File No: NA/564

2 February 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Thioimidodicarbonic Acid ((HO)C(O) NHC(S)(OH)), 1-ethyl, 3-hexyl ester, branched and linear
(AERO®5640 Promoter)

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

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(AERO®5640 Promoter)

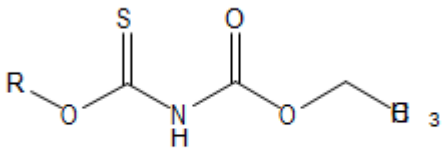
1. APPLICANT

Cytec Australia Holdings Pty Ltd of Suite 1, First Floor, 7-11 Railway Street BAULKAM HILLS NSW 2153 has submitted a standard notification statement in support of their application for an assessment certificate for Thioimidodicarbonic Acid ((HO)C(O) NHC(S)(OH)), 1-ethyl, 3-hexyl ester, branched and linear.

No claims for exempt information were made.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	Thioimidodicarbonic Acid ((HO)C(O) NHC(S)(OH)), 1-ethyl, 3-hexyl ester, branched and linear
Chemical Abstracts Service (CAS) Registry No.:	None assigned
Other Names:	CT-639-97
Marketing Name:	AERO®5460 Promoter; Reagent S-6588 Promoter
Molecular Formula:	$C_{10}H_{19}NO_3S$
Structural Formula:	



R = C_6H_{13} (isomers)

Molecular Weight:	233
Method of Detection and Determination:	Infra-red (IR) spectroscopy; Gel Permeation Chromatography analysis.

Spectral Data:	IR spectra: major absorbance peaks observed at approximately 3 255, 2 962, 1 769, 1 529, 1 466, 1 396, 1 327, 1 254, 1 173, 1 095, 1 058 cm^{-1}

Comments on Chemical Identity

AERO®5460 Promoter is a light yellow to orange-red clear non-viscous liquid with an alcoholic odour. AERO®5460 Promoter is synthesised by condensation of thioimidodicarbonic acid, 1-ethyl ester with a mixture of C6 alcohols. These alcohols are added in excess and remain as residual solvent at the end of the process. Thus, the concentration and composition of these alcohols may vary from batch to batch. However, the purity of AERO®5460 Promoter will remain between 73 to 75%.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	light yellow to orange-red, clear, non-viscous liquid with an alcohol odour
Freeze Point:	<-25°C
Boiling Point:	177.5°C
Specific Gravity:	1.04 at 23°C
Vapour Pressure:	0.271 kPa at 25°C
Particle Size:	Not applicable, substance is a liquid
Water Solubility:	0.0733 g/L at 20°C
Partition Co-efficient (n-octanol/water):	log P_{ow} = 3.53 to 3.71
Hydrolysis as a Function of pH at 25°C:	145 days at pH 4.0 169 days at pH 7.0 80.2 days at pH 9.0

Adsorption/Desorption:	Log_{10} K_{oc} = 3.08 to 3.15
Dissociation Constant:	Not determined (see comments below)
Flash Point:	67.5°C closed cup method
Flammability Limits:	Not determined, not classified as a Dangerous Good
Autoignition Temperature:	346°C (liquids and gases)
Explosive Properties:	Not explosive
Reactivity/Stability:	Stable

Comments on Physico-Chemical Properties

Tests were performed according to corresponding EEC and OECD test guidelines (European Commission, 1992, OECD, 1995-1996) at Huntingdon Life Sciences Testing Facilities, UK (HLS, 1998b). 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.

The vapour pressure of AERO®5460 Promoter was determined using the static method (OECD TG 104) to be 271 Pa at 25°C. The notified chemical without solvent is expected to be volatile since it has a low molecular weight with ester functionality. This is confirmed in the ecotoxicity studies where test media containing AERO®5460 Promoter were kept sealed to reduce loss by evaporation.

The maximum water solubility of AERO®5460 Promoter was determined to be 73.3 mg/L at 20°C using the flask method (OECD TG 105) which is to be expected given the notified chemical is an organic compound containing neither dissociable functionalities or hydrophilic groups.

