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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

FSH

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Holder of the origianl assessment certificate:
MITSUI & Co. (Australia) Ltd ABN 85 096 197 885
Level 24, Burke Place, 600 Burke Street,
MELBOURNE VICTORIA 3000

Applicant for an extension of the origianl assessment certificate:
Sola International Holdings Ltd ABN 47 007 719 708
Sherriffs Road
LONSDALE SOUTH AUSTRALIA 5160

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)

Data items and details claimed exempt from publication:
chemical name
other name(s)
CAS Number
molecular formula
structural formula
molecular weight
spectral data
purity
impurities
import volume
identity of sites

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
dissociation constant
flammability limits
acute inhalation toxicity

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
European Union

2. IDENTITY OF CHEMICAL

METHODS OF DETECTION AND DETERMINATION

METHOD Infrared (IR), Nuclear Magnetic Resonance (NMR) and Mass spectroscopy
TEST FACILITY Reference spectra were provided

3. COMPOSITION

DEGREE OF PURITY
High

HAZARDOUS IMPURITIES
The notifier reports that no hazardous impurities are present at or above the relevant cut offs for classification of the notified chemical as a hazardous substance.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Import as pure notified chemical in 200 L steel drums.

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

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

USE
A component of ophthalmic lenses.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Melbourne or Adelaide.

IDENTITY OF MANUFACTURER/RECIPIENTS
Confidential.

TRANSPORTATION AND PACKAGING
200 L drums will be transported from the dock by road or rail to a single plant.

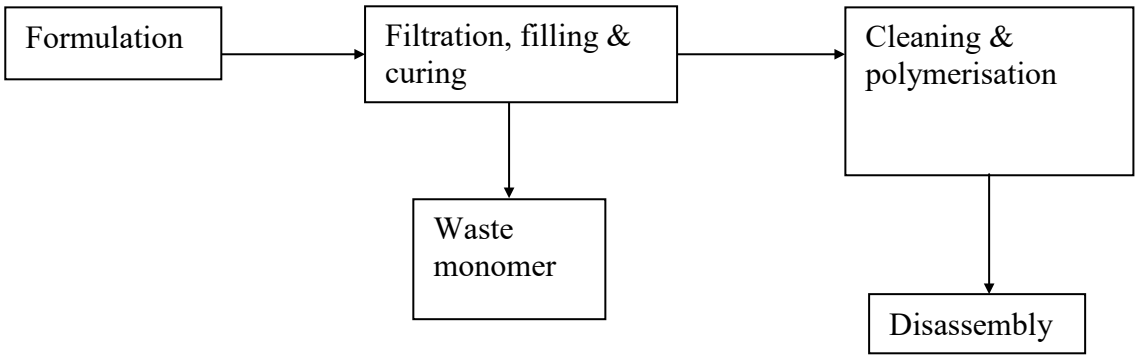
5.2. Operation description

Manufacture of articles using the notified chemical is carried out in the following four stages:

1. The notified chemical is formulated with other liquid resins and additives to produce a liquid resin.
2. Mould assemblies used to manufacture the final articles are filled with the resulting formulated liquid resin. Waste liquid resin is produced at this stage of the manufacturing process.
3. The liquid resin-containing mould assemblies are loaded into an oven for curing; and
4. The resulting cured assemblies are cleaned and disassembled to remove the final article.

The notified chemical is at room temperature until the commencement of stage 3 (the thermal curing stage) and remains in a liquid form until part way through stage 3. During stage 3 the notified chemical is incorporated into a polymer.

Transfer (stage 1) from 200 kg drums will be by means of an electrically driven pump or vacuum to closed systems. The transfer lines and filling machine are automated and enclosed. Automatic filling equipment will be used to fill the mould assemblies (stage 2). The curing oven area and curing ovens are under local ventilation (stage 3) and the latter are loaded manually. The filled mould assemblies are placed in racks on a trolley, which is rolled into the curing oven. The four stages of the manufacturing process are illustrated below:



5.3. Occupational Exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration (hrs/day)*	*Exposure Frequency (days/yr)*
Process Workers	6 - 10	2.5 - 5	241
Maintenance/Engineering	10 - 14	1 - 8	241
Quality Assurance	1 - 2	0.5 - 1	104
Supply Personnel	2	0.5 - 1	4
Emergency Personnel	10 - 15	0.5 - 1	1
Waste Disposal	2	2	12

Exposure Details

***Process Workers*:** Process workers will be formulating the liquid resin containing the notified chemical (stage 1), filling the formulated resin into mould assemblies (stage 2), transferring resin-filled mould assemblies into curing ovens (stage 3) and removing the cured articles from mould assemblies at the conclusion of the thermal curing process (stage 4). As a result of the oven-curing process, it is anticipated that the quantity of notified chemical will be reduced to negligible amounts at the conclusion of Stage 3. There is a potential risk of dermal exposure to the notified chemical via drips, spills and accidental releases of the liquid formulated resin until part way through the curing process (Stage 3). Formulation and filling is carried out in an area with local exhaust ventilation.

Maintenance and Engineering Workers: Maintenance and engineering workers will repair existing equipment and commission any new equipment that is introduced into the production area. There is a potential risk of dermal exposure to the formulated resin via drips, spills and accidental releases and from contact with contaminated equipment.

***Quality Assurance Workers**:* Quality assurance staff will be involved in sampling and testing of the notified chemical upon the arrival of the notified chemical at the production plant. There is a potential risk of dermal exposure to the notified chemical via drips, spills and accidental splashes during quality assurance sampling and testing.

***Supply Department Workers**:* Workers in the supply department will transfer sealed drums into storage and from there to the production area as required. There is a potential risk of dermal exposure

to the notified chemical via accidental releases, e.g., if a drum leaks or if an accident occurs during the transfer operation.

Emergency Personnel: Emergency personnel will be involved in clean up operations in the event of such accidental spills. There is a potential risk of dermal exposure to the notified chemical and the formulated resin during the clean up operation.

Cleaning and Waste Disposal Workers:
The process line is dedicated so that cleaning is not required unless the transfer lines require maintenance. If cleaning is required, the transfer lines and machine are flushed with a suitable solvent such as acetone. Maintenance work is commenced only after the equipment has been flushed. The plant operator redirects a valve within the transfer line, which switches the input from the monomer to the solvent. The solvent is then pumped through the system. The acetone washings are collected in 200 L drums.

