FACILITY: Ciba-Geigy (1986d)

8.2.2a. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE: Analogue (Irganox 1520)

METHOD: OECD TG 202 Daphnia sp. Acute Immobilisation Test - Freshwater.

Species: *Daphnia magna* Straus 1820 (Waterfleas)

Exposure Period: 24 hours

Auxiliary Solvent: DMF, alkylphenol polyglycolether

Water Hardness: 240 mg/L as $CaCO_3$.

Analytical Monitoring: Temperature, dissolved oxygen and pH measured at 0 and 24 hours. Actual concentrations measured at 0 and 24 hours. The results are based on the averaged of two measured test concentrations.

Remarks - Method: Toxicity Test Date: November 1986. Water pH 7.8-80. Temp. 20±1°C. Dissolved oxygen 8.3-8.7 mg/L. Light:dark 16:8 hours ~2000 lux). Semi-static test. Immobilisation referred to incapability of swimming. Reference toxicant substance: none used. 1.0 g of TK12229/1 was

dissolved in and made up to 10 mL with DMF. This solution was diluted to a concentration of 100 mg/L with water containing 2.3 mg/L of alkylphenol-polyglyocolether.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised (%)*
Nominal	*Actual (Average 0-24 h)*		*24 h*
Control blank, 0	0	4 x 10 per replicate	0
0.58	0.5	4 x 10 per replicate	40
1.00	0.9	4 x 10 per replicate	58
1.80	1.7	4 x 10 per replicate	65
3.20	3.1	4 x 10 per replicate	63
5.80	5.5	4 x 10 per replicate	53
Vehicle	0	4 x 10 per replicate	0

EC50	Not determined. EC50 Physical immobilisation in the range of 0.5 to 0.9 mg/L.
EC100	>5.5 mg/L at 24 hours (mean measured test concentration)
NOAEC (immobilisation)	<0.5 mg/L at 24 hours (mean measured test concentration)
Remarks - Results	The data do not allow for the calculation of an EC50. Most daphnids were at the surface of the water, particularly in lower test concentrations. Their immobility was affected by deposits of test substance on the body of the animals. This might explain their immobility and the lack of a clear dose/effect relationship. Nevertheless, 50 % of the *Daphnia* were physically immobilised by the test substance in the test concentration range of 0.5 to 0.9 mg/L. Poorly recorded test observations do not allow for greater interpretation of results at higher test concentrations.
CONCLUSION	Potentially harmful to aquatic invertebrates due to physical effects (Physical EC50 range of 0.5-0.9 mg/L).
TEST FACILITY	Ciba-Geigy (1986e)

8.2.2b.Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Irganox 1520
METHOD	OECD TG 211 *Daphnia magna* Reproduction Test.
Species	*Daphnia magna* Straus Clone 5 (Waterfleas)
Exposure Period	21 days
Auxiliary Solvent	DMSO (dimethylsulphoxide)
Water Hardness	Not stated
Analytical Monitoring	Temperature, dissolved oxygen and pH measured at abut every 2 days. Actual concentration of the highest test concentration was measured at 0, 48 and 72 hours age by HPLC.
Remarks - Method	There were no protocol amendments. Toxicity Test Date: January 2000. Water pH 7.6-80. Temp. 20-21 °C. Dissolved oxygen 8.1-9.0 mg/L. Light:dark 16:8 hours ~300-800 lux). Semi-static, renewal test. Mortality was monitored 3 times per week during the tests before renewal of the test media. Reference toxicant substance: none used.