Hydrolysis of the notified chemical was studied (Directive 92/69 EEC) at pH 4, 7 and 9 while at 50, 60 and 70ºC (HLS, 1999a). The notifier used the data from these tests to determine the hydrolysis rate constants at 25ºC using the Arrhenius relationship. The notified chemical was found to be hydrolytically stable with half-lives at 25°C of 145, 169 and 80.2 days at pH 4, 7 and 9, respectively. Ester groups are expected to undergo hydrolysis at extreme pH.

The partition coefficient log P_{OW} of AERO®5460 Promoter between n-octanol and water was estimated to range from 3.53 to 3.71 by the HPLC method (OECD TG 117), which is consistent with the hydrophobic nature of the chemical.

The notifier estimated the sorption behaviour of the notified chemical on soil by using HPLC in accordance with OECD TGP/94.75 (HLS, 1999d). The nature of the stationary phase in a HPLC column allows for the interaction of polar and apolar parts of a molecule in a similar way as with soil. This enables the relationship between the retention time on a column and the adsorption coefficient on the organic parts of the soil to be established. The notifier, therefore, determined the adsorption/desorption coefficient, K_{oc}, of AERO®5460 Promoter to range from 1 200 to 1 400 which indicate low mobility in soil.

The notifier indicates that AERO®5460 Promoter does not contain any group that can undergo dissociation.

4. PURITY OF THE CHEMICAL

Degree of Purity: 73-75%

Hazardous Impurities:

Chemical name:	Hexanol, branched and linear
CAS No.:	68526-79-4
Weight percentage:	6-24%
Toxic properties:	R41: Risk of Serious Damage to Eyes (notifiers MSDS)
Chemical name:	Isobutanol
Weight percentage:	1-19%
CAS No.:	78-83-1
Toxic properties:	Hazard Classification (NOHSC, 1999b): R10: Flammable; R20: Harmful by Inhalation. National Exposure Standard (NOHSC, 1995): 50 ppm (152 mg/m^3) TWA

Non-hazardous Impurities (> 1% by weight): none

Additives/Adjuvants:

Chemical name:	Quinoline
CAS No.:	91-22-5
Weight percentage:	1.0%

5. USE, VOLUME AND FORMULATION

AERO®5640 Promoter will not be manufactured in Australia. It will be imported by sea in either 200 L steel drums or one tonne international bulk containers (IBC) and transported by road to the notifiers warehouse at Arndell Park. AERO®5460 Promoter will be supplied to customers in the original containers and no repackaging of the product will occur.

AERO®5460 Promoter is to be used as a mineral-processing reagent during the processing of sulphide ores by flotation. The flotation process involves addition of the reagent to aqueous slurries of crushed and finely ground ore contained in a series of flotation tanks. During the use of AERO®5460 Promoter in the flotation process, the mineral particles become separated as froth from the tailings, which settle at the bottom of the flotation tank.

AERO®5460 Promoter will be either pumped or gravity fed from the 200 L drums and IBCs 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. The process will be completely automated.

The froth or float is collected and dried. Tailings are transferred as a slurry to a tailings dam where they ultimately settle, dry and consolidate. Spills and washings would also be directed to tailings dams. Tailings typically have a solids content of about 30%. In some operations, tailings may be intercepted in settling tanks so that wastewater containing low concentrations of the notified chemical can be recovered for reuse in flotation.

Projected import volumes for AERO®5460 Promoter are 10 to 50 tonnes per year for the first five years.

6. OCCUPATIONAL EXPOSURE

Transport and Storage (2 to 10 workers; 2 to 3 hours/day, 10-15 days/year)
Transport and storage workers may be exposed to the notified chemical 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®5460 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 7.5 to 37.5 ppm (0.00375%). The chelated metal, including AERO®5460 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).

7. PUBLIC EXPOSURE

There is little potential for exposure of the public to AERO®5640 Promoter 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®5640 Promoter in the event of an accident during transportation between dockside and the end customer site.

8. ENVIRONMENTAL EXPOSURE

Release

The notifier indicates that AERO®5460 Promoter maybe used at the Western Mining Corp. Ltd. Nickel operation at the Mt. Keith mine located in WA. It could also be possibly used at mine sites located at either Orange or Parkes in NSW, Kanowna Belle in WA and at the Normandy mine at Mt. Leyshon in QLD.