The waste-containing drums are sealed and dispatched off site for disposal by a licensed waste contractor. There is a potential risk of dermal exposure to the notified chemical via accidental splashes and releases of acetone washings containing the notified chemical and from contaminated waste drums.

Workers using the notified chemical wear latex gloves, disposable sleeves, protective garments, disposable aprons and wrap around safety spectacles. Quantities of the notified chemical greater than 50 kg are stored separately from the workplace. Storage of the notified chemical occurs in the original 200 L drum in a purpose built bunded area. The Material Safety Data Sheet is available to all production, maintenance and engineering, quality assurance, supply department and cleaning and disposal workers as well as the Emergency Response Team.

5.4. Release

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured in Australia and is transported by road from the dock to a single plant. Potential release may occur in the event of an accidental spill resulting from a transport accident.

At the plant the notified chemical is formulated with other liquid resins and additives. Then the formulated liquid resin is filled into mould assemblies, polymerised and finally disassembled. Traces of polymer will be removed from equipment using 25% potassium hydroxide solution at 75˚C. Potassium hydroxide solution will pass through a sedimentation tank and be neutralised before discharge to sewer. The pH of the effluent will be maintained between 5.5 and 10.5 by automatic equipment. Solids from the sedimentation tank are collected and sent to a secure landfill site for disposal. The notifier estimates that wastes from this process are anticipated to be no more than 50 g per day or about 20 kg per annum.

Specialised mixing and filling equipment will produce waste resin at up to 20 kg per annum. Waste resin will be collected, allowed to polymerise and incinerated. Further waste may be generated from the cleaning of filling lines and residue left in drums, of which a small amount may be disposed of to the sewer or landfill.

RELEASE OF CHEMICAL FROM USE

There is no risk of release to the environment from the final products made from notified chemical as the manufacturing process is designed to produce fully cured polymer. The finished articles will contain no residue of liquid resin used in the manufacturing process.

5.5. Disposal

A small amount of waste notified chemical is generated and although care is exercised to prevent release to watercourses a small amount may potentially be disposed to the sewer, however the main methods of disposal are landfill or incineration. Empty drums will be sent to a contractor, where they will be decontaminated with alkaline organic solvent (which will be incinerated) then washed with water, and the waste from this process is neutralised prior to discharge to the sewer. The drums are crushed and sent to a secure landfill site

5.6. Public exposure

The chemical will not be available to the general public. Excluding the potential for accidental spills, potential contamination of air, food or water is not expected to be significant because of the low vapour pressure and insolubility of the notified chemical. Nil residue of the notified chemical is expected in the finished lenses because the notified chemical is incorporated into a polymeric structure as a result of the curing process used during the manufacturing process.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Colourless liquid.

Freezing Point < -21ºC

METHOD EC Directive 92/69/EEC A.1 Melting/Freezing Temperature
TEST FACILITY Safepharm Laboratories Limited (1997m).

Boiling Point 313ºC at 101.3 kPa

METHOD EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Determined by differential scanning calorimetry. Decomposition at 222 ºC.
TEST FACILITY Safepharm Laboratories Limited (1997m).

Density 1292 kg/m^3 at 20ºC

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Pycnometer method.
TEST FACILITY Safepharm Laboratories Limited (1997m).

Vapour Pressure 9.4 x 10^{-13} kPa at 25ºC.

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Determined using a vapour pressure balance. Measurements were performed between 144°C and 169°C. Vapour pressure at 25°C was determined by extrapolation.
TEST FACILITY Safepharm Laboratories Limited (1997n).

Water Solubility < 0.0222 mg/L at 20ºC

METHOD EC Directive 92/69/EEC A.6 Water Solubility. Analytical Method: HPLC.
Remarks The flask method was used. Test material and glass double-distilled water mixtures were prepared and after shaking at 30°C for 24 hours and standing at 20° C for 24 hours, the samples were centrifuged and filtered.
TEST FACILITY Safepharm Laboratories Limited (1997m).

Hydrolysis as a Function of pH Not determined

No test was conducted as such tests of hydrolysis as a function of pH are not applicable for water insoluble substances. The notified chemical does not contain any functionality that is expected to hydrolyse appreciably at the environmental pH range of (4-9).

Partition Coefficient (n-octanol/water) Log Pow = 4.16 to 4.34

METHOD HPLC method. EC Directive 92/69/EEC A.8 Water Solubility.
Remarks Preliminary assessment of the partition coefficient could not be made due to the low solubility of the test material in n-octanol and in water. The preliminary assessment of the partition coefficient was determined visually and the value of the partition coefficients were <10 mg/L and <4 mg/L in n-octanol and water, respectively. A calibration curve was constructed from the retention time data of a range of different reference standards and the retention time of the sample

(containing a known amount of test material) was compared to these. The sample was eluted between naphthalene (log Pow 3.6) and phenanthrene (log Pow 4.5). Despite the preliminary test results, the relatively large log Pow value suggests that test substance will have an affinity for the organic phase.

TEST FACILITY Safepharm Laboratories Limited (1997m)

Adsorption/Desorption Log Koc = 4.30

METHOD HPLC Screening Method of Fraunhofer-Institut für Umweltchemie und Ökotoxikologie

Remarks A calibration curve was constructed from the retention time data of a range of different reference standards that were prepared in acetonitrile and eluted through a Zorbax column using a mobile phase of acetonitrile:water (55:45 w/w). The retention time of the sample was run under identical conditions and compared to these reference standards. The relatively large Koc value suggests that the test substance will most likely associate with sediments and soils

TEST FACILITY Safepharm Laboratories Limited (1997m)

Dissociation Constant Not determined.

The dissociation constant could not be determined due to the low solubility for FSH. It is expected that in the environmental pH range of 4 to 9, a small fraction of the notified chemical will be dissociated.

Flash Point 217°C at 101.3 kPa

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

Remarks Closed cup equilibrium method.

TEST FACILITY Safepharm Laboratories Limited (1997o).