RESULTS

Total Number of Alive, Young Daphnids Reproduced by All Adults (Cumulative Values). Exposure to Analogue

Exposure Day	Nominal concentration of the Test Substance (Analogue)						
	0[1]	0[2]	0.001	0.002	0.004	0.008	0.016
0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0
9	128	128	119	114	113	82	76
12	317	328	295	269	259	189	157
14	562	600	564	561	529	475	428
16	586	600	575	561	529	475	428
19	801	737	757	682	638	613	551
21	938	907	977	999	928	869	910
% of Solvent Control [3]	100	96.7	104.2	106.5	98.9	92.6	97.0

1. Solvent control. 2. Control (test water without any additions). 3. Based on the value of the last exposure day.

Total Number of Alive Offspring Reproduced Per Surviving Adult within 21 Days of Exposure to Analogue

Replicate No.	Nominal concentration of the Test Substance (Analogue)						
	0[1]	0[2]	0.001	0.002	0.004	0.008	0.016
1	119	82	98	93	102	99	90
2	77	95	128	97	101	95	90
3	116	80	78	101	69	102	92
4	90	83	100	117	107	83	91
5	118	99	102	100	82	72	*
6	78	78	113	106	89	52	85
7	76	83	85	80	104	106	111
8	86	81	87	102	107	98	89
9	93	118	75	99	70	80	86
10	85	108	111	104	97	82	84
Mean	93.8	90.7	97.7	99.9	92.8	86.9	90.9
±SD	17.4	13.7	16.8	9.5	14.6	16.5	8.0
n	10	10	10	10	10	10	10
CV %	18.5	15.1	17.2	9.5	15.7	19.0	8.8
Mean in %	100	96.7	104.2	106.5	98.9	92.6	96.9
STAT	---	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

1. Solvent control. 2. Control (test water without any additions). CV% coefficient of variation in percent: SD/mean). STAT: Statistical significance; results of a Williams-test with the mean values of alive offspring (one-sided smaller, $\alpha = 0.05$). n.s. Mean value not significantly lower than in the solvent control. * Test animal died during the test period.

EC50	>>0.0088 mg/L (not able to be calculated; this was the highest concentration tested).
NOAEC (reproduction)	>0.0088 mg/L in 21 days (the NOAEC exceeds the highest concentration tested)
Remarks - Results	In the controls and all tests concentrations up to and including 0.0088 mg/L (0.016 mg/L nominal) the survival rate of *Daphnia* was 90% or greater over the 21 test days.

CONCLUSION No toxic effects on survival or reproduction were observed at test concentrations that approximate the solubility limit of a chemical of similar physico-chemical properties to that of the notified chemical.

TEST FACILITY RCC Ltd (2000)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE	Irganox 1520
METHOD	Directive 92/69/EEC, C3, OECD TG 201 Alga, Growth Inhibition Test
Species	*Scenedesmus subspicatus* (unicellular)
Exposure Period	72 hours
Concentration Range - Nominal	Control (0) and 100 mg/L (limit test)
Time-weighted Mean Measured Concentration	0.013 mg/L. The mean analytically determined concentration of the analogue from the freshly prepared test medium of the main test (stock emulsion filtrate with a nominal concentration of 100 mg/L) in the test was 0.013 mg/L at the start of the test. A supersaturated stock emulsion of the analogue with a nominal concentration of 100 mg/L was prepared by dispersing 200 mg of the analogue by means of ultrasonic treatment for 15 minutes in 2 L water. No auxiliary solvent or emulsifier was used. The stock solution was stirred in the dark for 96 hours to dissolve and/or disperse a maximum concentration of the analogue in the stock emulsion. After stirring, the stock emulsion was allowed to stand at room temperature for 1 hour. Undissolved or unemulsified oily drops of the analogue were removed from the surface. The remaining stock emulsion was filtered (0.45 μm), and the first 100 mL of the filtrate was discarded to avoid potential loss of the analogue by adsorption onto the filter.
Auxiliary Solvent	None
Water Hardness	24 mg/L as $CaCO_3$
Analytical Monitoring	Temperature and pH measured at 0 and 72 hours. The actual concentration of the notified chemical was measured at 0 and 72 hours by HPLC with UV/VIS-detection.
Remarks - Method	Toxicity Test Date: May 1988. Water pH 8.0 at 0 hours increasing to pH 9.1-9.2 at 72 hours. The increase in pH is considered to be due to the amount of CO_2 required by the large number of algal cells in the log phase of growth exceeding the transfer rate of CO_2 from the gaseous phase. Temp. 24 °C ±1. Light:dark 24:0 hours 7060-8370 lux. Three replicate flasks per treatment concentration and 6 control replicates were tested. Chemical analysis at 72 hours showed a decline in measured concentration of the notified chemical from 0.013 to less than the detection limit (<0.005 mg/L), leading to a total mean test concentration of 0.0088 mg/L. However, biological results are reported on the basis of the nominal concentration of 100 mg/L. Losses may be attributed to the degradation of the test article resulting from the intense irradiation of the treatment samples, or oxidation of the analogue.

