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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Carbamothioic acid, 2-propenyl-, O-(2-methylpropyl)ester
(AERO® 5100 Promoter)

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

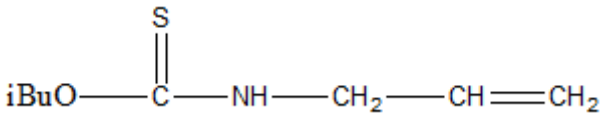
Carbamothioic acid, 2-propenyl-, O-(2-methylpropyl)ester
(AERO® 5100 Promoter)

1. APPLICANT

Cytec Australia Holdings Pty Ltd. has submitted a standard notification statement in support of their application for an assessment certificate for Carbamothioic acid, 2-propenyl-, O-(2-methylpropyl)ester.

No claims for exempt information were made.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	Carbamothioic acid, 2-propenyl-, O-(2-methylpropyl)ester
Chemical Abstracts Service (CAS) Registry No.:	86329-09-1
Other Names:	CT-637-97; Carbamate, N-allyl-O-isobutylthiono-; Carbamic acid, allylthio-, O-isobutyl ester; Isobutyl allylthionocarbamate.
Marketing Name:	AERO® 5100 Promoter (containing approximately 87% notified chemical)
Molecular Formula:	$C_8H_{15}NOS$
Structural Formula:	
Molecular Weight:	173

Method of Detection and Determination:	Infra-Red (IR) spectroscopy
Spectral Data:	IR spectrum: major absorbance peaks were at: 3 260, 2 964, 2 879, 1 646, 1 518, 1 470, 1 389, 1 324, 1 273, 1 198, 1 178, 1 149, 1 059 and 990 cm^{-1}

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C at 101.3 kPa:	Pale brown liquid with a garlic odour, non-viscous
Freezing Point:	< -25°C
Boiling Point:	225.5°C
Density:	0.994 g/cm^3
Vapour Pressure:	7.9 x 10^{-3} kPa at 25°C (see comments below)
Water Solubility:	497 mg/L at 25°C
Partition Co-efficient (n-octanol/water):	$Log_{10} P_{ow} = 2.84$
Hydrolysis:	Substance is hydrolytically stable at 25°C
Hydrolysis as a Function of pH:	$T_{1/2}$ > 1 year at pH 4.0, 7.0 & 9.0
Adsorption/Desorption:	$Log_{10}K_{OC} = 2.61$ ($K_{OC} = 407$)
Dissociation Constant:	Substance is a thiocarbanate and does not contain any groups which can undergo dissociation
Surface Tension:	49.0 mN/m
Particle Size:	Not applicable, substance is a liquid
Flash Point:	95°C
Flammability Limits:	Not available, but chemical is flammable
Autoignition Temperature:	344°C
Explosive Properties:	Not explosive
Reactivity/Stability:	React with strong acids and alkalies and also oxidising agents

Comments on Physico-Chemical Properties

Tests were performed according to corresponding EC and/or OECD test guidelines (European Commission 1992), (OECD 1995-1996) at Huntingdon Life Sciences testing facilities, UK. These facilities comply with the OECD principles of good laboratory practice and full test reports were submitted. All tests were performed on the notified chemical.

Vapour pressure was determined using the OECD static method and the substance is considered to be volatile. This relatively high volatility is likely to be due to the presence of the butanol and isobutanol solvents present in the end use product.

From a preliminary study, water solubility of the notified chemical was estimated to be greater than 100 mg/L. The definitive test was performed by the flask method. Supersaturated solutions were filtered and 2 mL sub-samples of each filtrate were diluted to 20 mL with ethanol for analysis by gas chromatography. From this, water solubility was determined to be 497 mg/L.

The results from a preliminary study showed that the hydrolysis rates at pH 4, 7 and 9 at 50°C were less than 10% at 5 days (HLS 1998). Although this level is low, it is likely that the notified chemical will degrade slowly.

$Log_{10}P_{OW}$ = 2.84 for the notified chemical was calculated by the Leo and Hansch procedure. This value indicates there is a potential for the notified chemical to partition into the n-octanol phase.

Adsorption/Desorption study was conducted in accordance with the OECD draft document TGP/94.75. Estimate for the adsorption coefficient K_{OC} was based on an empirical relationship with the partition coefficient. $Log_{10}K_{OC}$ = 2.61, indicating that the notified chemical will sorb moderately to soil colloids and organic matter and will be mobile through the soil profile.

Dissociation Constant of the notified chemical was not determined. However, no groups are present which are likely to lose or gain a proton.

By definition, a chemical has surface activity when the surface tension is less than 60 mN/m (European Commission 1992). The notified chemical has a surface tension of 49.0 mN/m and is expected to be surface active.