Flammability Limits Not determined

Remarks Not expected to be flammable based on vapour pressure. The flammability limits were not determined since the flash point was 217°C indicating that FSH is not flammable.

Autoignition Temperature 332°C

METHOD 92/69/EEC A.15 Auto-Ignition Temperature (Liquids).

TEST FACILITY Safepharm Laboratories Limited (1997o).

Explosive Properties Not explosive

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

Remarks Not sensitive to shock or heat. Friction test is not applicable to liquids.

TEST FACILITY Safepharm Laboratories Limited (1997o).

Reactivity

Remarks Stable under normal environmental conditions.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 > 2000 mg/kg bw	low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Inhalation	test not conducted
Rabbit, skin irritation	moderately irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – maximisation test	evidence of sensitisation.
Rat, oral repeat dose toxicity - 28 days.	NOAEL = 50 mg/kg/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberrations	non genotoxic

7.1. Acute toxicity – oral

TEST SUBSTANCE	notified chemical
METHOD	OECD TG 401 Acute Oral Toxicity – Limit Test. EC Directive 92/69/EEC B.1 Acute Toxicity (Oral) – Limit Test.
Species/Strain	Rat/Sprague-Dawley.
Vehicle	None.
Remarks – Method	No protocol deviations reported.

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	None.
Effects in Organs	None.
Remarks – Results	No signs of systemic toxicity were noted during the study. No abnormalities were noted at necropsy.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Safepharm Laboratories Limited (1997a).

7.2. Acute toxicity – dermal

TEST SUBSTANCE	notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	Rat/Sprague-Dawley.
Vehicle	None.
Type of dressing	Surgical gauze over the treatment area and semi-occluded with a piece of self-adhesive bandage and secured with BLENDERM™.
Remarks – Method	No protocol deviations reported.

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	Incidents of desquamation and/or small superficial scattered scabs were noted in females on days 6 to 14.
Signs of Toxicity - Systemic	None.
Effects in Organs	None.
Remarks – Results	No signs of systemic toxicity were noted during the study. No abnormalities were noted at necropsy.

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

TEST FACILITY Safepharm Laboratories Limited (1997b).

7.3. Acute toxicity –inhalation

The test was not conducted. Inhalation exposure would be unlikely due to the expected low vapour pressure of the notified chemical.

7.4. Irritation – skin

TEST SUBSTANCE notified chemical

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

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None.
Observation Period	14 days.
Type of Dressing	Semi-occlusive.
Remarks – Method	No protocol deviations reported.

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	2	2	2	7 days	0
Oedema	0	1	1.7	2	3 days	0

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

Remarks – Results No corrosive effects were noted. All signs of erythema/eschar and oedema formation in the test animals were resolved at day 7. The value of the Primary Irritation Index was 2.5.

A reaction extending approximately up to 3 cm beyond the treatment site was observed in two of three animals at 24-hours but was resolved at day 7. One of three animals displayed blanching of the skin accompanying a reaction extending approximately up to 3 cm beyond the treatment site at 24-hours but was resolved at day 7.

CONCLUSION The notified chemical is moderately irritating to the skin in rabbits.

TEST FACILITY Safepharm Laboratories Limited (1997c).

7.5. Irritation – eye

TEST SUBSTANCE notified chemical

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

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	3 days.
Remarks – Method	No protocol deviations were reported.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0	0.3	0	1	24 hours	0
Conjunctiva: chemosis	0	0	0	0		
Conjunctiva: discharge	0	0	0	1	1 hr	
Corneal opacity	0	0	0	0		
Iridial inflammation	0	0	0	0		

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

Remarks – Results	A maximum group mean score of 1.3 was determined

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Safepharm Laboratories Limited (1997d).

7.6. Skin sensitisation

TEST SUBSTANCE notified chemical

METHOD OECD TG 406 Skin Sensitisation – maximisation test.
EC Directive 96/54/EC B.6 Skin Sensitisation – maximisation test.

Species/Strain	Guinea pig/Dunkin-Hartley.
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: < 1% w/v in arachis oil topical: 25% and 50% v/v in arachis oil
MAIN STUDY	
Number of Animals	Test Group: 10 Control Group: 5
INDUCTION PHASE	Induction Concentration: intradermal injection 1% (w/v) topical application 25%, 50% (v/v)
Signs of Irritation	Well-defined or moderate to severe erythema was noted at the intradermal induction sites of all test group animals at the 24 and 48-hour observations. Very slight to well-defined erythema and incidents of very slight to slight oedema were noted at the induction sites of all test group animals at the 1-hour observation. Very slight erythema was noted at the induction sites of two test group animals at the 24-hour observation.
CHALLENGE PHASE	
1st challenge	topical application: 25% (v/v) topical application: 50% (v/v)
Remarks – Method	No protocol deviations reported. One death (day 17) occurred in the control group resulting in 4 control animals. No skin reactions were observed at the intradermal induction sites of control group animals at the 24- and 48-hour observations. No skin reactions were observed at the topical induction (treatment) sites of control group animals at the 1- and 24-hour observations.

RESULTS

Animal	*Challenge Concentration(w/v)*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	25%	10/10	9/10
	50%	10/10	10/10
Control Group[1]	25%	1/4	1/4
	50%	3/4	2/4

[1] one death (Day 17)

Remarks – Results

The death (unspecified cause) of one control animal on day 17 is not regarded as affecting the integrity of the study. For the remaining four control animals, in those treated with 25% (v/v) test substance, one showed slight erythema at both 24 and 48 hours and slight oedema at 24 hours. Accompanying desquamation was also noted in this animal. In those control animals treated with 50% (v/v), very slight erythema and incidents of very slight oedema were noted at the challenge site of three of four control group animals at the 24-hour observation and two of four control group animals at the 48-hour observation.

For the test group, responses were more pronounced and are indicated by average Draize scores of 2.1 and 1.5 for erythema at 24 and 48 hours, respectively, for those animals challenged with 25% (v/v) test substance. The corresponding average Draize scores for oedema at a challenge concentration of 50% (v/v) test substance were 1.6 and 0.9 at 24 and 48 hours, respectively.

At a challenge concentration of 50% (v/v), the average Draize scores were 2.2 and 1.6 for erythema and 1.8 and 1.3 for oedema at 24 and 48-hours, respectively.

