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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

TGBMA Monomer

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

TGBMA Monomer

1. APPLICANT

Sola International Holdings Limited of 19 Cooroora Crescent, LONSDALE SA 5160 has submitted a standard notification statement in support of their application for an assessment certificate for TGBMA Monomer.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae, molecular weight, method of detection and spectral data, purity, details of exact import volume, and specific details of the nature of work done have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Name:	TGBMA Monomer
Spectral Data:	Spectral data were submitted to characterise the identity of the notified chemical

3. PHYSICAL AND CHEMICAL PROPERTIES

All physico-chemical studies were performed on standard technical grade of the notified chemical in testing facilities that complied with OECD Principles of Good Laboratory Practice and methods that followed OECD test guidelines or EC guidelines (European Commission, 1992).

Appearance at 20°C and 101.3 kPa:	Colourless to pale yellow viscous liquid
Boiling Point:	Decomposes at 214°C
Pour Point:	-12°C
Specific Gravity:	1.38 at 20°C
Vapour Pressure:	7.1×10^{-8} kPa at 25°C

Water Solubility:	20.9 mg/L at 20°C
Partition Co-efficient (n-octanol/water):	log P_{ow} <1.6 to >6.2
Hydrolysis as a Function of pH:	Not determined (see comments below)
Adsorption/Desorption:	Log K_{oc} <1.25 to >5.63 at 20°C
Dissociation Constant:	Not determined (see comments below).
Surface Tension	72.5 mN/m (ca 21.8 mg/L at 20°C)
Particle size:	Not applicable (liquid)
Flash Point:	182+ 2°C (closed cup)
Flammability Limits:	Not determined; combustible liquid
Autoignition Temperature:	312+ 5°C
Explosive Properties:	Not explosive
Reactivity/Stability:	Considered stable.

Comments on Physico-Chemical Properties

The boiling point of the notified chemical was not determined as the notified chemical decomposes at 214°C. From vapour pressure data and the chemical structure the estimated theoretical boiling temperature is > 360°C (Hogg,1999).

The vapour pressure of the notified chemical was determined by a vapour pressure balance method similar to OECD TG 104 to be 7.1 x 10^{-8} kPa at 25°C (Tremain, 1998b).

The water solubility of the notified chemical determined by a flask shaking method similar to OECD TG 105 is 20.9 mg/L at 20+0.5°C (Hogg, 1999). It was noted that this value is an approximation of the results obtained because the notified chemical is a mixture of oligomers and monomers.

Hydrolysis of the notified chemical was not determined. The notifier indicates that not only is the notified chemical poorly soluble but that it is a multi-component system for which an adequate method could not be developed. The notified chemical contains ester linkages that could be expected to undergo hydrolysis under extreme pH. However, due to the low water solubility, this is unlikely in the environmental pH range of between 4 and 9.

The partition coefficient log P_{OW} of TGBMA determined using a reverse phase HPLC method similar to OECD TG 117 is < 1.6 to > 6.2 at 20°C (Hogg, 1999). The wide range represents values for the multiple components of the mixture.
The adsorption/desorption coefficient of the notified chemical determined by HPLC (OECD draft guideline, July 1997) is < 1.25 to > 5.63 at 20°C (Hogg, 1999). The wide range represents values for the multiple components of the mixture.

No dissociation constant data was provided for the notified chemical. The notifier indicates that the notified chemical is a complex mixture, which contains 2-mercaptoacetic acid with pKa values 3.7 and 10.4. The notifier, using the chemical structure for the notified chemical and employing Hammett and Taft equations, calculated the pKa of the notified chemical to be 6.5 to 9.3 (Hogg, 1999).

The surface tension of a 21.8 mg/L solution of the notified chemical was determined to be 72.5 mN/m at 20°C according to method A5 Commission Directive 92/69/EC (Hogg, 1999). The notified chemical is not considered to be a surface-active material.

4. PURITY OF THE CHEMICAL

Degree of Purity: Very high

Hazardous Impurities: Contains two impurities identified as hazardous:

the first impurity is present at 4% (w/w); the classification for the neat chemical is Toxic, R23/24/25- Toxic by inhalation, in contact with skin and if swallowed; Corrosive, R34- Causes burns; and

the second impurity is identified as a contact allergen and is present at 1% (w/w)

Non-hazardous impurities (>1%): None

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured in Australia, but will be imported by sea in 200 kg plastic lined steel drums. Import volumes by the fifth year will be less than 300 tonnes. The imported solution contains a high percentage of notified chemical. The notified chemical will be used in the manufacture of plastic ophthalmic lenses, whereby it will be formulated with other liquid resins and additives at a final concentration between 10-50%. During 1998, the notified chemical was in use in Australia under a commercial evaluation permit granted under section 21G of the Act.

6. OCCUPATIONAL EXPOSURE

Transport and storage: 0.25 hour/day
The notified chemical will be imported in 200 kg plastic lined steel drums by sea and will be transported from the dockside by road to the notifer's warehouse for storage and use. Waterside, transport and storage workers would only be exposed to the notified chemical in the event of a spill. The nature of the packaging used for transport minimises the likelihood of release or loss of the chemical in incidents.