RESULTS

Growth		*Biomass*	
NOAEC mg/L at 72h	*E_rC50 mg/L at 72h*	*NOAEC mg/L at 72h*	*E_bC50 mg/L at 0-72h*
>0.013 (>100 mg/L nominal, highest concentration tested)	>>0.013 (>>100 mg/L nominal)	Not determined due to a lack of toxic effects.	Not determined due to a lack of toxic effects.

Remarks - Results	Control cell numbers increased by a factor of 155, within the acceptable limits of the test procedure.
CONCLUSION	No algal cell growth inhibition was recorded through out the tests.
TEST FACILITY	RCC Ltd (1988).

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Irganox 1520
TEST FACILITY	None
METHOD	EEC L 133, p. 118-122 (30 May 1988).
Inoculum	Activated sludge from the sewage treatment plant of CH-4153 Reinach, Switzerland.
Exposure Period	3 hours
Nominal Concentration	92.0, 36.4, 12.0, 4.5, 1.75 mg/L. 18.4, 7.28, 2.40, 0.90 and 0.35 mg of the analogue were weighed and added to the test medium. The volume was adjusted to 200 mL with water and aerated for 3 hours. The sludge concentration in the test bottles was 1.7 g/L.
Remarks – Method	The test substance's capacity to inhibit microbial activity was determined by the measurement of oxygen consumption for a period of 3 h after the medium was inoculated with activated sludge and exposed to light at ~20°C. Standard Test Deviations: 1). Due to the poor water solubility of the analogue at the test concentrations, no stock solution was prepared. The test substance was given directly into the medium. 2). Instead of using a centrifuge, the activated sludge was separated from the aqueous layer by settling. 3,5-dichlorophenol was used as the standard reference material at concentrations of 32, 10 and 3.2 mg/L.
RESULTS	
IC50	> 100 mg/L
Remarks – Results	Exposure to the analogue at the highest test concentration (92 mg/L) did not inhibit microbial growth, as indicated by oxygen consumption.
CONCLUSION	The results indicate that the notified chemical is not inhibitory to sludge microorganisms.
TEST FACILITY	Ciba-Geigy (1990)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The notified chemical will be mixed with a range of other products to form a range of end use products. End products may contain up to 1 % of the notified chemical.

In the environment, the notified chemical is expected to be relatively persistent. The notified chemical is only very slightly volatile (1.8×10^{-19} Pa at 25°C) and loss to the atmosphere is unlikely to be significant process. The notified chemical has a low solubility in water (<0.1 mg/L). The notified chemical has a density lighter than water, and oily drops appear on the surface of super saturated solutions. It is not readily biodegradable, with only 3 – 4 % degradation after 28 days for 10 mg/L and 20 mg/L test solutions. However, it may degrade slowly over time at lower concentrations as it has not been shown to inhibit microbial activity. The notified chemical is unlikely to hydrolyse readily in natural waters at environmentally-relevant pH values. It has a potential to adsorb to particulate organic material and therefore

accumulate in sediments due to this sorption to suspended particulate matter and settlement. It is not expected to be very mobile in soils and groundwater due to its low sorption potential and very slight water solubility. It is also not expected to bioaccumulate in animals or plants due to its high Log Kow (14.1) and slight water solubility.