CONCLUSION

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

TEST FACILITY

Safepharm Laboratories Limited (1997e).

7.7. Repeat dose toxicity

TEST SUBSTANCE

notified chemical

METHOD

Japanese Ministry of Health and Welfare (MHW) Guidelines 1986 for a twenty-eight day repeat dose oral toxicity study as required by the Japanese Chemical Control Law 1973 of Japanese Ministry of International Trade and Industry (JMITI) amended 1986.

Species/Strain	Rat/Sprague-Dawley.
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days: 28 days. Dose regimen: 7 days per week.
Vehicle	Polyethylene glycol 400
Remarks – Method	No protocol deviations are reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5/sex	0	None
II (low dose)	"	50	"
III (mid dose)	"	250	"

IV (high dose)	"	1000	"
V (control recovery)	"	0	"
VI (high dose recovery)	"	1000	"

Mortality and Time to Death There were no deaths during the study.

Clinical Observations High dose male and female animals showed short-lived increased salivation either before or immediately after dosing from day 11 onwards.

High and intermediate dose males and males from the corresponding high dose recovery group showed a statistically significantly lower ($p < 0.05$-0.001) bodyweight gain (20-50%) compared to controls with the magnitude becoming more pronounced as the study progressed.

High dose recovery females showed a significantly ($p < 0.01$) lower bodyweight gain (~ 47%) than the satellite control group during week 4 compared to controls, although, in the absence of the similar adverse effect amongst the corresponding high dose female group, this finding was considered to be of equivocal toxicological significance. There was no adverse effect on body weight development amongst satellite high dose animals following cessation of treatment. A statistically significant increase in body weight gain identified amongst satellite high dose animals of either sex during the 14-day treatment-free period was consistent with the animals' recovery from the adverse effects during the 28-day dosing period.

High and intermediate dose males and recovery high dose males showed a reduced food efficiency (> 12%) compared with controls, mostly during the second half of the treatment period. Satellite high dose females showed a reduced food efficiency (11-58%) compared to controls with the magnitude becoming more pronounced as the study progressed but which resolved during the 2-week recovery period.

Intermediate dose females and low dose animals of either sex showed similar body weight gains to controls during the study.

No other treatment related clinical observations were observed in the study.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Clinical chemistry: A number of changes were observed but were within the normal range of historical controls, did not exhibit a dose-response or occurred only in recovery animals.

Haematology: A number of incidental changes were observed but were within the normal range of historical controls, did not exhibit a dose-response or occurred only in recovery animals.

Urinalysis: No changes observed.

Effects in Organs A number of statistically significant decreases ($p < 0.001 – 0.05$) in absolute organ weights (gonads, kidneys and spleen) in mid or high dose males were assumed to be an effect of reduced bodyweight. High and mid dose males showed lower absolute testes weights (14 – 32%) compared to controls, with two of five animals from each group showing abnormally low testes weights for rats of this strain and age. Normally this would be ascribed to the reduced bodyweight but recovery high dose

males showed significantly lower absolute ($p < 0.01$) and relative ($p < 0.05$) testes weights at the end of the recovery period compared to controls with several animals showing abnormally low individual values. No change in absolute organ weights in mid or high dose females were observed.

At necropsy, 2 of 5 high dose males showed small, discoloured testes and 1 of 5 mid dose males showed a slightly discoloured left testis. Two of 5 recovery high dose males showed discoloured and/or small testes at the end of the recovery period. Histopathology revealed testicular atrophy in mid and high dose males in 5 of 5 and 4 of 5 animals, respectively, and in 5 of 5 recovery high dose males. The only other macroscopic changes observed at necropsy in the mid or high dose males and females were one incident of a small malformed kidney and dark lung areas in a male and female rat, respectively, treated at the high dose.

Remarks – Results

Treatment related changes were observed amongst animals of either sex dosed at 1000 mg/kg bw/day and also amongst males dosed at 250 mg/kg bw/day. At 1000 mg/kg bw/day, the testes were identified as target organs for males. With the exception of these testicular changes, animals of either sex dosed at 1000 mg/kg bw/day showed only minimal signs of toxicity during the study. A reduced bodyweight gain and reduced food efficiency were evident amongst animals of either sex although the adverse effects amongst the females were confined to the satellite 1000 mg/kg bw/day group and were, therefore, of equivocal significance. The adverse effects on the testes persisted amongst satellite 1000 mg/kg bw/day males following an additional fourteen days without treatment whereas the other toxicologically significant changes identified at this dose had regressed fully by the end of the recovery period.

At 250 mg/kg bw/day, toxicologically significant findings were confined to males and were almost identical in nature to those observed at the higher dose level. Body weight gain and food efficiency were reduced during the study. In addition, histopathological examination showed testicular atrophy. Females dosed at 250 mg/kg bw/day and animals dosed at 50 mg/kg bw/day showed no toxicologically significant changes in the parameters measured.

CONCLUSION

With no changes detected at 50 mg/kg bw/day which could be considered indicative of a treatment related effect, the No Observed Effect Level (NOEL) for males may be considered to be 50 mg/kgbw/day.

With no changes detected at 250 mg/kg bw/day which could be considered indicative of a treatment related effect, the No Observed Effect Level (NOEL) for females may be considered to be 250 mg/kgbw/day.

TEST FACILITY

Safepharm Laboratories Limited (1997f).

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
Species/Strain	*S. typhimurium*: TA1538, TA1535, TA1537, TA98, TA100. *E. coli*: WP2 uvrA, WP2 uvrA (pKM101), WP2 (pKM101).
Metabolic Activation System	Rat liver S9 microsomal fraction from Aroclor 1254 treated rats.
Concentration Range in Main Test	a) With metabolic activation: 0 - 5000 µg/plate. b) Without metabolic activation: 0 - 5000 µg/plate.
Vehicle	Dimethylsulfoxide (DMSO).
Remarks – Method	No protocol deviations reported.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5000	> 5000	1500	Not observed
Present				
Test 1	> 5000	> 5000	1500	Not observed

Remarks – Results	Oily precipitate at and above 1500 µg/plate. No cytotoxicity was observed at any dose level. Negative and positive controls gave expected responses. No increase in revertant numbers was observed at any dose level either with or without S9.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Safepharm Laboratories Limited (1997g).