If spillage occurs, the notifier stated that spills will be contained with an absorbent material such as sand or vermiculite and stored in specified locations. Persons involved in clean up tasks would be required to wear thick nitrile gloves, wrap-around protective eyewear, appropriate footwear affording full splash protection to the feet, polyester/nylon protective coats, disposable plastic aprons and half face respirators equipped with organic vapour cartridges.

The chemical will be stored in a secured area separate from the workplace.

Process workers: 7 hours/day, approximately 260 days/year
Exposure to the notified chemical may occur during the multi-stage ophthalmic lens manufacturing process. Drums of the notified chemical are transferred from the storage area into an industrial loading cell by a special lifting device. The chemical is automatically pumped into mixing vessels and formulated with other liquid monomers and additives in a closed system, with automated stirring. Accordingly, operators may be exposed to the neat notified chemical during connection/disconnection of pump hoses.

The liquid resin formulation containing the notified chemical is then forced into mould assemblies via a semi-automatic filling machine. Operators may be exposed to the notified chemical (10-50% in liquid resin) during loading/unloading of mould assemblies from the filling machine (because waste liquid resin is generated at this stage) and when loading mould assemblies into ovens for curing. Exposure from handling, cleaning and disassembling the cured assemblies and plastic lenses is expected to be negligible as the notified chemical is polymerised into the solid lenses and is no longer separately available. The notifier stated that between 12 and 27 workers would be involved in the manufacturing process.

Maintenance and Cleaning: 0.5-1 hour/day
Workers will be exposed to the notified chemical during regular equipment maintenance and cleaning, and at disposal of waste liquid resin and acetone washings. The notifier stated that acetone is used to clean the equipment and areas where the chemical is formulated. Mixing and holding vessels and filling pots are cleaned annually, whereas filling lines are cleaned weekly. Between 3 and 5 workers would be involved in maintenance operations and 1-2 in clean up tasks.

QA Staff and Engineers: 0.5 hour/day
Formulation adjustment and QA testing of the liquid resin will involve one engineer and one

QA staff. Although not described in the submission, QA testing typically involves sampling of vessel contents during manufacture for laboratory analysis. Exposure to the notified chemical may occur via inhalation of aerosols, or by skin and/or eye contact, but is expected to be low given the engineering control measures and the use of personal protective equipment when handling the notified chemical.

Exposure to the neat and diluted notified chemical would mainly occur via skin contact from spills, drips or waste liquid resin. Ocular exposure may also occur either directly or indirectly through contaminated hands. Although aerosols and vapours may be generated, exposure by inhalation would be low because the notified chemical has a low vapour pressure and formulation occurs in an enclosed semi-automated system, and the operation area is fitted with local exhaust ventilation. Curing ovens are also locally exhausted to reduce odours generated during the manufacturing operation.

Workers involved in the manufacturing operations, particularly prior to the curing stage, are required to wear thick nitrile or rubber lined gloves[1], polyester/cotton laboratory coats and safety spectacles with side shields.

The notifier stated that safe job handling procedures have been developed for all production and maintenance tasks, and all workers are trained in the safe handling and use of hazardous chemicals.

7. PUBLIC EXPOSURE

TGBMA Monomer will enter the public domain as plastic ophthalmic lenses containing the notified chemical at a concentration of 10-50%. Although the public will make dermal contact with the notified chemical, exposure is likely to be negligible since the notified chemical in the plastic lens is in a cured state and is not expected to leach out. The potential for public exposure to the chemical during transport, formulation and use or from disposal is assessed as negligible.

8. ENVIRONMENTAL EXPOSURE

Release

After importation, the notified chemical will be transported *via* road without repackaging in the closed 200 kg steel drums; potential release would only be through accidental spills. The MSDS details procedures to protect the environment in these cases. Once received by the notifier, the drums are stored separately from the workplace until required.

The notifier indicates that some release of the notified chemical will occur during formulation *via* mixing vessels, holding vessels, filling pots, filling lines and empty drums. The notifier estimates that the amount lost will be 5 kg per day based on 100 tonnes of import volume per

[1] A glove permeation and degradation study revealed no breakthrough of the notified chemical was observed for thick nitrile or rubber lined gloves after an 8 hour exposure period.

year. Production will occur up to 260 days per year, so 1.3 tonnes of chemical will be lost per year. At a maximum import of < 300 tonnes per year, approximately 3 tonnes of notified chemical may be lost per year.

The notified chemical will not be directly marketed to the public, but formulated and polymerised into ophthalmic lenses only at the notifier's site.

Fate

All released TGBMA Monomer waste will be contained on-site and treated in accordance with the notifier's waste EPA licence. During the cleaning stage of the manufacturing process there is no release to the cleaning water as the chemical is in polymeric form. The notifier indicates that the TGBMA Monomer is completely polymerised with no residual monomer being contained within the final finished lenses. All waste water at the site is treated to remove sediments and adjusted to pH 5-10 before release to the sewage system.