Following landfill disposal, the notified chemical is likely to be persistent. Most of the import volume of the notified chemical is likely to eventually be disposed of to landfill over time (eg. 1000 kg/year); however, the actual rate of disposal each year may be extended beyond any one year.

A small fraction of the notified chemical (eg. <10 kg/year) may potentially be discharged to sewage treatment plants (STPs) where it is likely to mainly partition to biosolids. Using estimates for Australian STPs, which generate ~1423500 ML/year of effluent and ~142350 tonnes/year of biosolids, estimated maximum concentrations of the notified chemical in each of these media are 7×10^{-6} mg/L and 0.07 mg/kg (dry wt), respectively, assuming complete partitioning to one or the other media. On this basis, the concentration in STP biosolids and effluent is likely to be negligible. Furthermore, dilution by a factor of 10 is likely where STP effluents are discharged to the ocean via outfalls.

9.1.2. Environment – Effects Assessment

No aquatic toxicity data available for the notified chemical. However, data are available for a structurally similar analogue (Irganox 1520). In summary, the aquatic toxicity data for the analogue indicate:

Fish: 96-h LC50	Practically non-toxic to fish (LC50 >>100 mg/L nominal, solvent-enhanced)
Invertebrate 48-h EC50	Could not be determined due to physical interferences. The notified chemical may potentially be harmful to aquatic organisms due to adherence to external body parts resulting in immobilisation (physical IC50 range of 0.5-0.9 mg/L).
Invertebrate 21-d L(E)C50	No toxic effects on survival or reproduction were observed at test concentrations that approximated the solubility limit of a chemical of similar physico-chemical properties to that of the notified chemical (NOAEC >0.0088 mg/L). This was the highest concentration tested.
Alga 72-h E_rC50 (growth)	No lethal or reproductive toxicity observed at concentrations of 0.013 mg/L (100 mg/L nominal) or greater. EC50 >>0.013 mg/L. This was the highest concentration tested.

Based on data for an analogue of similar chemical structure (Irganox 1520), the notified chemical is likely to have a low toxicity to aquatic organisms (eg. fish, invertebrates, algae). The analogue was practically non-toxic to the fish and algal species tested. Over a 21-day period, the analogue was not toxic to the freshwater aquatic invertebrate tested (*Daphnia magna*) at test concentrations approximating the solubility limit of this compound (NOAEC >0.0088 mg/L). However, higher test concentrations used in the tests resulted in physical immobilisation due to adherence of the test substance to the external body surfaces of the *Daphnia*. Physical immobilisation of 40 % or more of the test organisms occurred at analogue concentrations of 0.5 mg/L or greater.

Using the lowest LC50 datum (ie. 100 mg/L), a predicted no effect concentration (PNEC - aquatic ecosystems) of 1 mg/L) has been derived by dividing the LC50 value by an uncertainty (safety) factor of 100. To account for the potential for physical effects due to adherence to external surfaces of biota, a PNEC (physical immobilisation) of 0.013 mg/L has been derived based on NOAEC for the chronic Daphnia magna test. Physical effects were observed at a concentration of 0.5 mg/L or greater.

No aquatic toxicity data were available for the notified chemical for Australian endemic aquatic species or marine species, and no chronic data were available. Acute aquatic toxicity data for three freshwater species (fish, invertebrate, alga) were available for this assessment. Rainbow trout are naturalised in temperate Australian freshwater systems. In accordance with Australian

guidance (ANZECC/ARMCANZ, 2000), the freshwater data have tentatively been adopted to assess risks to marine life.

The oral toxicological data available for the analogue for mammals indicates that the notified chemical has a low toxicity to wildlife.