7.9. Genotoxicity – in vitro

7.9.1. Chromosome aberration test in Chinese Hamster Lung Cells (Study 1)

TEST SUBSTANCE	notified chemical
METHOD	EC Directive 2000/32/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.
Cell Type/Cell Line	Chinese Hamster Lung cell line isolated by Koyama et al (1970) and cloned by Ishidate and Sofuni (1958).
Metabolic Activation System	Rat liver microsomal S9 fraction from Aroclor 1254 treated rats.
Vehicle	Dimethylsulfoxide
Remarks – Method	No protocol deviations reported.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 1.79, 3.58*, 7.15*, 14.3*, 28.6*, 57.3	12 hours	12 hours
Test 2	0*, 1.79*, 3.58*, 7.15*, 14.3*, 28.6, 57.3	12 hours	12 hours
Present			
Test 1	0*, 3.58, 7.15, 14.3, 28.6*, 57.3*, 114.6*	4 hours	12 hours

Test 2	0*, 7.15, 14.3, 28.6*, 57.3*, 114.6*, 229.2	4 hours	12 hours

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	14.3	7.15	-	Not observed
Test 2		1.79	-	Not observed
Present				
Test 1	114.6	57.3	-	Not observed
Test 2		-	114.6	Not observed

Remarks – Results

The preliminary cytotoxicity tests showed evidence of a dose-related increase in cell toxicity with and without activation. The notifier states the presence of a precipitate may have affected the electronic cell counter giving falsely elevated counts in some cases. Microscopic assessment of the slides prepared from the preliminary cytotoxicity test showed metaphases present up to 114.6 µg/mL and 14.3 µg/mL in the 12-hour with and without activation cases.

Experiment 1 showed the expected level of toxicity similar to that seen in the preliminary toxicity study. The results of the cell counts at 12-hours showed a mean percentage compared with solvent control of 106, 101, 80, 77, 83 and 84% at 1.79, 3.58, 7.15, 14.3, 28.6 and 57.3 µg/mL, respectively, without activation and 108, 115, 112, 110, 93 and 90% at 3.58, 7.15, 14.3, 28.6, 57.3 and 114.6 µg/mL, respectively, with activation. In the cases of activation, no scorable metaphases, were observed at the treatment doses of 57.3 and 114.6 µg/mL. The results of the mitotic index at 12-hours showed a mean percentage compared with solvent control of 144, 172 and 79% at 3.58, 7.15 and 14.3 µg/mL without activation and 72, 49 and 71% at 28.6, 57.6 and 114.6 µg/mL, respectively, with activation. In all treatment cases with and without activation, no significant change in mean frequency of polyploid cells was observed at treatment doses up to 114.6 µg/mL as compared with solvent control.

Experiment 2 showed expected levels of toxicity similar to that seen in the preliminary toxicity study and Experiment 1. The results of the cell count at 12-hours showed a mean percentage compared with solvent control of 89, 88, 75, 74, 73 and 80% at 1.79, .58, 7.15, 14.3, 28.6 and 57.3 µg/mL, respectively, without activation and 101, 95, 94, 94, and 87% at 7.15, 14.3, 28.6, 57.3, and 114.6 µg/mL, respectively, with activation. In the cases without activation, no scorable metaphases were observed at 28.6 and 57.3 µg/mL as compared with solvent control. The results of the mitotic index at 12 hours showed a mean percentage compared with solvent control to 80, 81, 31 and 15% at 1.79, 3.58, 7.15 and 14.4 µg/mL, respectively, without activation and 63, 59 and 49% at 28.6, 57.3 and 114.6 µg/mL, respectively, with activation. In all treatment cases, no significant change in mean frequency of polyploid cells was observed with and without activation at

treatment doses up to 114.6 µg/mL as compared with solvent control.

Negative and positive controls gave the expected results. No statistically or biologically significant increases in the percentage of aberrant cells, above the vehicle control values, were recorded for any cultures treated with the test substance in either the presence or absence of metabolic activation. Positive controls confirmed the sensitivity of the test system. The notified chemical was toxic to Chinese Hamster Lung cells in vitro in all treatment cases with a very steep dose response curve.

CONCLUSION The notified chemical was not clastogenic to Chinese Hamster Lung cells treated in vitro under the conditions of the test.

TEST FACILITY Safepharm Laboratories Limited (1997h)

7.9.2. Chromosome aberration test in Chinese Hamster Lung Cells (Study 2)

TEST SUBSTANCE notified chemical

METHOD Guidelines for Screening Toxicity Testing of Chemicals and Guidelines for Toxicity Testing of Chemicals, Japanese Ministry of International Trade and Industries (JMITI)

Cell Type/Cell Line Chinese Hamster Lung cell line isolated by Koyama et al (1970) and cloned by Ishidate and Sofuni (1958).

Metabolic Activation System Rat liver microsomal S9 fraction from Phenobarbital and 5,6-benzoflavone treated rats.

Vehicle Dimethylsulfoxide.

Remarks – Method No protocol deviations reported.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 0.5*, 1*, 2*, 4, 8	24 hours	24 hours
Test 2	0*, 0.5*, 1*, 2*, 4, 8	48 hours	48 hours
Test 3	0*, 2.5, 5*, 10*, 20*, 40	6 hours	24 hours
Present			
Test 2	0*, 12.5, 25*, 50*, 100*, 200	6 hours	24 hours

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	6	4	20	Not observed
Test 2	6	4	″	Not observed
Test 3	13	40	″	Not observed
Present				
Test 1	6	200	″	Not observed

Remarks – Results Positive and negative controls demonstrated the validity of the study.

CONCLUSION The notified chemical was not clastogenic to Chinese Hamster Lung cells treated in vitro under the conditions of the test.

TEST FACILITY Genetic Laboratory JBC Inc (1996).

8 ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

No test and report for Ready Biodegradability has been provided. It will be assumed that the notified chemical is not readily biodegradable.