4. PURITY OF THE CHEMICAL

Degree of Purity: Approximately 98%

Hazardous Impurities:

Chemical name:	Isobutanol
Synonyms:	Isobutyl alcohol
CAS No.:	78-83-1
Weight percentage:	0.6%
Regulatory Controls:	Hazard Classification (NOHSC 1999): R10 – flammable; R20 – harmful by inhalation; National Exposure Standard (NOHSC 1995): 50 ppm; 152 mg/m^3 TWA; Dangerous Goods Class (FORS 1998): Class 3; Packing Group III

Non-hazardous Impurities (> 1% by weight): Unidentified impurities constitute 1.2%

Additives/Adjuvants: None known.

5. USE, VOLUME AND FORMULATION

AERO® 5100 Promoter is intended for use as a mineral processing reagent. The notifier claims that the reagent is an improved sulfide collector used in mineral flotation processes to more efficiently float and separate copper, lead and zinc sulfides from certain milled ores.

The notified chemical will not be manufactured in Australia. It will be imported in 200 L steel drums or one tonne International Bulk Containers (IBC), coming in at 87% in butanol/isobutanol. It is transported from dockside to the notifiers warehouse for storage prior to being transported to the customer site. The estimated import volume of the notified substance will be 10 to 50 tonnes for the first two years increasing to approximately 100 tonnes per year in following years.

At the customers site, the notified chemical will be pumped or gravity fed from the 200 L drums to a storage tank. An automatically controlled ring main system will be used to regulate flow, mix reagents and deliver reagents to the addition points in the flotation circuits. AERO® 5100 Promoter selectively chelates to and enhances the floatability of the metal sulfide particles. The metal sulphides will then be mechanically collected and further concentrated by succeeding 'cleaner' flotation cells. The concentrate, including the metal sulphides and adsorbed notified chemical will be drawn off and transported to a smelter for metal recovery where the notified chemical will be destroyed by oxidation in the smelting process. The reagent storage, mixing and flotation processes are completely automated, continuous and recycling.

6. OCCUPATIONAL EXPOSURE

Transport and Storage (2 to 13 workers; 2 to 3 hours/day, 10-15 days/year)
Transport and storage workers may be exposed to AERO® 5100 Promoter in the event of a spill.

Plant Operators (6 to 12 workers, 1 to 8 hours/day, 300 days/year)
Ore treatment by plant operators involves transfer of AERO® 5100 Promoter from 200 L drums or IBC by pumping or gravity feed to a flotation cell where it mixes and chelates the ore. There is potential for skin and possibly eye contact during connecting and disconnecting lines and cleaning pumping and ancillary apparatus. The product is added at 10 to 50 g per tonne of ore equivalent to a concentration in slurry of approximately 8.7 to 43.5 ppm (0.00435%). The chelated metal, including AERO® 5100 Promoter is successively concentrated. The transfer, mixing and flotation processes are automated, continuous and recycling, with little need for worker intervention. The reagent storage and flotation areas are open and well ventilated. The notifier states that plant operators in the reagent storage area are required to wear respirators, impervious gloves, coveralls and eye protection due to the presence of other hazardous chemicals. The notifier states that personnel in other areas will be required to wear impervious gloves, coveralls and chemical splash goggles. The metal concentrate is stockpiled before removal from the mine to the smelter. The notifier estimates that 80% (70% after the metal is washed) of the chemical will remain with the ore, and 20% will remain with the waste. The chemical will be destroyed during smelting (900 to 10 000°C, 0.5 to 1 hour).

Worker Education and Training
The notifier states that workers receive induction training including sessions on safe handling of hazardous chemicals. MSDS are available for workers.

7. PUBLIC EXPOSURE

There is little potential for exposure of the public to the notified chemical used as a mineral processing agent as it will not be sold to the public and will only be used in the mineral processing industry. The public would only be exposed to AERO®5100 Promoter in the event of an accident during transportation between dockside and the end customer site.

8. ENVIRONMENTAL EXPOSURE

Release

AERO® 5100 Promoter is likely to be used at the following four mine sites: Cadia in Orange and Northparkes near Parkes in NSW, Kanowna Belle near Kalgoorlie in WA and Mt Leyshon near Charters Towers in QLD.

The notified chemical functions as a flotation reagent, and 70% is estimated to remain bound to the mineral surfaces, and become incorporated in the metal sulphide concentrates. These are smelted for recovery of the metal and the high temperature of the furnace would destroy the compound.

Some of the remaining reagent becomes attached to the surface of the gangue (waste) minerals, deposited into the tailings dams. The notifier indicates that typically, 10% of the reagent would be disposed of with the tailings. The remaining 20% will remain with the water and be returned to the process. Based on an annual import volume of 87 tonnes, this equates to 8.7 tonnes of notified chemical being released to tailings dams per annum.