The ready biodegradability of the notified chemical was examined by exposure to activated sewage sludge microorganisms at a concentration of 10 mg/L at 21°C for 28 days (Mead, 1999). Degradation of the notified chemical was assessed by the determination of carbon dioxide produced. The test material attained 64% degradation after 28 days. However, the 10 day window criterion was not met, therefore, the notified chemical cannot be considered to be readily biodegradable under the terms and conditions of the Modified Sturm Test OECD TG 301B.

The notifier indicates that all waste monomer containing odorous chemicals is disposed of by incineration. Residues from equipment and containers cleaned with acetone will also be incinerated. The notifier supplies no information concerning the fate of the notified chemical once incinerated. However, it is noted that it would experience the same temperature required for destruction of acetone and would be burnt to oxides of carbon and hydrogen as well as oxides of sulfur.

The bulk of the notified chemical will be associated with the lenses and the ultimate fate will be to landfill, in a very diffuse manner in locations country wide. In landfill, the chemical will be immobile as it exists in a solid, high molecular weight polymeric form that is expected to be very insoluble in water.

The notifier indicates that it would be difficult to predict the bioaccumulation of the notified chemical as it is a complex mixture with a wide range of molecular weights and partition coefficients. However, it is noted that the substance shows considerable potential for biotic transformation. It is reasonably biodegradable as well as unstable in aqueous solution and as such should not bioaccumulate.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of TGBMA Monomer

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	637 mg/kg bw (females); >500 mg/kg bw (males)	(Allen, 1999a)
acute dermal toxicity	rat	>2 000 mg/kg bw	(Allen, 1999b)
skin irritation	rabbit	very slightly irritating	(Allen, 1999c)
eye irritation	rabbit	moderately irritating	(Allen, 1999d)
skin sensitisation	guinea pig	strongly sensitising	(Allen, 1999e)

9.1.1 Oral Toxicity (Allen, 1999a)

Species/strain:	Rat/Sprague-Dawley CD
Number/sex of animals:	5/sex/dose; females were tested at three doses; males were tested at one dose
Observation period:	14 days
Method of administration and doses:	Oral (gavage); single doses (dose volume 10 mL/kg); females were administered doses of 500, 707 or 1 000 mg/kg bw; males were administered a dose of 500 mg/kg bw
Test method:	OECD TG 401
Mortality:	Within 24 hours of dosing, four females at 707 mg/kg bw and five females at 1 000 mg/kg bw were found dead
Clinical observations:	All dose groups were observed to share a hunched posture following dosing, which persisted to day 4. Other observed signs included lethargy, ataxia, diarrhea, decreased respiratory rate, laboured respiration and gasping respiration in animals belonging to the 500 and 707 mg/kg bw dose groups; incidents of loss of righting reflexes were also observed in the latter groups. All surviving animals appeared normal 3-5 days post dosing

Morphological findings:	Dosing related deaths: haemorrhagic lungs, dark liver, pale spleen, dark kidneys, pale gastric mucosa, sloughing of the non-glandular epithelium of the stomach and haemorrhage of the small intestines; Euthanised animals: no abnormalities noted
Comment:	Males were included in the test to assess potential differences between sexes in sensitivity to the test substance. From the findings of the study, males were considered as not markedly more sensitive to the test substance than females.
LD_{50}:	637 mg/kg bw (females); >500 mg/kg bw (males)
Result:	The notified chemical was of low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Allen, 1999b)

Species/strain:	Rat/Sprague-Dawley CD
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	A single 24 hour, semi-occluded dermal application to an area of shorn intact skin (equivalent to ~ 10% of total body surface area) at a dose of 2 000 mg/kg bw; after the exposure period, residual test material was removed with distilled water
Clinical observations:	No signs of systemic toxicity were observed during the study period.
Dermal reactions:	All females showed signs of skin irritation 3-12 days after dosing; these included superficial cracking of the epidermis, crust formation and glossy skin. However, erythema and oedema were not observed; all Draize scores were zero. Signs of skin irritation were not observed in the male group during the study period.
Mortality:	Nil
Morphological findings:	No abnormalities observed at necropsy

Test method: OECD TG 402

LD_{50}: > 2 000 mg/kg bw

Result: the notified chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

Claims were made and accepted by the notifier for variation of Schedule Requirements for this toxicological end-point as the inhalation route of exposure may not be relevant as the substance is described as viscous. The notifier considers that the acute oral and dermal toxicity were the most appropriate studies to evaluate the acute toxicity hazards of the notified chemical.

9.1.4 Skin Irritation (Allen, 1999c)

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 3 males

Observation period: 72 hours

Method of administration: 0.5 mL of test substance applied to an area (~ 6.25 cm^2) of shorn intact skin of the back of each rabbit and held under semi occlusive dressing. After 4 hours, residual test substance was removed with methylated spirits.

Test method: OECD TG 404

Draize scores (Draize, 1959):

Skin reaction/ Animal				
		Observation Time (hours)		
Erythema/Eschar	***1***	***24***	***48***	***72***
1	1	0	0	0
2	1	0	0	0
3	1	0	0	0
Oedema				
1	1	0	0	0
2	0	0	0	0
3	0	0	0	0

Result: the notified chemical was very slightly irritating to the skin of rabbits

9.1.5 Eye Irritation (Allen, 1999d)

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 3 males

Observation period: One animal was observed over a period of 7 days;
Two animals were observed over a period of 14 days.