8.1.2. Bioaccumulation

TEST SUBSTANCE	notified chemical
METHOD	OECD TG 305 Bioconcentration: Flow-through Fish Test. EC Directive 98/73/EC C.13 Bioconcentration: Flow-Through Fish Test.
Species	Carp
Exposure Period	Exposure: 8 weeks
Auxiliary Solvent	Dispersing medium: polyoxyethylene hydrogenated castor oil.
Concentration Range	Nominal: 0.001 – 0.01 µg/L Actual: 0.00099 – 0.0099 µg/L
Analytical Monitoring	IR spectroscopy, HPLC and liquid scintillation counting.
Remarks - Method	The test concentrations were chosen on the result of a preliminary test using the 48 h LC50 of 3.74 mg/L from orange killifish. A primary stock solution was prepared in acetonitrile with 100 mg of ^{14}C-labelled test substance and 5 g of dispersing agent. Aliquots of the primary stock were added to dechlorinated water to make the desired test concentrations. Test water was analysed twice a week and three fish were collected from both exposure aquaria on weeks 2, 4, 6 and 8 after the introduction.
RESULTS	
Bioconcentration Factor	Maximum values of 77 and 76 at the high and low exposure levels, respectively.
CT50	
Remarks - Results	No mortalities or changes in appearance or behaviour were observed throughout the study. The concentration of the test substance in water was generally within a range of ±10% of the nominal concentration in both test concentrations. The concentration in fish reached steady state plateau after about 4 weeks in the test group.
CONCLUSION	The notified chemical is slightly bioconcentrating.
TEST FACILITY	Mitsubishi Chemical Safety Institute (1997).

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static. EC Directive 92/69/EEC C.1 Acute Toxicty for Fish-statc
Species	Rainbow Trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	Dimethylformamide
Water Hardness	100 mg $CaCO_3$/L
Analytical Monitoring	HPLC for substance concentration, also temperature, dissolved oxygen and pH.
Remarks – Method	Based on the results of a range test (96 h, 1.0 mg/L) five test

concentrations were selected. The test substance was suspected to be unstable in water, so a dosing trial was carried out using dynamic, continuous flow test conditions. Stock solutions containing the test substance were prepared in dimethylformamide. Oxygen content, pH and temperature were all satisfactorily maintained.

The measured concentrations of the samples ranged from 133% to 89% of the nominal concentration. The analytical recovery in the filtered samples ranged from 27 to 86%. The low recoveries were considered to be due to the chemical instability caused by the dissolved oxygen and inorganic ions present in the test media. The detection limit of the test was determined to be 0.010 mg/L.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	<LOQ	10	0	0	0	0	0
0.10	<LOQ	10	0	0	0	0	0
0.18	<LOQ	10	0	0	0	0	0
0.32	0.150	10	0	0	0	0	0
0.56	0.226	10	0	0	0	2	8
1.0	0.713	10	0	0	10	72	10

LC50	>1 mg/L at 24 hours 0.75 mg/L at 48 hours (nominal) 0.67 mg/L at 72 hours (nominal) 0.45 mg/L at 96 hours (95% C.I. of 0.41-0.56 mg/L, nominal)
NOEC	0.18 mg/L at 96 hours (nominal)
Remarks – Results	Sub-lethal effects of exposure were observed at test concentrations of 0.32 mg/L and above. These responses were swimming at the bottom of test vessels, loss of equilibrium and the presence of moribund fish.

CONCLUSION The notified chemical is highly toxic to Rainbow Trout

TEST FACILITY Safepharm Laboratories Limited (1997i)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – semi-static
EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – semi-static

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Dimethylformamide
Water Hardness	270 mg $CaCO_3$/L
Analytical Monitoring	HPLC for substance concentrations, also temperature, dissolved oxygen and pH.
Remarks - Method	Based on the results of a range test (no immobilisation at test concentrations of 0.0010 and 0.010 mg/L) nine test concentrations were selected. Prestudy stability work showed the test substance to be unstable in water, so a semi static regime was selected. Oxygen content, pH and temperature were all satisfactorily maintained. The test substance was prepared using a preliminary solution in acetonitrile:dimethylformamide (98:2). The measured concentrations of

the samples ranged from 110% to less than the quantitation of the nominal concentration. The observed variations were considered to be due to the chemical instability caused by the dissolved oxygen and inorganic ions present in the test media.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	<LOQ	2 replicates of 10	0	0
0.010	<LOQ	"	0	0
0.018	<LOQ	"	0	0
0.032	<LOQ	"	0	0
0.056	<LOQ	"	0	2
0.10	<LOQ	"	0	14
0.18	0.122	"	0	20
0.32	0.136	"	0	20
0.56	0.402	"	8	20
1.0	0.709	"	16	20

LC50 0.65 mg/L at 24 hours (nominal)
0.085 mg/L at 48 hours (nominal)

NOEC 0.032 mg/L at 48 hours (nominal)

Remarks - Results Analysis of the test solutions throughout the study showed measured concentrations to range from less than the limit of quantitation to 110% of the nominal value and physical effects were not reported.

CONCLUSION The notified chemical is highly toxic to *Daphnia magna*.

TEST FACILITY Safepharm Laboratories Limited (1997j)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test.
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species *Scenedesmus subspicatus*

Exposure Period 72 hours

Concentration Range Nominal: 1 mg/L

Auxiliary Solvent Dimethylformamide.

Water Hardness Not stated.

Analytical Monitoring HPLC

Remarks - Method The test concentration of 1.0 mg/L was the highest attainable test concentration that could be prepared due to the limited solubility of the test substance in water and auxiliary solvent and having due regard the amount of auxiliary solvent permitted in the study under these guidelines.

The test substance was prepared using a preliminary solution in dimethylformamide. During preliminary solubility work performed, precipitation of the test substance occurred at concentrations in excess of 1.0 mg/L thereby indicating this to be the maximum limit of water solubility of the test substance under these test conditions. The measured concentrations of the samples ranged from 99% to 35%. The observed variations were considered to be due to the chemical instability caused by the dissolved oxygen and inorganic ions present in the test media.

