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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Phenol, 2,4-dimethyl-6-(1-methylpentadecyl)- (CGX AO 145)

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Director
Chemicals Notification and Assessment

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1. APPLICANT

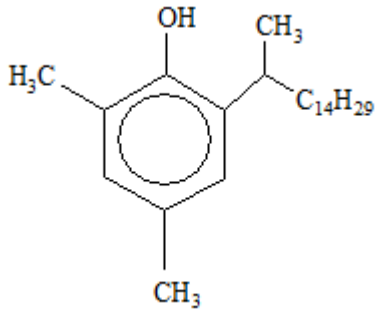
Ciba Specialty Chemicals of 235 Settlement Road Thomastown, Victoria 3074 (ABN No. 97 005 061 469) has submitted a standard notification statement in support of their application for an assessment certificate for **CGX AO 145**.

No request was made for any information relating to the notified chemical to be exempt from publication in the Full Public Report and Summary Report.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	Phenol, 2,4-dimethyl-6-(1-methylpentadecyl)-
Chemical Abstracts Service (CAS) Registry No.:	134701-20-5
Other Names:	CGX AO 145 CG 27-145 TKA 13267
Marketing Name:	CGX AO 145 Irganox 1141
Molecular Formula:	$C_{24}H_{42}O$

Structural Formula:



Molecular Weight:	347 g/mol
Method of Detection and Determination:	Infra-red (IR), Untraviolet (UV) and Nuclear Magnetic Resonance (NMR) spectroscopy.
Spectral Data:	IR peaks located at approximately 3600, 3550, 2900, 2850, 1480, 1450, 1370, 1300, 1250, 1195, 850, 770, 750, 730 cm^{-1}.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Colourless to yellow liquid with little or no odour (aqueous imported product).
Melting Point:	-14.3°C See comments below.
Boiling Point:	385°C See comments below.
Density:	0.900 g/ml at 20°C (OECD TG 109, EEC A.3)
Vapour Pressure:	1 x 10^{-7} kPa at 25°C (OECD TG 104)
Water Solubility:	< 0.15 mg/L at 25°C (less than detection limits)
Partition Co-efficient (n-octanol/water):	log P_{ow} >11
Hydrolysis as a Function of pH:	Not determined. See comments below.
Adsorption/Desorption:	Not determined. See comments below.
Dissociation Constant:	Not determined. See comments below.
Flash Point:	> 200°C (closed cup)
Particle Size:	Not determined. Chemical is imported in liquid form.
Flammability Limits:	Not flammable.
Autoignition Temperature:	365°C
Explosive Properties:	Not explosive.
Reactivity/Stability:	Stable
Fat Solubility:	98g/100g at 37°C
Surface Tension:	72.1mN/m (OECD TG 115)

3.1 Comments on Physico-Chemical Properties

The testing laboratory investigated the melting phenomena of the notified chemical and determined that the phase transition starts at -30°C and is completed by -15°C.

The boiling point of the new chemical could not determined by the test method approved by the OECD (TG 103) because it is out of the temperature range of the instrument used >280°C. Therefore, the boiling point was determined by extrapolation of the vapour pressure data.

A test for water solubility of the notified chemical was attempted using the flask method, in accordance with OECD TG 105 (Herzfeld, 1991). The solubility was found to be below the limits of detection of the method; therefore the water solubility of the chemical was given as <0.15 mg/L. Since the water solubility of the chemical was unable to be determined the hydrolysis test could not be performed, as an analytical method could not be developed with such a low detection limit (<4 ppb).

Measured fat solubility (EEC A.7) of the chemical was very high at 98g/100g indicating extreme lipophilicity.

The partition coefficient could not be determined experimentally due to the very high lipophilicity and very low water solubility of the notified chemical. Therefore the partition coefficient was calculated based on the fragmentation of the molecule into suitable substructures for which reliable log P increments are known, using the computer program CLOGP (Jakel, 1992).

Determination of a soil adsorption coefficient, K_{OC} and dissociation constant were not attempted presumably due to the low water solubility of the notified chemical. Based on low water solubility and very high lipophilicity the chemical is expected to partition into the organic phase of soil and sediment. Phenol will be only weakly acidic with pKa estimated between 10.5 and 11 and will therefore not impart significant hydrophilicity.

The surface tension of the notified chemical was measured in accordance with OECD guidelines (TG 115). The Wilhelmy plate method was used as it allows a better assessment of the time dependence of the surface tension, if present (Ryser, 1992). As the substance was not soluble in water the emulsion was shaken by mechanical agitator for 45 minutes and centrifugated for 45 minutes. The test was repeated twice using the separated water phase of the emulsions. The measured surface tension of 72.1 mN/m indicates that the chemical is not surface active.