Method of administration: One animal was tested initially to assess the initial pain reaction: 0.1 mL of the test substance was instilled into the conjunctival sac of the right eye; the left eye served as the control.

The remaining two animals were treated with local anaesthetic (one drop instilled into both eyes) prior to the instillation of the test substance following the procedure described above.

Test method: OECD TG 405

Draize scores (Draize, 1959) of non-irrigated eyes:

	Time after instillation																	
Animal	***1 hr***			***1 day***			***2 days***			***3 days***			***7 days***			***14 days***		
Cornea	***o***		***a***	***o***		***a***	***o***		***a***	***o***		***a***	***o***		***a***	***o***		***a***
1	0		0	[1]		2	1		2	1		1	(		0	-		-
2	0		0	1		3	2		2	2		2	(		0	0		0
3	0		0	1		1	1		1	1		1	(		0	0		0
Iris																		
1		0			1			1			0			0			-	
2		0			1			1			1			0			0	
3		0			1			1			0			0			0	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	2	2	2	2	2	3	2	2	2	2	2	1	0	0	0	-	-	-
2	2	2	2	2	2	3	2	2	2	2	2	1	1	1	0	0	0	0
3	2	2	3	2	2	3	2	2	2	2	2	1	1	1	0	0	0	0

[1] see Attachment 1 for Draize scales
o = opacity a = area r = redness c = chemosis d = discharge

Mean scores (24, 48, 72 hours observation):

Animal	*Corneal opacity*	*Iridial inflammation*	*Conjunctival redness*	*Conjunctival chemosis*
1	1	0.7	2	2
2	1.7	1	2	2
3	1	0.7	2	2

Comment: All rabbits were observed to have translucent corneal opacity, iridial inflammation and moderate conjunctival irritation. Treated eyes appeared normal at day 7 (one animal) or 14 (two animals)

Result: The notified chemical was moderately irritating to the eyes of rabbits

9.1.6 Skin Sensitisation-Magnusson and Kligman Maximisation Method (Allen, 1999e)

Species/strain: Guinea pigs/Albino Dunkin-Hartley

Number of animals: 20 males (test group), 10 males (control group);
10 females (rechallenge control group).

Induction procedure: test animals:
Day 1: three pairs of intradermal injections (0.1 mL) into the dorsal skin of the scapular region:

- Freund's complete adjuvant (FCA) 1:1 in distilled water;
- the test substance, 5% w/v in arachis oil BP;
- the test substance at 5% w/v emulsified in a 1:1 mixture of FCA and distilled water;

Day 7 - filter paper saturated with neat test substance was applied to the treated area and held under occlusive dressing for 48 hours;

control animals:
treated similarly to test animals omitting the test substance from the intradermal injections and topical application.

Skin reactions following, Intradermal (i.d.) and Topical Induction:

Adverse skin reactions were observed in test group animals after the *i.d.* and topical induction procedures.

No skin reactions were noted at induction sites of control group animals.

Comment:

Evaluation of erythema and oedema were not possible in some test group animals because of scab formation or bleeding wounds caused by animals scratching the test site.

No skin reactions were observed in the control group animals.

Challenge procedure:

test and control animals:
Day 21: filter paper saturated with 50% w/v or 25% w/v of test substance in acetone, was applied to sites on the right and left flank respectively, and held under occlusive dressing; after 24 hours the test sites were swabbed with cotton wool soaked in diethyl ether to remove residual test material.

Test method:

OECD TG 406

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hrs****	***48 hrs****	***24 hrs****	***48 hrs****
25%	14**/20	11/20	0/10	0/10
50%	18/20	14/20	0/10	0/10

* time after patch removal
** number of animals exhibiting positive response, ≥ Grade 1

Skin reactions after topical challenge:

Besides erythema and oedema, desquamation, loss of skin elasticity and small superficial scattered scabs were reported in some test group animals; desquamation only was observed in a few control group animals.

Re-challenge procedure

Day 42;
The challenge procedure was repeated on untreated skin areas of the test group and on 10 control animals that had received *i.d.* injections of FCA.

Re-challenge outcome:

Challenge concentration	Test animals		Control animals	
	*24 hrs**	*48 hrs**	*24 hrs**	*48 hrs**
25%	9**/20	7/20	0/10	0/10
50%	15/20	11/20	0/10	0/10

*time after patch removal
** number of animals exhibiting positive response, ≥ Grade 1

Skin reactions after topical re-challenge: Incidents of desquamation, loss of skin elasticity, small superficial scattered scabs, crust formation, superficial cracking of the epidermis, and hardened light brown coloured scabs were observed in some test group animals at the re-challenge site. The severity of these reactions prevented the evaluation of erythema and oedema at the re-challenge site in two animals.

No skin reactions were noted at the re-challenge sites of control group animals at 24 and 48 hours observations.

Result: the notified chemical was strongly sensitising to the skin of guinea pigs.