The chemical functions as a flotation reagent and most, around 70%, remains bound to the mineral surfaces, and becomes 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, with production of water and oxides of carbon, nitrogen and sulphur.

Some of the remaining reagent becomes attached to the surface of the gangue (waste) minerals, and these are deposited into 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 maximum import volume of 50 tonnes, this equates to 5 tonnes of AERO®5460 Promoter which is approximately 3.75 tonnes of the 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 expected to be released to the wider environment. Tailings dams are designed to "substantially" reduce the potential for seepage. All liner systems of tailing dams have a leakage rate and this rate will depend on the hydraulic conductivity of the liner.

Hydraulic conductivity is dependent on the properties of the liner material either soil or geotextile material. The properties include the size and frequency of either defects or discontinuity in the liner and 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 soil type used, including the texture, strength, plasticity and dispersion index. The integrity also depends upon the maintenance and age of the tailings dam. 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 and 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 IBCs. 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 1 tonne of the notified chemical could be released in a single event.

Fate

The notifier estimates approximately 20% of the notified chemical will be reclaimed and reused in the process.

The notifier claims 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 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 with production of sulphuric acid and solutions of metal sulphates. Consequently the water in the tailings dams becomes very acidic, pH between 1 and 2 is common, and highly polluted with heavy metal sulphates. The notified chemical was found to be hydrolytically stable with a half-life at 25°C of 145 days at pH 4 (see Physico-Chemical Properties). However, it is likely that the notified chemical will degrade slowly in the tailings dam 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 AERO®5460 Promoter was assessed by exposure to micro-organisms from a domestic sewage treatment plant in the Closed Bottle Method (OECD TG 310D) over a period of 28 days (HLS, 1999f). Bottles were filled with mineral salts medium inoculated with sewage effluent 1 mL/L and AERO®5460 Promoter was added at a nominal concentration of 4 mg/L. The concentrations of dissolved oxygen in the bottles were measured at the start of the test and after 5, 7, 11, 14, 18, 21, 25 and 28 days of incubation at 22ºC. Oxygen consumption in the bottles was at most 0.49 mgO_2/mg, which is 25% of its theoretical oxygen demand of 1.99 mgO_2/mg. A biodegradation plateau was achieved after approximately 10 days. Substances are considered to be readily biodegradable in this test if oxygen consumption is either equal to or greater than 60% of the theoretical value within ten

days of the level exceeding 10%. AERO®5460 Promoter cannot, therefore, be considered to be readily biodegradable.

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 3.53-3.71 indicates that the chemical is relatively hydrophobic. The adsorption/desorption coefficient, of AERO®5640 Promoter ranges from 1 200 to 1 400 indicating that the chemical has low mobility in soil. The notified chemical is unlikely to bioaccumulate particularly since exposure to natural waters is expected to be low.

The notifier indicates that approximately 0.5% of residual product will be left in the drums after emptying and that these residues will be rinsed out with water and the rinsate sent to the on-site wastewater treatment plant. This assessment believes that this is unlikely and expects that all residues and wastes will be sent directly to tailings dams. Licensed contractors will dispose of empty containers.

9. EVALUATION OF TOXICOLOGICAL DATA

Tests were performed according to corresponding EEC and OECD test guidelines (European Commission, 1992, OECD, 1995-1996) at Huntingdon Life Sciences Testing Facilities, UK, except for the mouse micronucleus assay which was conducted by Hazelton Laboratories, USA. 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 AERO®5460 Promoter

Test	*Species*	*Outcome*	*Reference*
Acute oral toxicity	Rat	Discriminating dose = 50 mg/kg	(HLS, 1998d)
Acute dermal toxicity	Rat	LD_{50}>2 000mg/kg	(HLS, 1998c)
Skin irritation	Rabbit	Moderate irritant	(HLS, 1998h)
Eye irritation	Rabbit	Slight irritant	(HLS, 1998f)
Skin sensitisation	Guineapig	Skin sensitiser	(HLS, 1998i)