The reagent disposed of with the tailings either attached to gangue particles or dissolved in the water is not be expected to be released to the wider environment. Tailings dams are designed to "substantially" reduce the potential for seepage. All liner systems, whether soil or geotextile material, have a leakage rate and this will depend on the hydraulic conductivity of the liner. Hydraulic conductivity is influenced by the size and frequency of defects or discontinuities in the liner and the underlying base material and the length of time the hydraulic head is applied to the liner (EPA 1995). Older tailings dam floors are usually constructed from soils. The integrity of these soil floors depends largely upon the texture, strength, plasticity, and dispersion index of the soil type used including. The degree of maintenance and the age of the tailings dam are also important factors. Regardless of the lining used, there remains a risk of tailings dam seepage which may ultimately lead to contamination of surface and ground water. This concern is reinforced by a 1998 environmental report for Mt Leyshon Operations that reported seepage from a new tailings dam contaminating ground water bores (Normandy Mining Limited 1998). In addition, the 1997 Environment, Safety and Health Report (North Limited 1998) for North Limited

indicated that for all Australian sites, cases of actual or potential ground water contamination were identified.

Release to the environment may also occur as a result of accidental spillage. The material will be transported from dockside to the notifiers chemical warehouse where it will be stored prior to transport to mining sites. Transport will be by road in either 200 L drums or IBC. Risk of exposure to the environment in the case of accident, increases as container size increases. In the case of an accident leading to a ruptured bulk container, up to one tonne of the notified chemical could be released in a single event.

Fate

Approximately 20% of the notified chemical will be reclaimed and reused in the process.

Approximately 70% of the notified chemical will be exported with the metal concentrates. The material exported with the concentrates will be destroyed during smelting, with production of water vapour and oxides of carbon, nitrogen and sulphur.

Approximately 10% of the reagent will be disposed of into the tailings dams. It is a characteristic of most sulphide metal mines that pyrite and other gangue metal sulphides will slowly oxidise when exposed to air producing sulphuric acid and solutions of metal sulphates. Consequently, the water in the tailings dams becomes very acidic, (pH 1 and 2 is common) and highly polluted with heavy metal sulphates. The results from a preliminary study indicated that hydrolysis rates at pH 4, 7 and 9 at 50°C were less than 10% at 5 days. Although this level is low, it is likely that the notified chemical will degrade slowly due to the very low pH. The products of this degradation are further expected to slowly degrade to simpler compounds through chemical and physical processes.

The Ready Biodegradability of the notified chemical was assessed using the Closed Bottle Method (OECD TG 310D) (HLS 1998). The notified chemical degraded by 1% after 28 days indicating slow degradation. Tests on the reference substance indicated the inoculum was viable and the notified chemical was not significantly inhibiting to the microbial medium.

In the case of accidental release to waterways, the notified chemical would be likely to persist, either hydrolysing or degrading only slowly. The partition coefficient of 2.84 indicates the chemical is relatively lipophilic and will moderately sorb to soil sediments therefore soil mobility is expected (Mensinck, 1995). According to Connell (1990), the above physico-chemical data and the low molecular weight (173) indicate that the notified chemical has the potential to bioaccumulate. However, exposure to natural waters is expected to be low.

9. EVALUATION OF TOXICOLOGICAL DATA

The toxicological studies performed on the notified chemical (purity 98%) were performed according to corresponding EEC and OECD test guidelines (European Commission 1992), (OECD 1995-1996) at Huntingdon Life Sciences testing facilities. These facilities comply with the OECD principles of good laboratory practice and full test reports were submitted. All tests were performed on the notified chemical.

9.1 Acute Toxicity

Summary of the acute toxicity of Carbamothioic acid, 2-propenyl-, O-(2 methylpropyl)ester

Test	*Species*	*Outcome*	*Reference*
Acute oral toxicity	Rat	LD_{LO} > 500 mg/kg	**(HLS 1998)**
Acute dermal toxicity	Rat	LD_{50} > 2 000 mg/kg	(HLS 1998)
Skin irritation	Rabbit	Moderate Irritant	(HLS 1998)
Eye irritation	Rabbit	Slight irritant	(HLS 1998)
Skin sensitisation	Guinea pig	Sensitising	(HLS 1998)

9.1.1 Oral Toxicity (HLS 1998)

Species/strain:	Rat/Sprague-Dawley origin
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Gavage, dose of 500 mg/kg bw
Test method:	OECD TG 420 – fixed dose method EC Directive 92/69/EEC – fixed dose method
Mortality:	Nil
Clinical observations:	Piloerection, increased salivation and ungroomed appearance were observed within 7 minutes of dosing and accompanied by hunched posture, unsteady gait, lethargy, partially closed eyelids, pallid extremities, walking on toes and dull colouring to eyes in all rats. Abnormal respiration, discoloured urine, increased lacrimation, increased sensitivity to touch, thin appearance, protruding eyes, body tremors, prostration, blue and cold extremities and swollen abdomen were observed in some rats.
Morphological findings:	No abnormalities revealed upon macroscopic examination

LD_{LO}:	500 mg/kg discriminating dose
Comment:	The discriminating dose, ie the dose which caused evident toxicity, but not mortality (100% survival) was determined at 500 mg/kg
Result:	The notified chemical was of low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (HLS 1998)