4. PURITY OF THE CHEMICAL

Degree of Purity: 85% (lower limit 82% and upper limit 90%)

Hazardous Impurities: None

Non-hazardous Impurities:

Chemical Name	*CAS No.*	*Weight %*

2,4-Xylenol	< 0.05
Hexadecene-1	< 0.05
2,4-Dimethyl-6-(1-methyl-tridecyl)-phenol	1.19 - 1.31
2,4-Dimethyl-1-[(1-methyl-pentadecyl)oxy]-benzene	1.64 – 1.76
2,4-Dimethyl-6-(1-ethyl-tetradecyl)-phenol	1.77 – 1.82
Methyl-6-(1-methyl-pentadecyl)-phenol	0.62
2,5-Dimethyl-6-(1-methyl-pentadecyl)-phenol	4.11 – 4.27
Dimethyl-6-(1-methyl-pentadecyl)-phenol isomers	2.10 – 2.16
2,4-Dimethyl-6-(1-methyl-heptadecyl)-phenol	0.98 – 0.99
Unidentified species	1.01 – 1.19

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical CGX AO 145 will be used as an antioxidant additive at 0.08-0.4% in polymers used for manufacture of plastic articles. The notified chemical also will be used at 300ppm as a chain terminator for polymerisation reactions. The chemical will be imported in a product Irganox 1141 at 50-80% in 200L steel drums. Assuming an 80% proportion, the notified chemical will be imported in the following volumes:

Year	Irganox 1141	CGX AO 145
1	< 1 tonne	< 800 kg
2 and 3	1 - 2 tonnes	800 - 1600 kg
4 and 5	3 - 4 tonnes	1.6 - 3.2 tonnes

6. OCCUPATIONAL EXPOSURE

Import, Transport and Storage

The notified chemical will be imported as a component of a liquid antioxidant product Irganox 1141 in 200 L steel drums at 50-80% w/w. Following import, the chemical will be transported by road to a storage warehouse and then to a single customer sites.

The notifier has provided no data on numbers of workers involved in initial importation and transportation of the polymer. Exposure of workers involved in initial import and transport will only occur following inadvertent puncture of the drums.

Formulation of Masterbatch

At the formulator site, 3 employees are expected to be involved for up to 50 days/year in the initial formulation of a polymer masterbatch using the notified chemical including operation of the extruder to produce masterbatch granules.

The employee involved in blending operations will manually open the 200L import drums and either pour the product containing the notified chemical into the blending vessel after weighing or transfer the liquid to the blending vessel via a metering system. Alternatively, the notified chemical may be transferred by injection directly into the cool end of the extruder using a pump connected to the import drum. "Empty" drums will be purged of chemical by rinsing with a plasticiser as part of the masterbatch formulation and then emptied manually into the blender. Another employee will be involved in quality analysis sampling.

For both employees, dermal and ocular exposure to the notified chemical may occur from slops and spills during these transfer procedures. Given the low vapour pressure of the notified polymer, inhalation exposure is unlikely. However, the very high lipophilicity of the notified chemical suggests that dermal exposure may lead to substantial absorption. To prevent exposure and possible absorption, workers will wear protective clothing, eye protection and long PVC or nitrile gloves. The imported drums will be opened at the point of transfer into the blending vessel where any fugitive vapours will be controlled by local exhaust ventilation.

After blending, the masterbatch will be transferred in a closed system to an extruder where molten strands are cooled and chopped into granules. These granules are then discharged via a closed system to a package-filling machine and poured into 25kg or 500-1000kg bags. Local exhaust ventilation is provided at the exit point of the extruder to capture fugitive vapours.

Once the polymer containing the notified chemical is extruded, the latter is bound within the polymer matrix and unavailable for absorption.

Dermal contact with the notified chemical may also occur during the cleaning and maintenance of process equipment and during the cleaning of the import drums. Exposure to small quantities may occur also during quality analysis sampling and testing.

Production of Articles

Masterbatch granules containing the notified chemical will be poured manually into the hopper of an injection moulder or extruder. The process including the operating temperature will then be monitored by the worker.

Dermal exposure to the notified chemical during article production is unlikely as the chemical will be bound within a fused polymer matrix. However, at recommended processing temperatures, the hot extrusion of polymer containing the notified chemical may produce vapours. If the polymer resin is overheated, more extensive decomposition and liberation of irritating carbonaceous oxide fumes may occur. Vapours liberated from hot sections of the extruder will be collected by local exhaust ventilation. Dermal and ocular exposure will be controlled by personal protective equipment consisting of protective clothing, eye protection and gloves.