9.1.1 Oral Toxicity (HLS, 1998d)

Species/strain: Rat/Sprague-Dawley

Number/sex of animals: 5/sex/group

Observation period: 14 days

Method of administration: Gavage, 500 mg/kg or 50 mg/kg

Test method:	OECD TG 420 – Fixed Dose Method; EC Directive 92/69/EEC.
Mortality:	One male died within 24 hours after administration of 500 mg/kg; There were no deaths at 50 mg/kg.
Clinical observations:	Piloerection became evident in all rats within 6 minutes of dosing. By day 1, there was hunched posture, pallid extremities, walking on toes and ungroomed appearance in all rats. A number of animals also exhibited a waddling/unsteady gait, lethargy, abnormal respiration, partially closed eyelids, abnormal faeces, discoloured bright yellow urine, increased salivation, increased lacrimation, increased sensitivity to touch, thin appearance, protruding eyes, body tremors, prostration, blue/cold extremities and dull colouring to eyes. The majority of signs had resolved by day 3 or day 6 and recovery was complete in surviving animals by day 9.
Morphological findings:	Macroscopic examination of the decedent revealed congestive changes to the majority of tissues and organs. No abnormalities were detected in animals that survived treatment and killed at termination.
Comment:	Body weight gain was normal in all surviving rats.
LD_{LO}:	50 mg/kg (discriminating dose[1])
Result:	The notified chemical caused evident toxicity[2] in rats at 50 mg/kg

9.1.2 Dermal Toxicity (HLS, 1998c)

Species/strain:	Rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Animals were dosed dermally with 2 000 mg/kg applied to clipped and unabraded skin and then covered with a gauze patch and secured with non-irritating adhesive tape. After 24 hours, the dressings were removed and washed of any residual test substance.

[1] Discriminating dose is the highest out of four fixed dose levels (5, 50, 500, 2 000 mg/kg) which can be administered without causing substance related mortality (including humane kills).
[2] Evident toxicity is used to designate toxic effects, after exposure to the substance tested, which are so severe that exposure to the next highest fixed dose would probably lead to mortality.

Test method: OECD TG 402

Mortality: Nil

Clinical observations: Slight to well-defined dermal irritation was first evident on removal of the dressing on Day 2 and persistent over the following days in three rats (2 males, 1 female), resolving completely by Day 7. In addition, desquamation was seen in one of the males and in one further female on Days 4 through 6. No dermal reactions were observed in the remaining six animals throughout the study.

Morphological findings: No abnormalities were recorded at the macroscopic examination on Day 15

Draize scores:

Time after treatment (days)	***Rat #***									
	1M	***2M***	***3M***	***4M***	***5M***	***6F***	***7F***	***8F***	***9F***	***10F***
Erythema	*									
2	2	0	0	1	0	0	0	1	0	0
3	2	0	0	1	0	0	0	1	0	0
4	2a	0	0	0	0	0a	0	1	0	0
5	1a	0	0	0	0	0a	0	1	0	0
6	1a	0	0	0	0	0a	0	1	0	0
7 to 15	0	0	0	0	0	0	0	0	0	0
Oedema		0	0	0	0	0	0	0	0	0
2	1	0	0	0	0	0	0	0	0	0
3	1	0	0	0	0	0	0	0	0	0
4	1	0	0	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0	0	0
6	1	0	0	0	0	0	0	0	0	0
7 to 15	0	0	0	0	0	0	0	0	0	0

* see Attachment 1 for Draize scales.
F = female. M = male.
[a] desquamation of the stratum corneum (characterised by dryness sloughing and/or scaling)

Comment: There was no evidence of a systemic response in any of the animals throughout the study. One female had a low bodyweight gain on Day 8 and another on Day 15.

LD_{50}: > 2 000 mg/kg

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

9.1.3 Inhalation Toxicity

The notifier has sought a variation to schedule requirements for data relating to inhalation toxicology on the basis that the notified chemical is not considered to be volatile. As the imported product will be used in a sealed, automated system, it is considered that mists are unlikely to occur and worker exposure by inhalation will not be significant.