Species/strain:	Rat/Sprague-Dawley origin
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	A single topical application of 2 000 mg/kg bw test article held under semi-occlusive dressing for 24 hours.
Test method:	OECD TG 402 EC Directive 92/69/EEC
Mortality:	Nil
Clinical observations:	Lethargy, partially closed eyelids and pallid extremities observed in one animal between 4 and 6 hours after dosing; slight body weight loss in two females on day 8 only
Morphological findings:	No organ abnormalities observed

Draize scores:

Time after treatment (days)	***Animal #***									
	1M	***2M***	***3M***	***4M***	***5M***	***6F***	***7F***	***8F***	***9F***	***10F***
Erythema										
2	1	0	1	2	2	2	2	2	0	2c
3	1	0a	1	1	1	2b	2a	1a	0	1c
4	0	0a	0	0	1	2ab	2a	1a	0	1c
5	0	0	0	0	0	2a	2a	1a	0	0
6	0	0	0	0	0	2a	2a	1a	0	0
7	0	0	0	0	0	1a	1a	0a	0	0
8	0	0	0	0	0	0a	0a	0	0	0
9-15	0	0	0	0	0	0	0	0	0	0
Oedema										
2	1	0	0	1	1	2	1	1	0	1
3	0	0	0	1	1	3	1	1	0	1
4	0	0	0	0	0	3	1	1	0	0
5	0	0	0	0	0	2	1	1	0	0
6	0	0	0	0	0	1	1	1	0	0
7	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0
9-15	0	0	0	0	0	0	0	0	0	0

[1] see Attachment 1 for Draize scales

M male
F female
a desquamation of the *stratum corneum* (characterised by dryness sloughing and/or scaling)
b necrosis (localised)
c patchy response (dry area of skin) at edge of dose site

Comment: Slight or well-defined erythema with or without slight to moderate oedema accompanied with localised desquamation of the *stratum corneum*, necrosis and a patchy response at the edge of the treated site from day 2 which was not visible after day 8

LD_{50}: > 2 000 mg/kg

Result: The notified chemical was of low dermal toxicity in rats.

9.1.3 Inhalation Toxicity

No studies were available. Claims were made and accepted for variation of schedule requirements of this toxicological end point, on the basis that the substance is a liquid with a low vapour pressure and it will be used in a closed, automated process which will minimise potential worker exposure.

9.1.4 Skin Irritation (HLS 1998)

Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	14 days
Method of administration:	A single topical application of 0.5 mL of test material to intact, shorn dorsal skin and held under semi-occlusive dressing for 4 hours
Test method:	OECD TG 404 EC Directive 92/69/EEC

Draize scores :

Animal #	***Time after treatment (days)***													
	1*	2	3	4	5	6	7	8	9	10	11	12	13	14
Erythema														
1	2	2	2	2	2	2a	2a	2a	2a	2	1	1	0	
2	0	2	2	2	2	2a	2a	2a	2a	2a	2a	2a	2a	1a
3	0	2	2	1	1	1	0							
Oedema														
1	1	1	1	1	1	1	1	1	1	1	1	1	0	
2	0	2	1	2	2	2	2	1	2	2	2	2	1	0
3	0	2	1	1	0	0	0							

[1] see Attachment 1 for Draize scales
*approximately 60 minutes after removal of the dressing
a desquamation of the *stratum corneum*

Mean individual score (24, 48 and 72 hours observation)	Erythema/Eschar Formation: 2, 2, 1.7 Oedema: 1, 1.7, 1.3
Comment:	Well-defined erythema with slight oedema was evident in all animals and accompanied by desquamation of the *stratum corneum* in two rabbits; the reactions persisted to day 6 or day 12 in two animals and until study termination in one animal
Result:	The notified chemical was a moderate irritant to the skin of

rabbits.

9.1.5 Eye Irritation (HLS 1998)

Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	3 days
Method of administration:	A single ocular dose of 0.1 mL of test material into one eye of each animal; the contralateral eye remained untreated and served as control
Test method:	OECD TG 405 EC Directive 92/69/EEC

Draize scores[1] *of unirrigated eyes:*

	Time after instillation											
Animal	***1 hour***			***1 day***			***2 days***			***3 days***		
Cornea	*All individual scores were zero*											
Iris	All individual scores were zero											
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	1	1	-	1	0	-	1	0	-	0	0	-
2	3	2	-	1	0	-	1	0	-	0	0	-
3	3	2	-	2	1	-	1	0	-	0	0	-

[1] see Attachment 1 for Draize scales
r = redness c = chemosis d = discharge

Mean individual score (24, 48 and 72 hour observation)	Redness of the conjunctivae: 0.7, 0.7, 1.0 Chemosis: 0, 0, 0.3
Comment:	No iridial or corneal effects were observed; a diffuse, beefy red coloration of the conjunctivae with partial eversion of the eyelids was evident in two animals after 1 hour exposure; transient hyperemia of blood vessels with slight swelling was observed in the remaining animal; the reactions had recovered by day 3 (72 hours)
Result:	The notified chemical was slightly irritating to the eyes of rabbits.