Dermal contact to the notified chemical may occur also during routine maintenance of extruder or injection moulder plant.

Polymerisation Termination

In addition to masterbatch extrusion, the notified chemical may be used as a polymerisation terminator in the manufacture of PVC. Here, the chemical will be transferred directly into the closed polymerisation reactor using a pump line connected manually to the import drums. To prevent occupational exposure during this procedure, the worker will wear protective clothing, eye protection and long PVC or nitrile gloves. In this process, the notified chemical will be consumed.

7. PUBLIC EXPOSURE

The notified chemical will not be sold to the public, but will be used in the manufacture of plastics. The public will come into contact with the notified chemical only when it has been incorporated into the polymer matrix of finished articles. There is predicted to be little "blooming" of the notified chemical from articles during their lifetime. Consequently, the potential for public exposure to the notified chemical during all phases of its life cycle is considered to be very low.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

The notifier estimates that the wastage generated from residual material in the 200 L import drums will be negligible as the drums are rinsed with plasticiser at the compounding plant, and the rinses passed to the blending process. The drums virtually free of the notified chemical are sent to an accredited drum reconditioner.

Spillage of the notified chemical during transport, storage and processing is expected to be minimal and largely due to accidents. Release to the aquatic environment from spills during processing is expected to be negligible, as the material would be taken up in dry absorbent, packed and labelled for proper disposal.

It is estimated that the quantity of chemical released during the compounding process will be no more than 10–20 kg per year. This will be limited to disposal of waste from purging for maintenance runs. It is not normally necessary to purge equipment between runs, but if required the purged polymer can be circled into the next batch.

Waste from article manufacturing is limited as most scrap is recycled with only a trace proportion disposed of to landfill.

The majority of the notified chemical will share the fate of the plastic articles into which it is incorporated. At the end of the product's useful lifetime it is expected to be disposed of to either landfill or incineration if recycling facilities are not available.

8.2 Fate

Spillage of raw product containing the notified chemical during transport, storage and processing is expected to be minimal and largely accidental. In this situation the compound would be taken up by dry absorbent. The granules produced during masterbatch formulation are easily collected and release to the aquatic compartment is unlikely. However, if released to water, the granules containing the notified chemical would be expected to float and, as the

notified chemical is minimally soluble in water, release to the aquatic compartment would be negligible. After incorporation into final products, the chemical will be bound in an inert, thermoplastic matrix and release to the aquatic environment is not expected.

It is unlikely that the notified chemical would be released to the environment from final products disposed of to landfill, as the chemical is encapsulated within the polymer matrix. Therefore there is no likelihood of dispersion or migration of the chemical from the plastic.

Incineration would destroy the chemical, and create typical decomposition products of water and oxides of carbon and nitrogen.

The biodegradability of the notified chemical was investigated in a Ready Biodegradability Modified Sturm Test (OECD TG 301B, Grade, 1991 a), using bacteria activated sludge from a domestic waste-water treatment plant. TK 13267 (CGO AO 145) 10.9 mg test substance/L attained 28% biodegradation after 28 days and did not pass the test for ready biodegradability, ie. $\geq$ 60% biodegradation within 28 days. Therefore the notified chemical is described as not readily biodegradable.

A study of the potential for CGO AO 145 to bioaccumulate was not conducted. Although the estimated log P_{ow} for the chemical indicates that potential exists for bioaccumulation, release of the chemical into the environment is expected to be minimal, thereby reducing the potential for bioaccumulation. As an additive to plastic products, the substance will be encapsulated within the polymer matrix and it is expected that either leaching or extraction from the polymer would be low. Therefore, under normal use and handling of the notified substance there should not be a significant release into the environment.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of phenol, 2,4-dimethyl-6-(1-methylpentadecyl)-.