The notified chemical is not inhibitory to activated sludge microorganisms at the highest concentration tested (92 mg/L).

9.1.3. Environment – Risk Characterisation

Location	PEC (mg/L) or mg/kg	PNEC (mg/L)[c]	Risk Quotient (RQ)[a]
Australia-wide STPs			
Ocean outfall	7×10^{-7} mg/L	1 mg/L (0.013)	7×10^{-7} (5×10^{-5})
Inland River	7×10^{-6} mg/L	1 mg/L (0.013)	7×10^{-6} (5×10^{-5})
Soils			
Irrigation reuse	<0.001 mg/kg	1.0 mg/kg[b]	<0.001
Biosolids reuse	<0.01 mg/kg	1.0 mg/kg[b]	<0.01

a. RQ = PEC ÷ PNEC. b. No data available - trigger level estimation. c. $PNEC_{aquatic}$ for toxicological and physical effects (in brackets).

On the basis of the PEC/PNEC ratios, low volumes used and nationwide and diffuse use of the notified chemical, it is not considered to pose an unacceptable risk to the health of aquatic life based on its reported use and estimated disposal patterns. The low RQ value for marine life indicates that the absence of marine ecotoxicity data is unlikely to affect this conclusion.

Based on low exposure potential, reuse of biosolids is unlikely to pose an unacceptable risk to the health of soil organisms. Reuse of effluent for agricultural purposes is unlikely to result in unacceptable health risks to soil organisms.

The low toxicity to mammalian species and low exposure potential indicates that the notified chemical is unlikely to pose an unacceptable risk to the health of wildlife.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

The highest occupational exposure is expected to be for workers handling the essentially pure notified chemical during formulation of adhesives. Dermal exposure to drips and spills of the notified chemical may occur while pumping the imported chemical from drums to mixing vessels. This is expected to be occasional (approximately 5 days per year) and the use of gloves and other protective equipment should minimise exposure. All other workers are expected to handle the notified chemical only in sealed containers, or the handle only the finished products containing up to 1 % notified chemical. No inhalation exposure is expected based on the use pattern and properties of the notified chemical.

Workers using hot melt adhesives for lamination may handle the notified chemical at low concentrations on a regular basis, but the chemical will be contained within a solid matrix both before and after melting, and user contact with the molten adhesive will not occur. Water and solvent based adhesives containing the notified chemical are not expected to have industrial use. Quality control and formulation workers may have some contact with these on a infrequent basis, as the packing process is automated and quality control will involve only small quantities of adhesive.

9.2.2. Public health – exposure assessment

Public exposure to the notified chemical is expected to be low as the concentration of the notified chemical in the final adhesives is a maximum of 1 % and it is likely to be quickly immobilised in the adhesive matrix after release from its container. Use will normally be infrequent. Public exposure to adhesive used in packaging is likely to be rare, and the notified chemical will be immobilised in the solid matrix.

9.2.3. Human health - effects assessment

Information on the health effects due to the notified chemical have been drawn almost completely from studies performed on a close analogue, Irganox 1520. The analogue is considered to represent all of the toxicologically relevant properties of the notified chemical.

The notified chemical was not mutagenic when tested in the bacterial reverse mutation test. No test for inhalation toxicity was conducted (for the notified chemical or analogue), but the properties of the notified chemical (low melting solid with low volatility) indicate that aerosol formation and vapour inhalation are very improbable.

The analogue showed low acute toxicity in rats by the oral and dermal routes (LD50 > 5000 and 2000 mg/kg bw, respectively). It was a slight irritant to rabbit skin and eyes. Sensitisation testing resulted in up to 7 of 20 guinea pigs showing responses on challenge, which, for an adjuvant test, would indicate that classification should occur. However, a rechallenge at the same concentration resulted in dermal responses in only 1 of 20 animals, which indicates that the original result was not indicative of true sensitisation; the study authors suggested that it may have been due to hypersensitivity resulting from use of the adjuvant.