9.1.6 Skin Sensitisation (HLS 1998)

Species/strain:	Guinea pig/Dunkin/Hartley albino
Number of animals:	Test group: 20 males Control group: 10 males
Induction procedure:	
Test group: Day 1	Intradermal induction: Three pairs of intradermal injections (0.1 mL) into the dorsal skin of the scapular region: - Freund's complete adjuvant (FCA) 50:50 in water for injection - test material, 2.5% v/v in Alembicol D - The test material, 2.5% v/v in a 50:50 mixture of FCA and Alembicol D;
Day 8	Topical induction: Filter paper patch saturated with 0.4 mL test material applied to the scapular area and held under occlusive dressing for 48 hours;
Control group:	Treated similarly to the test animals omitting the test material from the intradermal injections and topical application
Challenge procedure:	
Day 22	An anterior site of the shorn flank of each animal was treated with 0.2 mL of test material, 75% v/v in Alembicol D, and a posterior site treated in 37.5% v/v in Alembicol D using filter paper patch and held under occlusive dressing for 24 hours
Test method:	OECD TG 406 – Maximisation Test EC Directive 96/54/EEC
Clinical observations:	No signs of ill health or toxicity were recorded; bodyweight increased in all animals over the period of the study

Challenge outcome:

Challenge concentration	*Dermal Reaction*	*Test animals*				*Control animals*	
		*24 hours**		*48 hours**		*24 hours*	*48 hours*
		E	O	E	O	E+O	E+O
37.5%	Grade 1	**9/20	4/20	8/20	2/20	0/10	0/10
	Grade 2	2/20	0/20	0/20	0/20	0/10	0/10
75%	Grade 1	12/20	8/20	11/20	8/20	0/10	0/10
	Grade 2	2/20	0/20	2/20	0/20	0/10	0/10

* time after patch removal
** number of animals exhibiting response
E = erythema
O = oedema
Grade 1 = slight erythema/ oedema
Grade 2 = well-defined erythema/ oedema

Comment: Dermal reactions observed in test animals were not observed in control animals. Thirteen of the 20 test animals scored Grade 1 or Grade 2, that is evidence of skin sensitisation.

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

9.2 Repeated Dose Toxicity (HLS 1998)

Species/strain: Rat/Sprague-Dawley

Number/sex of animals: 5/sex/group

Method of administration: oral (gavage); vehicle – corn oil

Dose/Study duration: 0, 15, 50 and 150 mg/kg bw/day (5 mL/kg bw/day) of the test substance administered once a day for 28 consecutive days

Test method: OECD TG 407
EC Directive 92/69/EEC

Clinical observations:
Dose-related, transient post-dose salivation was observed in all animals receiving 150 mg/kg bw/day from the second week of treatment. Piloerection, walking on toes and hunched posture were occasionally seen in 150 mg/kg bw/day animals. Body weight gain was reduced in a generally dose-related manner among all treated male groups and females at 50 and 150 mg/kg bw/day groups. Food consumption was affected in males receiving 50 and 150 mg/kg bw/day during the first week of the treatment. Slightly reduced efficiency

of food consumption for male animals at 150 mg/kg bw/day was observed, reflecting the reduced bodyweight gain at this dose. Increased water intake was seen among both sexes at 150 mg/kg bw/day.

No behavioural changes indicative of neurotoxicity were observed.

Clinical chemistry/Haematology
Cholesterol was significantly increased among both sexes receiving 150 mg/kg bw/day. Other changes observed in clinical chemistry parameters or hematological indices were either considered to be of no toxicological significance or within historical control ranges.

Pathology:

Organ weight: Liver weight was slightly increased among both sexes at top dose and females receiving 50 mg/kg bw/day. Decreased thymus weights among all treated animals (dose-related in males) were observed.

Macroscopy: No macroscopic pathological changes were seen.

Microscopy: Microscopic changes in the liver were found in both sexes at 150 mg/kg bw/day and consisted of minimal/slight cell loss and/or inflammatory cell infiltration in the centrilobular region and hypertrophy of centrilobular hepatocytes. Involution/atrophy of the thymus was observed among all treated animals, while a slight reduction in colloid in the follicles of the thyroid was seen among both sexes receiving 150 mg/kg bw/day.

Comment:
Changes observed at 150 mg/kg bw/day were indicative of systemic toxicity. The liver was identified as the target organ. Treatment related changes, reduced bodyweight gain and involution/atrophy of the thymus, were observed at 15 mg/kg bw/day.