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 2000mg/kg	Hartmann (1991a)
acute dermal toxicity	rat	LD_{50} > 2000mg/kg	Hartmann (1991b)
skin irritation	rabbit	Irritating	Hagemann (1991a)
eye irritation	rabbit	Slightly irritating	Hagemann (1991b)
skin sensitisation	guinea pig	Sensitising	Hagemann (1992c)

9.1.1 Oral Toxicity (Hartmann, 1991a)

Species/strain: Rats, Tif:RAIf

Number/sex of animals: 5 males, 5 females

Observation period: 14 days

Method of administration:	Gavage
Test method:	OECD TG 401
Mortality:	None
Clinical observations:	Hunched posture, piloerection, dyspnea; symptoms resolved within 5 days.
Morphological findings:	No deviations from normal morphology were observed.
Comment:	None
LD_{50}:	> 2000mg/kg
Result:	The notified chemical was of very low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (Hartmann, 1991b)

Species/strain:	Rats, Tif:RAIf
Number/sex of animals:	5 males, 5 females
Observation period:	14 days
Method of administration:	Test substance applied to shaved intact skin under semiocclusive dressing.
Test method:	OECD TG 402
Mortality:	None
Clinical observations:	Piloerection; symptoms resolved within 2 days.
Morphological findings:	No deviations from normal morphology were observed.
Comment:	No assessments of skin irritation were provided.
LD_{50}:	> 2000mg/kg
Result:	The notified chemical was of low dermal toxicity in rats.

9.1.3 Inhalation toxicity

No information was provided.

9.1.4 Skin Irritation (Hagemann, 1991a)

Species/strain: Rabbits, New Zealand White

Number/sex of animals: 3 males

Observation period: 72 hours

Method of administration: Test substance (0.5mL) applied to shaved intact skin under semiocclusive dressing.

Test method: OECD TG 404

Draize scores:

Time after Treatment (hours)	***1***	***24***	***48***	***72***
Erythema				
1	1[a]	3	3	3
2	2	3	3	3
3	1	2	2	2
Oedema				
1	1	2	2	2
2	2	2	2	2
3	1	2	2	2

[a] see Attachment 1 for Draize scales

Comment: Erythema was still apparent at 7 days. However, this was resolved at 10 days after application.

Result: The notified chemical was irritating to the skin of rabbits.

9.1.5 Eye Irritation (Hagemann, 1991b)

Species/strain: Rabbits, New Zealand White

Number/sex of animals: 3 males

Observation period: 7 days

Method of administration: Test substance (0.1mL) instilled into conjunctival sac of unirrigated left eye.

Test method: OECD TG 405

Draize scores of unirrigated eyes:

	Time after instillation									
Animal	***1 hour***		***24 hours***		***48 hours***		***72 hours***		***7 days***	
Cornea	***o***	***a***	***o***	***a***	***o***	***a***	***o***	***a***	***o***	***a***
1	0[1]	-	0	-	0	-	0	-	0	-
2	0	-	0	-	0	-	0	-	0	-
3	0	-	0	-	0	-	0	-	0	-
Iris										
1	0		0		0		0		0	
2	0		0		0		0		0	
3	0		0		0		0		0	

Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	1	0	-	1	0	-	1	0	-	0	0	-	0	0	-
2	1	0	-	1	0	-	1	0	-	1	0	-	0	0	-
3	2	1	-	1	1	-	1	0	-	1	0	-	0	0	-

[1] see Attachment 1 for Draize scales
o = opacity a = area r = redness c = chemosis d = discharge - = not reported

Irrigated eyes: Not determined

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

9.1.6 Skin Sensitisation (Hagemann, 1991c)

Species/strain: Guinea Pig, Pirbright White

Number of animals: 10 male, 10 female

Induction procedure: Intradermal injections followed by dermal application

test group:
day 0 Three pairs of 0.1ml intradermal injections into the shaved neck region:

- Freunds complete adjuvant (FCA)/saline 1:1
- Test substance 5% in Oleum arachidis
- Test substance 5% in FCA/saline 1:1

day 7
- 0.4g of 30% test substance in vaseline applied via filterpaper patch to shaved neck region and held under occlusive dressing for 48 hours.

control group: Treated similarly to test animals omitting test substance

from intradermal injections and topical applications

Challenge procedure:

day 28 — 0.2g of 10% saline in vaseline applied via filterpaper patch to shaved neck region and held under occlusive dressing for 24 hours.

day 35 — 0.2g of 5% saline in vaseline applied via filterpaper patch to shaved neck region and held under occlusive dressing for 24 hours.

Test method: OECD TG 406, Magnusson and Kligman maximisation test

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
10% (first challenge)	8/20**	11/20	3/10	2/10
5% (second challenge)	12/20	11/20	-	-

* time after patch removal
** number of animals exhibiting positive response
\- test not conducted

Comment: After first challenge application using 10% test substance, test animals showed strong stress responses. A second challenge was conducted in test animals using 5% test substance to verify first challenge results.