Remarks - Results The 72 h EbC50 was >1 mg/L as was the 0-72 h ErC50. Therefore the

	NOEC was ≥1 mg/L. As no parent test substance was detectable in the test samples, the EC50 values were expressed in terms of the nominal concentrations.
CONCLUSION	The NOEC for the alga *Scenedesmus subspicatus* was 1 mg/L. The notified chemical is not toxic to algae up to the level of its water solubilty.
TEST FACILITY	Safepharm Laboratories Limited (1997k)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE	notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated sewage sludge, synthetic sewage.
Exposure Period	3 hours
Concentration Range	Nominal: 0 - 1000 mg/L
Remarks – Method	Following a preliminary range-finding test using test concentrations of 100 and 1000 mg/L, activated sludge was exposed in the definitive test to an aqueous solution of the test material at the test concentration of 1000 mg/L in a "limit test" for a period of 3 hours at 21°C with the addition of a synthetic sewage as a respiratory substrate. The rate of respiration was determined after 30 minutes and 3 hours contact time and compared to data for the control and a reference material, 3,5-dichlorophenol.
RESULTS	
IC50	>1000 mg/L
NOEC	100 mg/L
Remarks – Results	Inhibition at 100 mg/L was 3% at 3 hours.
CONCLUSION	The effect of the substance on the respiration of activated sewage sludge microorganisms gave a 3-hour EC50 of >1000 mg/L. The validation criteria for the control respiration rates and reference material EC50 value (8 mg/L) have been satisfied. It was considered unnecessary and unrealistic to test at concentrations in excess of 1000 mg/L.
TEST FACILITY	Safepharm Laboratories Limited (1997l)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

It is expected that very little exposure to the environment is likely to occur during the use of the imported notified chemical. The majority of wastes containing the notified chemical generated during formulation and moulding are expected to be disposed of to landfill or incinerated. Up to 50 kg per annum of the notified chemical could be disposed of to landfill, including as residues in empty containers of hardener. Most of this waste would be cured polymeric resin in which case the chemical will be incorporated into the inert matrix of the resin and be unavailable to the environment. If the containers are destroyed in landfill the notified chemical is unlikely to leach into the water compartment dues to its low solubility. The calculation of the Predicted Environmental Concentration (PEC) could not be done.

At the end of their useful lives articles made from the resin containing the notified chemical would be disposed of to landfill.

9.1.2. Environment – effects assessment

The ecotoxicological data provided by the notifier indicate that the chemical is highly toxic to fish and aquatic invertebrates. The most sensitive species were *Daphnia magna* with a reported EC50 of 85 µg/L at 48 hours, so a PNEC may be calculated to be 0.85 µg/L, using a safety factor of 100.

9.1.3. Environment – risk characterisation

The notified chemical does not pose a significant risk to the environment based on its reported use pattern because there will be very low environmental exposure. The majority of the chemical will form the cured polymeric matrix of the lenses in which it is proposed to be used. The majority of the notified chemical will eventually be disposed of to landfill as a constituent of the final products at the end of their useful lives.

Despite the very low PNEC, it is appreciated that there is unlikely to be any release of the chemical into the aquatic environment under the proposed use patterns and levels are expected to be well below the safety margin.

Tests show that the notified chemical has a low potential to bioaccumulate. Abiotic or slow biotic processes are expected to be largely responsible for the eventual degradation of the notified chemical as it is not expected to be readily biodegradable.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Skin contact will be the main route of exposure, although eye contact via inadvertent splashes, e.g, during quality assurance testing of the 200 L steel drums, is also possible. Given the molecular weight of the notified chemical, absorption through intact skin cannot be excluded. All workers handling the notified chemical wear PPE such as safety glasses, gloves and protective clothing and have access to the Material Safety Data Sheet.

Transport, Storage and Supply

Exposure to the notified chemical is not expected during transport, storage and supply provided the 200 L drums containing the notified chemical remain intact. Transport, storage and supply workers would only be exposed to the notified chemical in the event of an accidental spill or breach of the 200 L steel drums. The nature of the packaging used for transport, i.e. steel drum, minimises the likelihood of release or loss of the notified chemical.

Processing

Exposure to the notified chemical may occur during transfer of the notified chemical from the 200 L drums into the mixing vessel via residual or leaking solution from transfer hoses, fittings, and/or pumps.

Mixing occurs mechanically in a closed system and thus exposure is limited. Exposure to the notified chemical and formulated resin containing the notified chemical during manufacturing is controlled through the use of automatic equipment, engineering control measures, such as sealed vessels and the use of PPE such as safety glasses, gloves and protective clothing. Inhalation exposure is expected to be low given the notified chemical's low vapour pressure and the use of general exhaust ventilation.

Exposure to the formulated resin containing the notified chemical is not expected to occur during automated filling of mould assemblies. Whilst exposure to the notified chemical via the formulated resin from accidental spills and splashes may occur during the manual loading of the curing ovens, this is expected to be limited due to the use of PPE such as safety glasses, gloves and protective clothing.

Exposure to odours and vapours generated during the curing operation and at high temperatures is expected to be low, given that curing ovens are located in a remote area of the workplace with exhaust ventilation and curing-oven fume extraction.

Exposure to the notified chemical is not expected when handling the finished plastic lenses as no residual polymer nor residual constituents are identified in the finished lenses.

Maintenance and Engineering
Maintenance and engineering workers will have limited exposure to the notified chemical by skin contact and a potential for accidental ocular exposure as they are required to repair existing equipment and commission any new equipment that is introduced into the production area. Any dermal exposure to the formulated resin via drips, spills and accidental splashes/releases and from contact with contaminated equipment or accidental ocular exposure will be mediated by the use of PPE such as safety glasses, gloves and protective clothing.

Quality Assurance
Quality assurance workers will have low exposure to the notified chemical by skin contact and a potential for accidental ocular exposure as they are required to take samples for quality control purposes upon arrival of the 200 L drums containing the notified chemical at the plant. This exposure, however, is expected to be limited due to the use of PPE such as safety glasses, gloves and protective clothing.

Emergency
Emergency Personnel will be involved in clean up operations in the event of an accidental spill. There is a risk of dermal (and ocular) exposure to the notified chemical and the formulated resin via accidental splashes during such clean up operations. This exposure, however, is expected to be limited due to the use of PPE such as safety glasses, gloves and protective clothing.