Result:
No suitable No Observed Effect Level (NOEL) has been established from this study as treatment related changes were observed at the lowest dose tested, 15 mg/kg bw/day. Therefore, the Lowest Observed Adverse Effect Level (LOAEL) is 15 mg/kg/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (HLS 1998)

Strains:	*Salmonella typhimurium* TA 1535, TA 1537, TA 98, TA 100 and *Escherichia coli* CM 891
Metabolic activation:	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254, 10% or 20%
Concentration range:	Two independent tests were performed: Test 1: 0, 5, 15, 50, 150, 500, 1 500 and 5 000 μg/plate with and without S9 mix (10% S9 fraction); Test 2: 0, 50, 150, 500, 1 500 and 5 000 μg/plate with and

	without S9 mix (20% S9 fraction) Test substance was diluted in ethanol and used as a negative control; appropriate strain specific positive control reference substances were used
Test method:	OECD TG 471 - plate incorporation assay EC Directive 92/69/EEC
Comment:	Inhibition of bacterial growth occurred in both Tests in all strains at 5 000 μg/plate; substantial dose-related increases in revertant colony numbers over control counts were observed in strain TA 1535 in both Tests and in strain TA 100 in Test 1 in the presence of S9 mix; slight increases (less than 2- fold) in strain TA 100 in Test 2 with S9 mix were also obtained; these results were maximal at 1 500 μg/plate
Result:	The notified chemical tested in ethanol showed evidence of mutagenic activity in *Salmonella typhimurium* strains TA 1535 and TA 100 in the presence of metabolic activation, under the conditions of the experiment.

9.3.2 *In Vitro* Mammalian Cell Mutation Assay (HLS 1998)

Species/strain:	L5178Y mouse lymphoma cells
Concentration range:	Two independent experiments were performed. Experiment 1 (without S9 mix): Test 1: 0, 5, 10, 20, 30, 40 and 60 μg/mL; Test 2: 0, 1, 2.5, 5, 7.5, 10, 20, 40 and 60 μg/mL. Experiment 2 (with S9 mix): Test 1: 0, 5, 10, 20, 30, 40 and 50 μg/mL; Test 2: 0, 2.5, 5, 10, 15, 20, and 30 μg/mL. Vehicle was ethanol; appropriate positive control reference substances were used.
Metabolic activation:	Liver fraction (S9 mix) from rat pretreated with Aroclor 1254
Test method:	OECD TG 476 EC Directive 88/302/EEC
Comment:	Toxicity was observed in treated cultures in all preliminary toxicity tests, both with and without S9 mix. Increases in mutation frequency were observed in treated cultures in both experiments, with and without S9 mix, but an increase of

	100 over the control value was not achieved. All mutation frequency values were within the normal control ranges with one exception. In Experiment 1 with presence of S9 mix, there was evidence of mutagenic activity in cultures treated with test substance at 30 μg/mL, but the Relative Total Growth (RTG) value of 0.4% was considerably below the required value of 10-20%.
Result:	The notified chemical showed non-conclusive evidence of mutagenic potential at the thymidine kinase locus on L5178Y mouse lymphoma cells *in vitro*

9.3.3 Micronucleus Assay in the Bone Marrow Cells of the Mouse (HLS 2000)

Species/strain:	mouse/Crl:CD-1 (ICR) BR
Number and sex of animals:	5/sex/dose group
Doses/Method of administration:	By intraperitoneal injection: Test substance: 25 mg/kg (low), 50 mg/kg (mid) or 100 mg/kg (high); Vehicle control: corn oil; Positive control, by intragastric gavage, Mitomycin C 12 mg/kg.
Sampling schedule:	Vehicle control, low, mid and high dose animals were sacrificed 24 hours after dosing; Remaining animals of the vehicle control group and high dose animals were sacrificed 48 hours after dosing; Positive control group animals were sacrificed 24 hours after dosing
Micronuclei score:	No significant increase in micronucleated polychromatic erythrocytes (PCE) due to treatment with test substance at either sampling time. The positive control caused a significant increase in micronucleated PCE.
Test method:	OECD TG 474
Result:	The notified chemical did not induce a significant increase in micronucleated PCE in bone marrow cells of the mouse *in vivo.*

9.4 Overall Assessment of Toxicological Data

The notified chemical has low acute oral toxicity (LD_{L0} > 500 mg/kg) and low dermal toxicity (LD_{50} > 2 000 mg/kg) in rats. Acute inhalation studies have not been conducted for the notified chemical. In rabbits, the notified chemical was a skin irritant but not an eye irritant. The notified chemical was sensitising to guinea pig skin.

In a 28 day repeat oral dose study, the notified chemical produced systemic toxicity and pathological effects in rats at dose of 150 mg/kg bw/day. These included reduced body weight gain, slight impairment of food utilisation, increased water intake, slight increased cholesterol level, increased liver weight and decreased thymus weight. Microscopic examination revealed slight liver cell loss and/or inflammatory cell infiltration in the centrilobular region and hypertrophy of centrilobular hepatocytes, slight reduction in colloid in the follicles of the thyroid and involution/atrophy of the thymus. No suitable NOEL has been established from this study as treatment related changes were observed at the lowest dose,15 mg/kg bw/day. The LOAEL is 15 mg/kg bw/day.