9.1.4 Skin Irritation (HLS, 1998h)

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 3 females

Observation period: 13 days

Method of administration: Dermal application of 0.5 mL of AERO®5460 Promoter under semi-occlusive conditions for four hours

Test method: OECD TG 404

Draize scores:

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

* see Attachment 1 for Draize scales

[a] desquamation of the stratum corneum (characterised by dryness and sloughing of the skin)

Mean individual score Erythema: 1.7, 1.7, 1.7;

(24, 48, 72 hours observation): Oedema: 1.3, 0, 0.3.

Comment: There were no signs of toxicity or ill health in any rabbit during the observation period. Well-defined erythema with or without very slight to slight oedema was seen in all three animals. Additionally, desquamation of the stratum corneum (characterised by dryness and sloughing of the skin) developed in all rabbits, and resolved completely by either Days 9, 10, or 13.

Result: The notified chemical was a moderate irritant to the skin of rabbits.

9.1.5 Eye Irritation (HLS, 1998f)

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 3 females

Observation period: 3 days

Method of administration: 0.1 mL of the notified chemical was placed into the lower everted lid and held in place for one second. The contralateral eye served as control.

Test method: OECD TG 405

Draize scores of unirrigated eyes:

	Time after instillation											
Rabbit #	***1 hour***			***24 hours***			***48 hours***			***72 hours***		
Cornea	*All scores were zero*											
Iris	*All scores were zero*											
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	1*	0	0	1	0	0	0	0	0	0	0	0
2	2	1	0	1	0	0	0	0	0	0	0	0
3	2	1	0	2	0	0	1	0	0	0	0	0

* 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: 0.3, 0.3, 1;
Chemosis: 0, 0, 0.

Comment: There were no signs of toxicity or ill health in any rabbit during the observation period. No corneal damage or iridial

	inflammation was observed. A diffuse crimson colouration of the conjunctivae with slight swelling was seen in two animals. Transient hyperaemia of blood vessels only was observed in the remaining animal. These reactions completely resolved by either two or three days after instillation.
Result:	The notified chemical was slightly irritating to the eyes of rabbits

9.1.6 Skin Sensitisation (HLS, 1998i)

Species/strain:	Guineapig/albino
Number of animals:	30 males (20 test; 10 control)
Induction procedure:	Day 1-intrademal injections on the scapular region where three pairs of injections were made. Freund's Complete Adjuvant (FCA) in distilled water, 2.5% AERO®5460 Promoter in Alembicol D, and 2.5% of AERO®5460 Promoter in a 50:50 mixture of FCA and Alembicol D. Day 7 - 0.5 mL of 10% w/w sodium lauryl sulphate in petrolatum gently rubbed onto the treatment site; Day 8 - 48 hour occluded application of 0.4 mL of test substance as supplied. Control animals were treated as above, omitting the test substance.
Challenge procedure:	Day 21 - 24 hour occluded application of 0.2 mL of test substance as supplied to the anterior left flank; 50% v/v Alembicol D applied similarly to the posterior left flank.
Test method:	OECD TG 406/ Magnusson and Kligman Maximisation Test
Comment:	Dermal reactions were seen in 19/20 test animals compared with 0/10 in the controls. There were no signs of ill health or toxicity and all guinea pigs recorded bodyweight gains.
Result:	The notified chemical was severely sensitising to the skin of guinea pigs.

9.2 Repeated Dose Toxicity (HLS, 1998j)

Species/strain:	Rats/Sprague-Dawley albino
Number/sex of animals:	5/sex/group
Method of administration:	Oral (gavage)
Dose/Study duration:	0, 15, 50 and 150 mg/kg day of the notified chemical in corn oil for 28 consecutive days.
Test method:	OECD TG 407

Clinical observations:

Transient post-dose salivation was observed in all animals from the second week of treatment, in a dose-related manner. Alopecia was observed in all animals at the 150 mg/kg/day dose, decreasing in incidence at the lower doses. The high dose group exhibited behavioural changes suggestive of neurotoxicity but these were not substantiated by histopathology.

During the first few days of treatment actual bodyweight loss was noted in the 150 mg/kg/day groups and remained notably lower than controls for the duration of the study. Bodyweight gain was also slightly reduced for females receiving 50 mg/kg/day over the entire treatment period. Food consumption for the 150 mg/kg/day group was also adversely affected.