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

9.2 Repeated Dose Toxicity (Gerspach, 1992)

Species/strain: Rats, Tif:RAIf

Number/sex of animals: 10 males, 10 females (dose groups 1 and 4); 5 males, 5 females (dose groups 2 and 3)

Method of administration: Test substance, 0.5% carboxymethylcellulose and 0.1% Tween 80 in distilled water by gavage

Dose/Study duration: 0, 10, 50, 1000 mg/kg/day for 28 days, observation for additional 28 days for doses 0 and 1000 mg/kg/day.

Test method: OECD TG 407

Clinical observations:
At the end of treatment, mean bodyweights of males in groups 3 (50mg/kg/day) and 4

(1000mg/kg/day) were decreased by 5% compared to control males (group 1). In the subsequent 28 day recovery period, mean body weights for group 4 males were decreased by 7-8% compared to controls.

During treatment weeks 2-4, mean body weights of females in groups 2 and 4 (10, 1000mg/kg/day respectively) were increased by 6-12% and 4-7% respectively. For these findings in female animals, no clinical relevance was attributed due to the absence of a dose relationship.

No clinical signs related to the treatments were noted. No deaths occurred during the study period.

Clinical chemistry/Haematology
In group 4 (1000mg/kg/day), both males and female animals showed slightly reduced values for red blood cell counts and associated haemoglobin values. In males of group 4, prothrombin times were also prolonged. These effects were reversible during the 28 day recovery period. Haematocrit values were also decreased in group 3 (50mg/kg/day) males.

Alterations in blood chemistry were observed in animals of group 4 (1000mg/kg/day). Elevated cholesterol, triglyceride and albumin levels and albumin/globulin ratios were observed in both males and females. Total protein concentrations were increased and plasma glucose concentrations were decreased in female animals. In male animals, alanine aminotransferase activities were slightly decreased and alkaline phosphatase activities were increased. These effects were reversible within the recovery period. No significant effects on urinalysis parameters were observed.

Morphology and Histopathology:
Macroscopic examination at the end of the treatment period detected enlarged livers in 1/5, 2/5, and 4/5 male animals from groups 2, 3 and 4 (10, 50 and 1000 mg/kg/day) and 5/5 female animals from group 4, respectively. Comparisons with microscopic findings showed the enlargements treatment-related in 1/5 animals in group 3 and all animals of both sexes in group 4.

At the end of the treatment period, both mean absolute liver and kidney weights were increased slightly in males in group 3 (50mg/kg/day) and markedly in both males and females in group 4 (1000mg/kg/day) compared to animals in the control group. After the 28 day recovery period, group 4 animals still showed increased liver weights and group 4 males still showed increased kidney weights compared to controls.

At the end of the treatment period, 1/5 male animals from group 3 (50mg/kg/day) and 5/5 male animals and 5/5 female animals from group 4 (1000mg/kg/day) showed slight centrilobular hepatocellular hypertrophy. Hypertrophy remained observable in 2/5 male animals in group 4 after the 28 day recovery period.

Comment:
The liver was identified as a target organ by macroscopic and microscopic findings, liver weight changes and clinical chemistry.

Result:

Based on incidence of liver hypertrophy, a no-observed-adverse-effect-level (NOAEL) for the test substance was established at 10mg/kg/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium*, *Escherischia coli* Reverse Mutation Assay (Ogorek, 1991)

Strains:	*Salmonella typhimurium* TA98, 100, 1535, 1537; *Escherischia coli* WP2 uvrA
Metabolic activation:	Aroclor 1254-induced rat liver microsomal fraction S9
Concentration range:	312.5, 625, 1250, 2500, 5000μg/plate
Test method:	OECD TG 471, 472
Comment:	A range finding toxicity test performed with and without microsomal activation determined a maximum test substance concentration without toxicity of 5000μg/plate. In both initial and confirmatory experiments, no significant increase in the incidence of mutations was observed compared to negative controls.
Result:	The notified chemical was non mutagenic under the conditions of the test.

9.3.2 Chromosomal Aberration Assay in Chinese Hamster Ovary Cells (Ogorek, 1992)

Cells:	Chinese hamster ovary CCL 61
Metabolic activation system:	Aroclor 1254-induced rat liver microsomal fraction S9

Dosing schedule:

Metabolic Activation	Experiment/ Study Number	Test concentration (μg/mL)	Controls
-S9	Original study	Treatment time = 18 hours 5.1*, 10.2*, 20.3*, 40.6, 81.3, 162.5, 325, 650 μg/ml	Positive: Mitomycin C
	Confirmation study	Treatment time = 42 hours 5.1*, 10.2*, 20.3*, 40.6, 81.3, 162.5, 325, 650 μg/ml	Negative: Ethanol vehicle
+S9	Original study	Treatment time = 3 hours. Recovery time = 15 hours. 5.1*, 10.2, 20.3, 40.6, 81.3, 162.5*,	Positive: Cyclophosphamide