In a 28-day repeat dose study in rats, a NOEL of 50 mg/kg bw/day was established for the analogue, with small changes in alkaline phosphatase levels and liver weights above this dose.

The analogue was not clastogenic to CHO cells in vitro.

The analogue was tested for reproductive and developmental toxicity in two studies. In a teratogenicity study, where the dams were treated only during gestation, a NOEL of 150 mg/kg bw/day was established, with embryotoxicity but no teratogenicity seen at 300 mg/kg bw/day. In a one generation reproductive study (originally designed for a longer study but terminated at one generation), no significant effects were seen and a NOAEL of 200 mg/kg bw/day was established.

Several other studies on the analogue chemical were summarised in a European notification statement for the analogue which was submitted by the notifier. The original studies were not provided. In a 90-day oral repeat dose study in rats, a NOEL of 10 mg/kg bw/day was established; the only reported observations at higher doses (100 and 1000 mg/kg bw/day) were changes in liver weight. In a similar study in beagle dogs, histopathological studies showed biliary cell proliferation which did not reverse after 28 days; also reversible changes in neutrophils and aminotransferase and/or alkaline phosphatase activities were seen at 100 and 1000 mg/kg bw/day; a NOEL of 10 mg/kg bw/day was established. A bone marrow micronucleus test in Chinese hamsters showed no evidence of mutagenicity at 5000 mg/kg bw.

Based on this data the notified chemical is not classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999b).

9.2.4. Occupational health and safety – risk characterisation

There is expected to be little occupational exposure to the notified chemical, as workers who handle it in concentrated form will do so on an infrequent basis, and workers will only handle it regularly in the form of hot melt adhesive granules, in which it is immobilised.

The notified chemical is not classified as a hazardous substance, and the effects of occupational exposure to the concentrated substance by the dermal and ocular routes are likely to be limited to low level skin or eye irritation, which should be prevented by use of personal protective equipment. The notified chemical is expected to have very low hazard at the concentration used in adhesives, resulting in low risk from the notified chemical for users of the adhesives.

9.2.5. Public health – risk characterisation

The notified chemical is expected to have very low hazard at the concentration used in adhesives, and this is the only form in which it is used by the public. Use would normally also be on an infrequent basis. Therefore the risk to the public resulting from use of the notified

chemical is expected to be very low.

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

10.1. Hazard classification

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

10.2. Environmental risk assessment

On the basis of the low volumes used (ie. < 1000 kg/year) and nationwide and diffuse use of the notified chemical, it is not considered to pose an unacceptable risk to the environment based on its reported use pattern and likely potential re-use/disposal pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

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

10.3.2. Public health

There is Negligible Concern to public health when the notified chemical is used in packaging and consumer adhesives at levels of 1 % or less.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994a). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

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

12. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - protective gloves, safety glasses or goggles, industrial clothing and footwear

  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

- The following water quality assessment benchmark may be used by the notifier and regulatory agencies for assessment of accidental release of the notified chemical to the aquatic environment:
  - 1 mg/L (based on PNEC)

Disposal

- The notified polymer should be disposed of in accordance with the methods described in the Material Safety Data Sheet, including by licensed waste contractor and in accordance with local jurisdiction waste management guidance.

Emergency procedures

- Spills/release of the notified polymer should be handled by trained personnel in accordance with the material safety data sheet provided by the manufacturer.
- Spills/release of the notified chemical should be contained with suitable absorbent material. Scoop into marked containers for disposal as chemical waste in accordance with relevant Government regulations.
- Avoid release of chemically contaminated water into drains, soil or surface water. Dispose of contaminated water and soil according to local regulations.

Transport and Packaging

- The following precautions should be taken by the manufacturer regarding transport and packaging of the notified polymer:
  - Australian Code for the Transport of Dangerous Goods by Road and Rail (DOTARS, 1996).

12.1. Secondary notification

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

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

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

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