During Week 2 of treatment, three females in the 150 mg/kg/day group were killed on humane grounds, due to their poor clinical condition.

Clinical chemistry/Haematology
At the end of the study, the two surviving females in the 150 mg/kg/day group had reduced leucocyte indices compared with controls, with a smaller reduction seen in males of the same group.

Activated partial thromboplastin time (APTT[3]) was significantly reduced among all treated females and among males in the 50 and 150 mg/kg/day groups. There was a marginally increased prothrombin time (PT) in males of the 150 mg/kg/day group, compared with controls, but this was not considered to be treatment-related. There were a number of other noted haematological variations, which were also considered to be toxicologically insignificant.

Both sexes at 150 mg/kg/day had elevated alanine transferases (ALT), aspartate transaminase (AST) and alkaline phosphatase (AP) activity, believed to reflect liver pathology. Increased bilirubin, albumin[3] and albumin/globulin ratio[3] values were also observed. Cholesterol levels were also higher for males in this group but the significance of this was considered to be unimportant.

[3] Followed a dosage related change.

Macroscopic findings:
The group mean thymus weights among all sexes and treatment groups were decreased compared with controls, but male values were not statistically significant.

Other macroscopic findings in the 150 mg/kg/day group:
- Brown staining in 5/5 male rats;
- Alopecia in 5/5 males and 2/2 females;
- Reduced adipose tissue in 2/2 females;
- Pitting of the liver 5/5 males;
- Enlarged and pale kidneys in 1/2 females;
- Thin uterus in _ females;

There was a zero incidence of these findings in controls.

Histopathology:
Liver:
There was a dose-related cell loss and/or inflammatory cell infiltration in the centrilobular regions, present in all animals at 150 and 50 mg/kg/day and in one male and one female at 15 mg/kg/day. In the high-dose animals, the finding was accompanied by single cell necrosis of hepatocytes and pigmented sinusoidal cells. Eosinophilia of the cytoplasm of centrilobular hepatocytes was seen in most of the females receiving 150 mg/kg/day, while males at 150 and 50 mg/kg/day had dose-related centrilobular hepatocyte hypertrophy and/or vacuolation. Centrilobular hepatocyte vacuolation was also present in two males at 15 mg/kg/day.

Kidney:
Tubular changes were dose-related in females, occurring in all treatment groups, and were present in males at 150 mg/kg/day. At this dose level, changes were generally more severe and extensive in females. Tubular basophilia with nuclear crowding in the cortex was reported in three males and all females; in females, tubular basophilia extended into the outer medulla, and affected tubules were sometimes dilated or contained casts. Focal tubular necrosis was also seen in the two females that were killed for humane reasons. All rats at 150 mg/kg/day showed minimal fine vacuolation of cortical tubular epithelium. In females at 50 mg/kg/day, slight tubular basophilia with nuclear crowding in the cortex and minimal fine vacuolation of cortical tubular epithelium were reported in all five animals. The only treatment-related change seen in the 15 mg/kg/day females was minimal fine vacuolation of cortical tubular epithelium.

Spleen:
Extramedullary haemopoiesis was reported in all males at 150 mg/kg/day and in two males in each of the other two treatment groups. This effect was absent in females. Haemosiderosis was seen in a small number of males and females dosed at 150 mg/kg/day and in a single female at 50 mg/kg/day. The only significant effect was considered be in the 150 mg/kg/day group.

Thymus:
Involution/atrophy was recorded in two male and all female rats at 150 mg/kg/day, and also in other animals of the lower-dosed groups. These findings were considered to be treatment-related and associated with the decreased group mean thymus weights[3] recorded

for all treated groups.

Thyroid:
In all males and two females receiving 150 mg/kg/day, and in two males each of the 50 and 15 mg/kg/day groups, the follicular cells of the thyroid did not show the normal fine vacuolation present in controls. This finding has been reported as cytoplasmic basophilia.

Findings considered probably to be secondary:

Male genital tract:
All males at 150 mg/kg/day and a single male at 50 mg/kg/day had reduce colloid in the prostate. Reduced seminal colloid in the seminal vesicles was also noted and considered to be significant at the 150 mg/kg/day level.