	Confirmation study	325*, 650* µg/ml Treatment time = 3 hours. Recovery time = 15 or 39 hours. 5.1*, 10.2, 20.3, 40.6, 81.3, 162.5*, 325*, 650* µg/ml	Negative: Ethanol vehicle

* - cultures selected for metaphase analysis

Comment: In experiments without metabolic activation, the highest concentration of test substance yielding metaphase plates of sufficient quantity for analysis was 20.3µg/plate. For experiments with metabolic activation, the highest concentration for analysis was 650µg/plate. At higher concentrations in both experiments, insufficient cells resulted from toxic effects of the test substance.

Test method: OECD TG 473

Result: The notified chemical was non clastogenic under the conditions of the test.

9.4 Overall Assessment of Toxicological Data

In acute toxicity tests, the notified chemical was shown to possess very low oral and low dermal toxicity with a rat LD_{50} for both tests established at >2000mg/kg.

A skin irritation test in rabbits showed persistent significant erythema and oedema indicating that the notified chemical was dermally irritating. In contrast, an eye irritation test revealed only minimal ocular lesions. A skin sensitisation study in guinea pigs revealed that the notified chemical was capable of inducing dermal allergic responses.

In a repeated dose oral toxicity test in rats, the liver was identified as a target organ. A NOAEL of 10mg/kg/day was established, based on incidence of liver hypertrophy.

In genotoxicity tests, the notified chemical was shown to be neither mutagenic nor clastogenic *in vitro*. *In vivo* genotoxicity tests were not available.

On the basis of these toxicological data, the notified chemical should be determined hazardous and classified Irritant (Xi) according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999b). The notified chemical should carry the risk phrases R38 – Irritating to skin and R43 – May cause sensitisation by skin contact.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Tests were performed according to EEC/OECD test guidelines at facilities complying with OECD Principles of Good Laboratory Practice. The notifier has supplied the following ecotoxicity studies.

Test	*Species*	*Results (Nominal) mg/L*	*References*
Acute Toxicity (Semi-Static Test) (OECD TG 203)	Zebra Fish (*Brachydanio rerio)*	96 h LC_{50} > 7.19 NOEC > 7.19	Vial (1992)
Acute Toxicity– Immobilisation (Static Test) (OECD TG 202 & EEC Directive 92/69)	Water Flea (*Daphnia magna*)	48 h EC_{50} > 0.045 mg/L NOEC > 0.045 mg/L (dissolved concentration)	Memmert (2000a)
Growth Inhibition - (Static Test) (OECD TG 201)	Green Algae (*Scenedesmus subspicatus*)	50mg/L<EC_{50}<100 mg/L 72 h NOEC < 6.25 mg/L (loading rates)	Memmert (2000b)
Activation Sludge Respiration Inhibition Test (OECD 209)	Activated sludge from sewage treatment plant	EC_{50} >100 mg/L	Grade (1991b)

* NOEC - no observable effect concentration

Fish (*Brachydanio rerio*)

Groups of 10 fish were exposed to TK 13267 (CGO AO 145) at nominal concentrations of 10, 18, 32, 58 and 100 mg test substance/L (OECD TG 203, Vial, 1992). Due to the low water solubility of the chemical, actual measured concentrations, drawn from the centre of the test vessels, were 0.60, 0.98, 3.43, 6.31 and 7.19 mg/L, and the non-solubilized parts of the test substance were apparent "swimming" at the surface of the test vessels. Measured concentrations are well above actual water solubilities as the stock solution for preparation of the dilutions contained the test substance and a co-solvent containing dimethylsulfoxide and polyoxyethylene-sorbitan-monooleate. No mortalities or sublethal effects were observed at any time for the duration of the test, so it can be concluded that the 96 h LC_{50} > 7.19 mg/L. Therefore the chemical is non-toxic to this fish species up to the limits of its solubility.

Aquatic Invertebrates *(Daphnia magna)*

The tests on immobilisation of the daphnia were conducted using a static method (OECD TG 202, Memmert, 2000a). Due to low water solubility of the test substance, a supersaturated emulsion of the test substance was created. The test item was mixed into test water at 100 mg/L by intense stirring for over 17 hours, then the dispersion was filtered through a glass microfibre filter, with only the undiluted filtrate with the maximum concentration of dissolved test item used as the test medium. Filtration was necessary in this test due to the potential adverse effect of non-dissolved matter on the test species. The separated water soluble fraction was found to have a mean concentration of 0.045 mg/L. A limit test was performed in accordance with Commission Directive 92/69/EEC to demonstrate that the test item had no toxic effect on the test organisms up to the highest concentration that could be dissolved in the test water. Therefore the chemical may be regarded as non-toxic to this species up to the limits of its solubility, and no values for 48 h EC_{50} or NOEC could be determined.