The notified chemical tested in ethanol revealed mutagenic activity in a bacterial test system but demonstrated non-conclusive evidence of mutagenic potential at the thymidine kinase locus on L5178Y mouse lymphoma cells *in vitro.* Further investigation of mutagenic activity revealed that the notified chemical was non genotoxic in the *in vivo* mouse micronucleus test.

Based on the submitted data the notified chemical is classified a hazardous substance under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 1999). Risk phrases R22 (likely to be 'harmful if swallowed'), R38 (irritating to skin), R43 (may cause sensitisation by skin contact), and R48/22 (harmful: danger of serious damage to health by prolonged exposure if swallowed) are appropriate.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Tests were performed according to corresponding EEC and OECD test guidelines (OECD 1995-1996), (European Commission 1992) at Huntingdon Life Sciences testing facilities, UK. These facilities comply with the OECD principles of good laboratory practice and full test reports were submitted. All tests were performed on the notified chemical.

10.1 Summary of Ecotoxicity Test Results

Test	***Species***	***Test Substance Concentration* mg/L***	***Result mg/L***
Acute Toxicity (Semi-Static Test); (OECD TG 203)	Rainbow trout (*Oncorhynchus mykiss*)	0.46, 1.0, 2.2, 4.6, 10.0	96 hour: $1.9 < LC_{50} < 4.1$ NOEC** = 0.38
Acute Toxicity - Immobilisation (Static Test) (OECD TG 202 part I)	Water Flea (*Daphnia magna*)	0.0001, 0.00022, 0.00046, 0.001, 0.002, 0.0046, 0.01, 0.022	48 hour EC_{50} = 0.006 NOEC = 0.0022 LOEC*** = 0.0051
Growth Inhibition - Growth (μ) & Biomass (b) (Static Test) (OECD TG 201)	Alga (*Selenastrum capricornutum*)	0.33, 0.74, 1.6, 3.4, 7.2, 16.0	0-72 hour E_RC_{50} = 9.3 72 hour E_BC_{50} = 3.9 NOEC < 0.33

* Actual concentration.
** NOEC - no observable effect concentration.
*** LOEC – lowest observable effect concentration.

The submitted EC_{50} values for all test organisms were calculated using the Thompson and Weil model, a model not favoured in this environmental assessment. Probit analysis could not be undertaken on fish and alga toxicity tests due to the experimental design. Consequently, the EC_{50} values for these species are estimated from the data provided.

10.2 Fish Acute Toxicity (HLS 1998)

Results reported are actual and not nominal concentrations. At 96 hours, actual concentrations ranged from 82 to 85% of nominal. At 96 hours, the highest test concentration resulting in 0% mortality was 1.9 mg/L. At this concentration, sub-lethal effects were observed at 2 hours. These effects included increased pigmentation, swimming at the surface, hyperventilation, lethargy, loss of equilibrium and distended abdomen. The lowest test concentration resulting in 100% mortality was 4.1 mg/L. These values indicate that the slope of the dose response curve is very steep. From the data provided the estimated EC_{50} lies between 1.9 and 4.1 mg/L.

10.3 Aquatic Invertebrate Acute Toxicity (HLS 1998)

Measured test concentrations ranged from 144 to 107% of nominal concentrations at 0 hours and 91-83% at 96 hours. Under the conditions of the study, 10% immobilisation was not considered to be biologically significant. Therefore, 0.10 µg/L was considered to be a close approximation of the highest test concentration resulting in 0% immobilisation. Due to the limited sensitivity of the analytical method of analysis (limit of quantification < 4 µg/L) it was not possible to verify the aqueous test concentrations below 4.6 µg/L. However, stock solutions used to prepare all the exposure concentrations were analysed and found to be 97 to 72% of nominal at 0 hours, which inferred that near nominal concentrations were achieved at the start of the study. This assessment reanalysed the daphnia test data using Probit analysis. The NOEC, LOEC and EC_{50} provided in the above table were calculated using the Bonferroni t-Test. The EC_{50} ranges from 3.46 to 11.16 µg/L (95% CI). Values provided by the notifier using the Thompson and Weil model were 6.8 µg/L (EC_{50}, 95% CI 3.2-15) and 0.22 µg/L (NOEC). It should be noted that the 24 hr EC_{50} value provided by the notifier (>22 µg/L) is markedly higher than the 48 hour value (6.8 µg/L). This suggests that equilibrium may not have been reached and that the actual EC_{50} value may be even lower. Results for testing of chronic effects to daphnia are not available.