Female genital tract:
All females at 150 mg/kg/day had endometrial atrophy, the majority also showing epithelial inflammatory cell infiltration and mucus and inflammatory cells in the lumen and in the vagina, and sparse/few corpora lutea in the ovaries. These findings were considered to indicate suppression of normal cyclic activity associated with the clinical condition of the animals.

Other findings:
The three females in the 150 mg/kg/day group that were killed due to poor clinical condition had microscopic lesions that were thought not to be treatment-related.

Comment:
Changes were observed in leucocyte indices, APTT activity, blood enzyme activity (ALT, AST and AP) and albumin levels. Pathological changes were observed in the liver, kidneys, spleen, thyroid and thymus. The liver and kidneys were the main target organs for these changes; with changes in the kidneys being more severe in females. Alopecia and pitting of the liver surface were noted in both sexes. At the lower dosage levels of 15 or 50 mg/kg/day, the principal changes consisted of reduced APTT values, increased albumin and Albumin/Globulin ratios, reduced thymus weights and microscopic changes in the liver, kidneys, thymus and thyroid.

No suitable no observed adverse effect level (NOAEL) can be established from this study because treatment-related microscopic changes were observed among animals receiving the lowest test dose of 15 mg/kg/day. Therefore, a lowest observed adverse effect level (LOAEL) of 15 mg/kg/day is established for this study.

Result:
The LOAEL established for the notified chemical is 15 mg/kg/day.

9.3 Genotoxicity

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

Strains:	*Salmonella typhimurium* TA1535, TA1537, TA98 TA100; *Escherichia coli* CM891
Concentration range:	Initial test: 0, 5, 15, 50, 150, 500, 1 500, 5 000 μg/plate; Repeat test: 0, 50, 150, 500, 1 500 and 5 000 μg/plate; Test solutions were prepared in ethanol
Metabolic activation:	10% and 20% (for initial and repeat assay, respectively) rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors
Positive controls:	TA98 + S9: 5 μg/plate benzo[a]pyrene; TA98 – S9: 1μg/plate 2-nitrofluorene; TA100 + S9: 5 μg/plate benzo[a]pyrene; TA100 – S9: 3 μg/plate N-ethyl-N'-nitro-N-nitrosoguanidine TA1535 +S9: 2 μg/plate 2-aminoanthracene; TA1535 – S9: 5 μg/plate N-ethyl-N'-nitro-N nitrosoguanidine; TA1537 + S9: 5 μg/plate benzo[a]pyrene; TA1537 – S9: 80 μg/plate 9-aminoacridine; CM891 + S9: 10 μg/plate 2-aminoanthracene; CM891 – S9: 2 μg/plate N-ethyl-N'-nitro-N-nitrosoguanidine.
Test method:	OECD TG 471
Comment:	All concentrations were tested in triplicate. In both initial and repeat tests, there was inhibition of bacterial growth at 5 000 μg/plate, indicated by thinning of the background lawn and reduction in revertant colony numbers. Under the conditions of the study, the notified chemical caused no substantial increases in revertant colony numbers over control counts at any concentration in either the presence or absence of the rat liver microsomal enzymes.

All positive and negative controls responded appropriately.

Result: The notified chemical was considered to be non-mutagenic under the conditions of the assay.

9.3.2 Chromosome aberration assay in human lymphocytes *in vitro* (HLS, 1998g)

Cells: Lymphocytes from healthy male donors

Metabolic activation 10% rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors.

Dose range:

1st experiment:
with S9: 100, 150 and 170 μg/mL (3 hours treatment, 16 hours recovery);
without S9: 50, 100 and 150 μg/mL (3 hours treatment, 16 hours recovery).

2nd experiment:
with S9: 170, 190 and 200 μg/mL (3 hours treatment, 16 hours recovery);
without S9: 50, 100 and 150 μg/mL (19 hours continuous treatment).

The test substance was dissolved in ethanol.

Positive controls: With S9: cyclophosphamide 6 μg/mL;
without S9: mitomycin C 0.1 μg/mL.