9.2 Repeated Dose Toxicity (Jones *et al*. 1999)

Species/strain: Rat/ Sprague-Dawley Crl:CD BR

Number/sex of animals: 10/sex/group (control and treatment groups); there were no recovery groups.

Method of administration: Oral (gavage); vehicle: anhydrous polyethylene glycol 400; dose volume: 2 mL/kg bw.

Dose/Study duration:: 0, 1.5, 15, 150 mg/kg bw /day for 28 consecutive days.
Test method: OECD TG 407

Mortality: One female at 150 mg/kg/day bw was found dead on day 13; no obvious clinical signs were observed prior to death. No other unscheduled deaths occurred at this or other doses.

Clinical observations

No toxicologically significant clinical findings were observed in treated or control animals. Animals at 150 mg/kg bw showed increased salivation approximately two minutes after dosing from day 13 to day 24, which on occasions was found to persist up to one hour

after dosing. In addition, at the same dose level a female developed transient noisy respiration on day 10 followed by red/brown staining of the fur from day 14 to day 23; another female revealed noisy respiration five hours after dosing on day 21 only.

No significant differences were identified between the control and test groups in all other functional observations, behavioural assessments, functional performance tests, sensory reactivity assessments, body weight, and food/water consumption.

Clinical chemistry/Haematology

No treatment related changes were detected in blood chemical or haematological parameters.

Pathology

Organ weights
Group-mean absolute and relative organ weights for both test and control group animals revealed no treatment related organ weight changes. However, a statistically significant increase in absolute kidney weight was observed for males at 150 mg/kg bw/day. This result was considered by the authors to be incidental in light of the bw absence of a similar effect in relative kidney weight. Also observed was a reduction in the relative testes weight for one animal in the 1.5 mg/kg bw /day group. In the absence of a dose related response the authors considered this difference to be incidental.

Necropsy
No abnormalities were detected in control and test groups at necropsy. Normal postmortem changes were detected in the 150 mg/kg/day bw female found dead on day 13 together with a pale spleen and gastric changes identified as reddening of the glandular gastric epithelium and a raised limiting ridge.

Histopathology
Examination of tissues from the control and 150 mg/kg/day bw groups revealed no significant treatment related histopathological changes. The single unscheduled death (see above) was due to haemorrhage from gastric erosion; pulmonary, thymus and adrenal terminal haemorrhage was also present.

Other morphological changes were reported to be those commonly observed in laboratory animals. No differences occurred in incidence or severity between controls and test animals that were considered to be toxicologically relevant.

Range finding study: In the seven days range finding study mortality was observed at 400 and 700 mg/kg bw/day. Necropsy of animals at these doses revealed thinning or pallor or reddening of the glandular/non-glandular gastric epithelium. Reddening of the non-glandular epithelium was also observed in one animal treated at 150 mg/kg bw/day.

Comment:	Test substance administration at 150 mg/kg bw/day resulted in a possible treatment related effect (local direct irritation) on the gastric epithelium. Macroscopic changes to the gastric epithelium were also observed at all treatment doses in the range finding study, and in in-study decedents in the acute oral toxicity study (section 9.1.1).
Result:	Based on possible treatment related mortality at 150 mg/kg bw /day, the NOEL determined for this 28 day study was 15 mg/kg bw/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Thompson, 1998)

Strains:	*Salmonella typhimurium*: TA1535, TA1537, TA98 and TA100; *Escherichia coli*: WP2uvrA$^-$
Concentration range:	0, 50, 150, 500, 1 500 and 5 000 µg/plate
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Test method:	OECD TG 471 and 472-plate incorporation method
Comment:	No toxicity was observed at the concentrations tested. No significant increase in the frequency of revertant colonies was observed in any of the bacterial strains, at any concentration, with or without S9 metabolic activation. All positive controls used in the study confirmed the sensitivity of the various strains and the efficacy of the S9-mix. Colony counts in the vehicle controls were within historical limits.
Result:	The notified chemical was considered non-mutagenic in the bacterial strains tested in the presence or absence of metabolic activation.

9.3.2 Chromosomal Aberration Assay in Human Lymphocytes *in vitro* (Durward, 1999a)

Cells:	Human Peripheral Lymphocytes
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Dosing schedule:	Duplicate cultures were used to test each concentration, with or without metabolic activation (S9), in two independent experiments. asterisk* indicates cultures selected for metaphase analysis <u>Experiment 1:</u> without S9, 0*, 80, 160, 320, 640*, 1 280*, and 2 560* µg/mL; treatment/harvest time: 4/20 hr; Positive control: Ethylmethanesulphonate, 750 µg/mL with S9: 0*, 80, 160, 320, 640*, 1 280*, and 2 560* µg/mL; treatment/harvest time: 4/20 hr, Positive control: Cyclophosphamide, 25 µg/mL, <u>Experiment 2:</u> without S9, 0*, 80, 160*, 320*, 640*, 960, 1 280, 1 920 and 2 560 µg/mL; continuous treatment: 20 hr without S9, 0*, 640*, 1280*, 1 920* and 2 560* µg/mL; treatment/harvest time:4/20 hr Positive control: Ethylmethanesulphonate, 500, 750* µg/mL In all cases the vehicle control was dimethyl sulphoxide (DMSO)
Test method:	OECD TG 473