Details of a second experiment were provided in the summary in which higher dilutions were

tested: 1:16, 1:32, 1:64, 1:128 and 1:256. The test dilution of 1:256 substance concentration = 0.09 mg/L, 1:128 = 0.14–0.18 mg/L, 1:64 = 0.25–0.30 mg/L. However, no adverse effects on daphnia were reported for this additional experiment.

Algae

An algal growth inhibition test was carried out using *Scenedesmus subspicatus*, (Memmert, 2000b). A filtrate from a supersaturated stock dispersion (loading rate 100 mg/L) with the maximum concentration of dissolved test item (0.07 mg/L) was used as the highest concentration test medium (as described above). This filtrate was progressively diluted to give water with the loading rates of 6.25, 12.5, 25 and 50 mg/L. At a loading rate of 12.5 mg/L, the growth in algal biomass decreased to 80% of the control, at 50 mg/L the growth rate was 77%, reaching a low of 40 % of the control at maximum loading of 100 mg/L. This suggests that 50 mg/L < EC50 < 100 mg/L loading rate although the test report suggests 175.2 mg/L. Measured concentrations in the test solutions were apparently linearly related to the loading rate ranging from 0.004 mg/L to 0.07 mg/L for the loadings of 6.25 to 100 mg/L.

The test item TK 13267 (CGO AO 145) was also found to have a statistically significantly inhibitory effect on the growth of the algae after the test period of 72 hours at the loading rate of 12.5 mg/L (measured concentration = 0.011 mg/L). These results indicate the chemical shows some toxicity to algae below its water solubility, possibly due to a more soluble impurity.

Micro-organisms

Assessment of the toxic effect of the notified chemical on sewage sludge micro-organisms (OECD TG 209) was performed (Grade, 1991b). Due to the insoluble nature of the test substance no stock solution was prepared. Instead the test substance was given directly into the medium. Graphically determined results based on nominal concentrations found that the EC50 (3 h) > 100 mg/L. Therefore, it can be concluded that the chemical is non-toxic to activated sludge bacteria up to the limits of solubility.

Conclusion

The ecotoxicity data for TK 13267 (CGO AO145) indicate that based on the conditions of the individual tests, the chemical is not toxic to fish or daphnia up to the apparent limit of its water solubility. However, the chemical is toxic to algae, with the 72 h LOEC at a loading rate of 12.5 mg/L (measured concentration = 0.011 mg/L).

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical will be used as an antioxidant additive in polymers. Once incorporated into these products the notified chemical is expected to remain within the product matrix. Hence, the majority of the notified chemical will share the fate of the articles into which it is incorporated. It is anticipated that these will be disposed of either to landfill or incineration at the end of their useful lifetime. In landfill, it is expected that the notified chemical will remain immobile within the plastic polymer matrix. Incineration would destroy the chemical, and create typical decomposition products of water and oxides of carbon.

The only waste expected is 10–20 kg per year from purging of the equipment for maintenance purposes during the compounding process. The polymer will be immobile

within the polymer matrix and will not pose a hazard when disposed of to landfill. Therefore, as the chemical is determined to be non toxic to fish and daphnia at the limits of its solubility, the overall environmental hazard of the chemical with the usage patterns described by the notifier can be rated as low, given the low environmental exposure. While the chemical appears to be toxic to algae below its water solubility limit, environmental exposure will be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard assessment

Toxicological data have been provided for the notified chemical. The notified chemical was shown to possess very low oral and low dermal toxicity. In a repeated dose oral toxicity test in rats, a NOAEL of 10mg/kg/day was established based on incidence of liver hypertrophy.

A skin irritation test in rabbits showed persistent significant erythema and oedema indicating that the notified chemical was dermally irritating. An eye irritation test revealed minimal ocular injury. A skin sensitisation study in guinea pigs revealed that the notified chemical was capable of inducing dermal allergic responses. In genotoxicity tests, the chemical was shown to be neither mutagenic nor clastogenic *in vitro*.

Lipophilicity of the notified chemical is very high suggesting that dermal exposure is likely to result in substantial absorption.

According to the NOHSC *Approved Criteria* (NOHSC, 1999b), on the basis of these toxicological data the notified chemical should be determined hazardous and classified Irritant (Xi) with the risk phrases R38 – Irritating to skin and R43 – May cause sensitisation by skin contact.