Cleaning and Waste Disposal
Dermal and a potential for accidental ocular exposure to the notified chemical in a dilute solution may occur during solvent rinsing of manufacturing equipment via residual or leaking solution from hoses, fittings, and/or pumps and the collection of this rinsate into drums. This exposure, however, is expected to be minimal as all cleaning and cleaning and waste disposal workers wear PPE such as safety glasses, gloves and protective clothing.

9.2.2. Public health – exposure assessment

Consumers of the ophthalmic lenses are expected to make dermal and ocular contact with the notified chemical in its final polymerised form but such contact is not via a bioavailable form of the notified chemical. Residual notified chemical in the ophthalmic lenses is negligible due to the oven-curing process, which results in the incorporation of the notified chemical into a biologically unavailable polymer matrix. Exposure to the notified chemical is, therefore, assessed as low due to the inert nature of the notified chemical in its final cured form.

9.2.3. Human health – effects assessment

Toxicological data for the notified chemical for the following health end points were submitted:

- acute oral and dermal toxicity
- primary dermal irritation

- eye irritation
- skin sensitisation
- 28-day subacute oral toxicity (gavage); and
- mutagenicity.

An acute oral and dermal toxicity study in the rat and rabbit, respectively, indicated the notified chemical is of low toxicity via the oral and dermal routes. A primary dermal irritation test in rabbits showed the notified chemical is moderately irritating to skin with a Primary Irritation Index value of 2.5. An eye irritation study in the rabbit showed a maximum group mean score of 1.3 and indicated the notified chemical is slightly irritating to the eye. A skin sensitisation (Magnusson & Kligman Maximisation) test in guinea pigs, showed sensitisation in 10 of 10 animals and indicated evidence of reactions indicative of skin sensitisation under the conditions of the test. A reverse mutation test in *Salmonella typhimurium* and chromosomal aberration tests in Chinese Hamster Lung Cells (*in vitro*) indicated the notified chemical was not mutagenic to bacteria nor clastogenic under the conditions of the tests.

Based on a 28-day subacute oral toxicity study in rats, a NOEL in male rats of 50 mg/kg/day was indicated based on increased salivation, reduced body weight gain, reduced food efficiency, macroscopic findings and/or discoloured testes, reduced absolute testes weight and histopathological findings of testicular atrophy at 250 and 1000 mg/kg bw/day. In addition, a NOEL in female rats of 250 mg/kg/day was indicated based on a decrease in bodyweight gain at 1000 mg/kg bw/day (the highest dose used in the study).

Based on the available data, the notified chemical is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004) on the basis of its skin sensitisation and skin irritant effects.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is moderately irritating to skin and displayed evidence of reactions indicative of skin sensitisation. The main concerns for occupational health are skin irritation and sensitisation effects. Any products containing equal to or more than 1% notified chemical are classified as hazardous, and any workers who become sensitised to the notified chemical should avoid further handling of it. Risk from repeated exposure is considered to be low since at 50 mg/kg/day (the NOAEL), the amount of product equivalent will be large and workers would not be expected to be exposed repeatedly to large amounts.

Dermal contact will be the main route of exposure and the occupational exposure is considered to be low. Pumps are used for transferring processes and automatic equipment and a closed production system is used for the formulation and filling of the mould assemblies with the liquid resin containing the notified chemical. In addition, the engineering controls such as automation and enclosure are in place and workers will wear personal protective equipment. Therefore, the adverse health risk for workers handling the notified chemical is assessed to be low, however, precautions are necessary as the notified chemical is a skin irritant and sensitiser.

9.2.5. Public health – risk characterisation

The notified chemical is not available to the general public and nil residue of the notified chemical is expected in the finished lenses because the notified chemical is incorporated into a polymeric structure as a result of the thermal curing process used during the manufacturing process. Consequently, the notified chemical is not bioavailable and as such unlikely to penetrate biological membranes and is not expected to cause irritation of the skin nor sensitization. Based on the notified use, the notified chemical will not pose a significant hazard to public health when used in the proposed manner.

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

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*. The classification and labelling details are:

R38: Irritating to skin
R43: May cause sensitisation by skin contact

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	*Hazard statement*
Skin sensitisation	1	May cause an allergic skin reaction

Based on the available data, the notified chemical does not meet the criteria for skin irritation under the GHS system. Based on the available data for the aquatic environment it should be classified: Chronic category 1.

10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

Based on the strong evidence of the sensitisation potential of the notified chemical and the essential requirement for PPE to mitigate such a hazard, there is Moderate 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 based on reported use patterns.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

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

12. RECOMMENDATIONS

REGULATORY CONTROLS
Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - R43: May cause sensitisation by skin contact
  - R38: Irritating to skin
- Use the following risk phrases for products/mixtures containing the notified chemical:
  - concentration ≥ 1%: R43: May cause sensitisation by skin contact
  - concentration ≥ 20%: R38 Irritating to skin
- Use the following risk and safety phrases for products/mixtures containing the notified

chemical:

– R38 Irritating to skin
– S 37 Wear suitable gloves
– ≥ 20% R38 Irritating to skin
– ≥ 1% S24 Avoid contact with skin

Suppliers should label the notified chemical with the signal word 'Hazardous' and the risk phrases listed above.

Health Surveillance

- As the notified chemical is a skin irritant and displayed evidence of reactions indicative of skin sensitisation, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of irritant contact dermatitis.

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 in the product FSH and liquid resin:

  – Protective clothing
  – Chemical resistant gloves or gauntlet
  – Chemical gloves or safety glasses

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

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:

  – sensitised workers should be advised not to further handle the notified chemical
  – MSDS should be provided to the authorised medical practitioner responsible for health surveillance in the workplace

- 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 control measures should be implemented by the applicant to minimise environmental exposure during use of the notified chemical and liquid resin:

  – not allow material or rinsates from lens manufacturing equipment to enter drain, sewers or water course.

Disposal

- The notified chemical should be disposed of by incineration or secure landfill.

Emergency procedures

- Spills of the notified chemical and liquid resin should be contained with suitable adsorbent material and care should be exercised not to allow material to enter drains and watercourses. The adsorbent material should be transferred to plastic bags sealed

inside a drum and incinerated.

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(1) of the Act; if
- Due to the very high toxicity to fish and aquatic invertebrates a secondary notification should be lodged if uses are intended where there is a more significant release to water.

or

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

The Director will then decide whether secondary notification is required.

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