Comment:	In experiment 1, a 50% mitotic inhibition was observed at the highest concentration both in the presence and absence of metabolic activation. The notified chemical induced a small, dose-related increase in chromosome aberrations (excluding gaps) in the absence of metabolic activation, which was statistically significant at the high dose treatment. A similar result was reported in the presence of metabolic activation at 640 µg/mL and 2 560 µg/mL, although no clear dose-relationship was discernible. The second experiment demonstrated similar data of chromosome aberrations for both exposure scenarios, however, the response level was more marked than that in the first experiment. Also, discrepancies were noted in the toxicity and mitotic inhibition index between the repeat culture treatment within and between the experiments. It is not possible to determine whether this is caused by the insolubility of the notified chemical, which was only reported to occur at the highest concentration (precipitate formation), or due to other factors. In both experiments, no significant increase in the number of polyploid cells was observed at any concentration of the test substance. All vehicle control cultures had frequencies of chromosome aberrations within the expected range. Positive controls induced statistically significant increases in the incidence of aberrant cells and the activity of the S9 fraction was found to be satisfactory.
Result:	The notified chemical was considered to be clastogenic under the conditions of the chromosomal aberration assay.

9.3.3 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Durward, 1999b)

Species/strain:	Mice/Albino Crl:CD-1(ICR)BR
Number and sex of animals:	7 males/24 hour exposure: vehicle control, low, mid and high dose group; 7 males/48 hour exposure: vehicle control and high dose group; 5 males per positive control group
Doses:	Test substance 300 (low), 600 (mid) or 1 200 (high) mg/kg bw;

	Vehicle control- arachis oil; Positive control cyclophosphamide- 50 mg/kg bw.
Method of administration:	Oral (gavage); single dose volume of 10 mL/kg bw
Test method:	OECD TG 474
Comment:	One premature death occurred in the 48 hours high dose group. This was not considered to affect the statistical power of the test since seven animals were used in each group, which is above the minimum recommended in the OECD guidelines. The reported death and clinical observations indicated that systemic absorption had occurred. Hunched posture was observed at 24 and 48 hours in the high dose group. No other signs were noted in either test or control groups. No significant increase in the mean frequency of micro-nucleated polychromatic erythrocytes (PCE) was observed at any dose of the test substance. Also, no statistically significant decrease in the PCE/NCE ratio was observed in the 24 or 48 hr test groups when compared to controls. One animal in the 48 hours high dose group revealed a higher frequency (9 micronuclei per 2 000 PCE) of micronuclei than that for the vehicle control groups. However, this value was within the upper range of the historical control and was considered by the study author to be of no toxicological significance.
Result:	The notified chemical was considered non-genotoxic in the *in vivo* mouse micronucleus assay.

9.4 Overall Assessment of Toxicological Data

The notified chemical was of low acute oral toxicity in rats with LD_{50} of 637 mg/kg bw females and >500 mg/kg bw males. The notified chemical was of low dermal toxicity in rats (LD_{50} > 2 000 mg/kg bw). The notified chemical was very slightly irritating to the skin of rabbits for the first hour following 4 hours exposure and moderately irritating to the eyes of rabbits. The notified chemical was strongly sensitising to the skin of guinea pigs.

Oral administration of the notified chemical to rats in a 28 day repeated dose toxicity study resulted in a possible treatment-related mortality due to gastric haemorrhage at the highest dose of 150 mg/kg bw/day. No other significant toxicological findings were observed. Based

on mortality at 150 mg/kg bw/day, the NOEL for the notified chemical was determined to be 15 mg/kg bw /day.

The notified chemical was considered non-mutagenic to the bacterial strains tested. The potential genotoxicity of the notified chemical, namely clastogenic activity in a chromosomal aberration study *in vitro*, was further investigated with a mouse micronucleus test, which was negative.

The notified chemical is classified as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999b) based on the findings of the acute oral toxicity study, conjunctival effects in an eye irritation study and the potential for skin sensitisation observed in an adjuvant type test. The overall classification is Harmful (Xn) and risk phrases R22- Harmful if Swallowed, R36- Irritating to Eyes, R43- May Cause Sensitisation by Skin Contact, are assigned.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Results of ecotoxicity studies are summarised in the table below. The tests were performed in compliance with OECD/EC Test Methods (OECD, 1995-1996) and according to OECD Principles of Good Laboratory Practices.