10.4 Alga Growth Inhibition Test (HLS 1998)

All results are based on mean measured concentrations of notified chemical which ranged from 74 to 80% of nominal at 0 hours and 68 to 77% of nominal at 72 hours. The NOEC of less than 0.33 mg/L (determined using the Williams' test) indicated statistically significant inhibition of growth at the 5% level. However, the mean % inhibition was less than 10% and not considered biologically significant. The notifier indicated that the E_RC_{50} was 9.3 mg/L. However, in the absence of Probit analysis, the E_RC_{50} value should be estimated to lie between 2.3 and 16 mg/L.

10.5 Activated Sludge

Whilst there were no data presented regarding Activated Sludge-Bacterial Inhibition, the three hour EC_{50} of the notified chemical is reported in the Material Safety Data Sheet (MSDS) to be 137.5 mg/L.

10.6 Conclusion

The ecotoxicity data indicate that the notified chemical is moderately toxic to fish and algae, highly toxic to daphnia but not toxic to water treatment bacteria.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

AERO® 5100 Promoter will be contained within the tailings dam and release to the environment of the notified chemical is expected to be minimal. The notifier has stated that tailings storage dams are designed to "substantially" reduce the potential for seepage to occur. Regardless of the type of floor employed there remains some risk of tailings dam seepage which may lead to contamination of surface and ground water. These factors, combined with the high toxicity to aquatic organisms, suggest that the notified chemical poses a significant

environmental risk if accidentally released regardless of the remoteness of the site of use.

In the event of accidental spillage, transporters will rely on the MSDS for instructions to minimise exposure to the environment, and for clean up and disposal.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Based on the available toxicity data, the notified chemical is acutely toxic by the oral route, elicits well defined skin irritation and is a skin sensitiser. In a 28 day oral (gavage) repeat dose study a NOEL could not be established. The LOAEL was 15 mg/kg/day. Hence, the notified chemical may pose a danger of serious damage to health by prolonged exposure. The notified chemical tested in ethanol revealed mutagenic activity in a bacterial test system but demonstrated non-conclusive evidence of mutagenic potential at the thymidine kinase locus on L5178Y mouse lymphoma cells *in vitro.* Genotoxic activity was not observed *in vivo* in a mouse micronucleus test.

Under the NOHSC *Approved Criteria for Classifying Hazardous Substances,* the notified chemical is classified as Harmful (Xn) with the following risk phrases assigned: R22 – Harmful if Swallowed; R38 – Irritating to Skin; R43 – May Cause Skin Sensitisation; and R48/22 Harmful: Danger of Serious Damage to Health by Prolonged Exposure if Swallowed.

Occupational Health and Safety
Given the nature of the chemical, it is critical that worker exposure does not occur either accidentally or in routine use. Transport and storage of the 200 or 1 000 L import containers should not result in worker exposure except in the event of accidental spillage.

Worker exposure during normal use of the notified chemical is most likely to occur from drips and spills when connecting or disconnecting lines or cleaning pumps and ancillary equipment. The notifier states that plant operators involved in transferring the notified chemical to the flotation cell and overseeing the flotation process are required to wear respirators, impervious gloves, chemical splash goggles and coveralls. It is critical that employers ensure that workers wear the personal protective clothing as specified, to minimise the potential for exposure and the risk of adverse health effects. Once mixed in with the ore slurry, the notified chemical is contained within an automated process requiring little worker intervention. The initial maximum concentration of reagent is 0.00435% in the slurry, however, as the slurry becomes more concentrated, the reagent concentration will increase. The maximum concentration is not known. Therefore, any worker who may potentially come in contact with the slurry should wear the personal protective equipment specified above. The subsequent processes also require little worker intervention. Chemical incorporated during process operations is ultimately destroyed during subsequent off-site metal processing.

Public Health
There is little potential for exposure of the public to the notified chemical used as a mineral processing agent as it will not be sold to the public and will only be used in the mineral processing industry. The public would only be exposed to the notified chemical in the event of an accident during transportation between dockside and the end customer site. The low exposure potential indicates a negligible risk to public health.

13. RECOMMENDATIONS

Occupational Health and Safety
To minimise occupational exposure to AERO®5100 Promoter the following guidelines and precautions should be observed:

- Workers receive regular education and training on handling techniques, good hygiene practices and potential adverse health effects associated with use of AERO®5640 Promoter;
- As potential for skin sensitisation exists the notifier's MSDS should be provided to the authorised medical practitioner responsible for health surveillance in the workplace;
- 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 1998);
- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand 1994);
- 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;
- A copy of the MSDS should be easily accessible to employees.

Environmental
Where seepage is known to occur, monitoring of ground and surface waters for the presence of the notified chemical or general tests for toxicity using daphnia should be conducted.

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

Recommendation to NOHSC
The notified chemical may be recommended to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC *List of Designated Hazardous Substances*.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the AERO®5100 Promoter, containing the notified chemical, was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 1994).

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

15. 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.

16. REFERENCES

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Standards Australia/Standards New Zealand (1994) AS/NZS 2210-1994, Australian/New Zealand Standard Occupational Protective Footwear. Sydney/Wellington, Standards Australia and Standards New Zealand.

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