Occupational Health and Safety

The notified chemical will not be manufactured in Australia but imported in liquid form (50-80%) in steel drums. Occupational exposure to the notified polymer is unlikely during import, transport and storage and would only be envisaged following accidental puncture of the drums. If exposure does occur, skin irritation would be expected. Repeated dermal exposure could result in dermal sensitisation. Eye irritation might also occur. Drums will remain unopened prior to use and so repeated exposure to the notified chemical with the risk of allergic sensitisation of transport and storage workers is unlikely. Thus, the health risk for these workers is low.

The notified chemical will be either used as a PVC polymerisation terminator or incorporated into a polymer masterbatch for processing into moulded articles. Dermal and ocular exposure to the notified chemical from spillage may occur during initial weighing and charging of the blender vessel or polymerisation reactor with the imported liquid product. Dermal exposure to the notified chemical may also occur following contact with extrusion masterbatch granules. However, at this point, the notified chemical is embedded in the polymer matrix. In addition, inhalation exposure is possible from fugitive dusts generated from packaging of masterbatch granules or from vapours liberated from the hot extrusion process.

Maintenance workers are likely also to experience dermal contact with the notified chemical during routine machinery upkeep. Similarly, skin contact may occur during cleaning and quality analysis testing.

Severe health effects may occur following exposure to the notified chemical. Dermal exposure may induce skin irritation and in the long term, skin sensitisation. High lipophilicity suggests the chemical would be absorbed via the skin. If eye contact occurs, local irritation may also result. The dermal sensitisation potential also indicates the possibility of respiratory sensitisation following repeated inhalation. Liver effects were observed also after exposure to the notified chemical in a repeat dose study. Notwithstanding the seriousness of acute dermal and ocular irritation, the unpredictable nature of allergic reactivity and long-term consequences of occupational sensitisation together with possible liver effects with repeated exposure indicate that contact with the notified chemical must be prevented. For these reasons, it is essential that exposure is controlled through a combination of personal protective equipment and engineering controls such as local exhaust ventilation at transfer points and hot sections of the extruder. The MSDS for the imported product containing the notified chemical recommends personal protective equipment consisting of overalls, eye protection and long PVC or nitrile gloves. Use of a barrier cream on exposed skin is recommended on the MSDS. However, no information has been provided to allow an assessment of the effectiveness of this measure in preventing exposure or absorption.

Following curing of moulded articles, the notified chemical will be immobilised in a polymer matrix. In this form, it is unavailable for absorption and thus the health risk to workers from the notified chemical during handling of masterbatch granules and moulded articles would be negligible.

Public Health

The potential for public exposure to CGX AO 145 during all phases of its life cycle is considered to be very low. It is considered that the notified chemical will not pose a significant risk to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to **CGX AO 145** the following guidelines and precautions should be observed:

- Skin contact with unpolymerised notified chemical should be eliminated during occupational use;
- Protective eyewear, chemical resistant industrial clothing and footwear and impermeable gloves should be used during occupational use of the products containing the notified chemical. Where engineering controls and work practices do not reduce vapour and particulate exposure to safe levels, an organic vapour negative pressure respirator should also be used;
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;
- A copy of the MSDS should be easily accessible to employees.

- As the notified chemical is a skin sensitiser, health surveillance should be conducted for any workers who have been identified in the workplace risk assessment as having significant potential or actual exposure to the chemical.

The following regulatory action is recommended:

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

If products containing the notified chemical are hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999b), workplace practices and control procedures consistent with State and territory hazardous substances regulations must be in operation.

Guidance in selection of protective eyewear may be obtained from Australian Standard (AS) 1336 (Standards Australia, 1994) and Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); for industrial clothing, guidance may be found in AS 3765.2 (Standards Australia, 1990); for impermeable gloves or mittens, in AS 2161.2 (Standards Australia/ Standards New Zealand, 1998); for occupational footwear, in AS/NZS 2210 (Standards Australia/ Standards New Zealand, 1994a); for respirators, in AS/NZS 1715 (Standards Australia/ Standards New Zealand, 1994b) and AS/NZS 1716 (Standards Australia/ Standards New Zealand, 1994c).

14. MATERIAL SAFETY DATA SHEET

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

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 may be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. In particular, clarification of the algal toxicity would be required if a new use resulted in greater contamination of the aquatic environment. No other specific conditions are prescribed.

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Attachment 1

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

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

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

CORNEA

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

CONJUNCTIVAE

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

IRIS

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

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