Test	*Species*	*Test concentrations (nominal) mg/L*	*Results (nominal) mg/L*
Acute Toxicity (Semi-Static Test) (OECD TG 203)	Rainbow trout (*Oncorhynchus mykiss*)	10, 18, 32, 56 & 100	96 hours LC_{50} = 23 96 hours NOEC = 10
Acute Toxicity - Immobilisation (Static Test) (OECD TG 202)	Water Flea (*Daphnia magna*)	1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56 & 100	48 hours EC_{50} > 20 48 hours NOEC = 10
Growth Inhibition Growth (μ & Biomass (b) (Static Test) (OECD TG 201)	Green Algae (*Pseudokirchneriella subcapitata*)	6.25, 12.5, 25, 50 & 100	96 hours $E\mu C_{50}$ = 80 96 hours E_bC_{50} = 72 96 hours NOEC = 50
Respiration Inhibition (OECD TG 209)	Activated Sludge - Aerobic Waste Water Bacteria	1.0, 3.2, 10, 32 & 100	3 hours EC_{50} > 100

10.1 Fish, Acute Toxicity Test (Sewell & Mullee, 1999a)

Rainbow trout were exposed to Water Accommodated Fractions (WAFs) of the notified chemical at nominal loading rates of 10, 18, 32, 56 and 100 mg/L for 96 hours under semi-static test conditions. WAFs were obtained by stirring the notified test material for 47 hours at each nominal concentration followed by standing for 1 hour prior to removal of the aqueous phase. Based on these nominal loading rate WAFs, the 96 hour LC_{50} was 23 mg/L with 95% confidence limits of 21-25 mg/L. The no observed effect concentration (NOEC) was 10 mg/L loading rate WAF. Sub-lethal effects of exposure were observed at the 18 mg/L loading rate WAF and above. These responses were increased pigmentation, swimming at the bottom, swimming at the surface and loss of equilibrium.

Chemical analysis of the test samples by HPLC showed that the measured concentrations of the freshly prepared test loading rates at 0 and 72 hours ranged from less than the limit of quantification to 36% of nominal. Analysis of the 24 hour old loading rates at 24 and 96 hours showed that the measured concentrations ranged from less than the level of quantification to 6%. The low and variable results obtained in the freshly prepared loading rates and the decline in measured concentrations over the 24 hr test media renewal period is considered to be due to the instability of the notified chemical components in water.

10.2 *Daphnia magna*, Acute Immobilisation Test (Sewell & Mullee, 1999b)

Daphnia magna were exposed to WAFs of the notified chemical at nominal loading rates of 1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56 and 100 mg/L for 48 hours. Based on these nominal loading rate WAFs, the 48 hours LC_{50} was 20 mg/L with 95% confidence limits of 17-24 m/L. The NOEC was 10 mg/L loading rate WAF. WAFs were made according to the method outlined above. Chemical analyses were also carried out on test samples with similar results to those above.

10.3 Algal Growth Inhibition Test (Mead & Mullee, 1999)

After 96 hours exposure of the notified chemical to green algae *Pseudokirchneriella subcapitata*, the $E\mu C_{50}$ was 80 mg/L and the E_bC_{50} was 72 mg/L. The no observed effect concentration at 96 hours was 50 mg/L WAF concentration. WAFs were made according to the method outlined above but chemical analysis was not carried out to determine measured concentrations.

10.4 Activated Sludge, Respiration Inhibition Test (Mead, 1999b)

The effect of the notified chemical on the respiration of activated sewage sludge microorganisms was studied. The test material was dispersed in dimethylformamide and water and subjected to ultrasonication for 30 minutes. Synthetic sewage, activated sewage sludge and water were added to a final volume to give the test concentrations of 1.0, 3.2, 10, 323 and 100 mg/L. A 3 hr EC_{50} of greater than 100 mg/L was observed, the NOEC was 3.2 mg/L.

10.5 Conclusion

The ecotoxicity data for the notified chemical suggests that it is moderately to slightly toxic to fish and aquatic invertebrates and slightly toxic to algae and microorganisms. However, it is noted that

the studies on fish, daphnia and algae all use WAFs which could very well have much lower test substance concentrations, due to low water solubility and instability in solution, than the nominal ones provided. This is confirmed by chemical analyses carried out by the notifier for the fish and daphnia studies. The test substance is, therefore, likely to be at least moderately toxic to fish and aquatic invertebrates and at least slightly toxic to algae. The analytical results indicate that the notified chemical is unstable in water.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The intended use pattern of the TGBMA Monomer is not expected to result in a significant release to the environment, as waste will be incinerated, resulting in oxides of carbon, hydrogen and sulfur. The MSDS of the chemical contains information on procedures to enable clean up operators to reduce environmental contamination from spills and minor releases during transfer operations.

There is no direct data to support the claim of complete combustion of the chemical to oxides of carbon, hydrogen and sulfur when the fuel is burnt within the incinerator. However, it is evident that the notified chemical, which is made up of hydrocarbon and sulfur, will not survive the temperatures at which the acetone washings will be burnt.

The bulk of the notified chemical will be found as part of a cross-linked polymer matrix used to make the lenses. When ultimately disposed of to landfill, the chemical will be immobile, as it exists in a solid, high molecular weight polymeric form that is expected to be very insoluble in water.
Given the above, environmental exposure and the overall environmental hazard is expected to be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical was of low acute oral and dermal toxicity. The notified chemical was a very slight skin irritant and a moderate eye irritant in rabbits, and was a strong skin sensitiser in guinea pigs. Possible treatment-related mortality at 150 mg/kg bw/day was observed in a 28-day oral (gavage) repeated dose toxicity study in rats. The NOEL was 15 mg/kg bw/day for 28 days. The notified chemical was considered non-mutagenic to the bacterial strains tested. The potential genotoxicity of the notified chemical, namely clastogenic activity in a chromosomal aberration study *in vitro*, was further investigated with a mouse micronucleus test, which was negative.

The submission indicates that skin irritation, possibly attributable to the handling of the notified chemical, have been noted in some personnel using the notified chemical.

The notified chemical, TGBMA Monomer, is determined to be a hazardous substance, Harmful (Xn), R22 - Harmful if Swallowed, R36 - Irritating to Eyes, R43 - May cause Sensitisation by Skin Contact according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999b) in

terms of the toxicological data supplied.

Occupational Health and Safety

Transport and Storage
The risk of adverse health effects to waterside, transport and storage workers is expected to be negligible, except in the event of a spill. Exposure after a spill would be controlled by use of the recommended practices for spillage clean up given in the MSDS supplied by the notifier. The risk of adverse health effects for transport and storage workers is considered low.

Occupational Exposure
Exposure to neat TGBMA Monomer may occur during connection/disconnection of transfer hoses. The neat TGBMA Monomer is a hazardous substance, with eye irritant and skin sensitising effects. Exposure to the chemical at 10-50% after dilution and mixing with other liquid resins and additives is expected during ophthalmic lens manufacturing operations. The diluted chemical is also a hazardous substance, with similar adverse effects. Workers handling the notified chemical will need to be strictly protected against skin and eye contact.

Exposure during mixing and filling stages is controlled as these occur in enclosed, semi-automated systems. Of greatest concern is exposure during the loading/unloading of mould assemblies from filling machines into ovens because waste liquid resin containing the notified chemical is generated.

Inhalation exposure is negligible because the notified chemical has low vapour pressure and aerosol formation can only occur within enclosed semi-automated operation systems. Skin contact will be the main route of exposure, although eye contact is also possible. Given the low molecular weight (< 500) absorption through intact skin cannot be excluded. Workers handling the notified chemical will need to wear thick nitrile or rubber lined gloves, polyester/cotton laboratory coats and safety spectacles with side shields.

Exposure during manufacturing is controlled through the use of semi-automatic equipment, engineering control measures, such as sealed vessels and local exhaust ventilation, the use of personal protective equipment and good industrial hygiene.

Exposure to the notified chemical and high temperatures during QA testing, maintenance and cleaning procedures is also controlled through the use of engineering control measures and personal protective equipment.

It is noted that acetone will be used in the clean up of areas and equipment. Acetone is a hazardous substance as it is moderately toxic by various routes, is a skin and severe eye irritant and causes headaches from prolonged inhalation (Lewis, 1996). The NOHSC exposure standard for acetone will need to be adhered to in the workplace.

Overall, the controls employed in the workplace are designed to minimise dermal and ocular exposure and therefore reduce the risk of topical effects of irritation and sensitisation.

According to the notifier, workers involved in the manufacturing operation are trained in aspects of health and safety practices, use of personal protective equipment and will be instructed on the safe handling of the notified chemical, its hazardous nature and main routes of entry into the body. In addition, safe job procedures have been developed and are reviewed, updated and added to by the notifier's occupational health and safety management system. These practices will need to ensure that exposure in the workplace is appropriately controlled and measures are continuously updated to minimise the risk of adverse effects to the health of workers.

Adequate precautionary measures should also be implemented in the disposal of the notified chemical and acetone washings to ensure that exposure to these is avoided.

Public exposure
Although members of the public will make dermal contact with plastic ophthalmic lens containing the notified chemical (10-50%), exposure is likely to be negligible because of the cured state of the notified chemical in the plastic from which the chemical is not expected to leach out. For the same reason, although the notified chemical is an eye and skin irritant, a skin sensitiser, and is clastogenic (*in vitro* only), these effects are unlikely to occur during normal use of the lens.

Based on the above information, it is considered that the polymer in TGBMA Monomer will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to **TGBMA Monomer** the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);

- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990);

- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia/Standards New Zealand, 1998). The notifier recommends thick nitrile or rubber lined gloves (the brand and type is identified on the MSDS);

- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994);

- Respiratory protection should conform to AS/NZS 1715 (Standards Australia/Standards New Zealand, 1994), and AS 1716 (Standards Australia/Standards New Zealand, 1994);

- Local exhaust ventilation should conform to AS 1668.2 (Standards Australia, 1994);

- Storage of the notified chemical when not in use, in closed containers, in a well ventilated area and away from strong oxidising agents, ketones, aldehydes, epoxides and olefins is required to avoid the potential for hazardous reaction products;

- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;

- Good personal hygiene should be practised to minimise the potential for ingestion;

- Exposure to acetone during clean up procedures should be maintained below the NOHSC exposure standard of 500 ppm (1 185 mg/m^3) Time-Weighted Average (TWA) (National Occupational Health and Safety Commission, 1995);

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

- The notified chemical is recommended to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC List of Designated Hazardous Substances.

If the conditions of use are varied from the notified use, greater exposure of the public may occur. In such circumstances, further information may be required to assess the hazards to the public health.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical, TGBMA Monomer, was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (National Occupational Health and Safety Commission, 1994).

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

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

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

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

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

CONJUNCTIVAE

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

IRIS

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