Test method: OECD TG 473

Comment:

1st experiment:
In the absence of S9, the test material did not cause a statistically significant increase in cells with chromosomal aberrations, compared with solvent controls. In the presence of S9, the test substance induced a statistically significant increase in cells with chromosomal aberrations at 150 μg/mL when gaps were included, and 170 μg/mL including and excluding gaps.

2nd experiment:
In the absence of S9, the test substance caused a statistically significant increase in cells with chromosomal aberrations at all dose levels when gaps were included and at 150 μg/mL , excluding gaps. In the presence of S9, significant results were observed at 200 μg/mL when gaps were included and at 190 μg/mL excluding gaps.

	Responses in most cases appeared to be dose-related. Both positive and negative controls responded appropriately.
Result:	The notified chemical was considered to be clastogenic in human peripheral lymphocytes *in vitro.*

9.3.3 Micronucleus Assay in the Bone Marrow Cells of the Mouse (HLA, 1990)

Species/strain:	Mouse/ICR strain
Number and sex of animals:	5/sex/group (11 groups)
Doses:	25.0, 83.0 and 250 mg/kg test substance in corn oil; 80 mg/kg cyclophosphamide (positive control) in water.
Method of administration:	Test substance: intraperitoneal injection; Cyclophosphamide: oral gavage.
Test method:	Code of Federal Regulations
Comment:	Test substance-dosed animals were sacrificed at 24, 48, and 72 hours post-treatment. The positive and vehicle control animals were sacrificed 24 hours post-treatment. Immediately prior to the 72 hour sacrifice, three animals in the high dose group were found dead and were replaced by animals from a secondary group. The test substance did not induce a significant increase in micronucleated polychromatic erythrocytes over the levels observed in the vehicle controls in either sex, at any harvest time. The positive and negative controls fulfilled the requirements for a valid assay.
Result:	The notified chemical was considered to be negative in the mouse bone marrow micronucleus assay.

9.4 Overall Assessment of Toxicological Data

The notified chemical, AERO®5460 Promoter, was administered at 500 mg/kg by gavage to rats in an acute oral toxicity study. As one male died within 24 hours of treatment, a discriminating dose of 50 mg/kg was established. Surviving animals had various symptoms that persisted up till Day 9 before complete resolution.

In the dermal toxicity study conducted at 2 000 mg/kg, well-defined dermal irritation accompanied by desquamation was seen in some animals. Under the conditions of the study, the LD_{50} was >2 000mg/kg.

Data relating to inhalation toxicology were not provided on the basis that the notified chemical is not considered to be volatile. As the imported product will be used in a sealed, automated system, it is considered that mists are unlikely to occur and worker exposure by inhalation will not be significant.

In a skin irritation assay, there were no signs of toxicity or ill health in any rabbit during the observation period. Prolonged, well-defined erythema with or without very slight to slight oedema was seen in all three animals. Additionally, desquamation of the stratum corneum developed in all rabbits, and resolved by Days 9, 10, or 13. In an eye irritation study, no corneal damage or iridial inflammation was observed. A diffuse crimson colouration of the conjunctivae with slight swelling was seen in two animals. Transient hyperaemia of blood vessels only was observed in the remaining animal. These reactions completely resolved by either two or three days after instillation. Based on these two assays, the notified chemical was considered to be a slight eye irritant and a moderate skin irritant.

The notified chemical is severe skin sensitiser, with 19/20 animals responding to challenge in an adjuvant type study.

In a repeat dose toxicity study, rats of both sexes were gavaged with 15, 50 and 150 mg/kg/day of the notified chemical, for 28 days. There was systemic toxicity in all animals at 150 mg/kg/day warranting termination of three females on humane grounds, with some treatment-related changes occurring at 50 and 15 mg/kg/day. The principal toxicity findings at 150 mg/kg/day included severely reduced food consumption and bodyweight gain and disturbances in leucocyte indices, APTT activity, and blood enzyme and albumin levels. Pathological changes were observed in the liver, kidneys, spleen, thyroid and thymus. The liver and kidneys were the main target organs for these changes, with changes in the kidneys being more severe in females. At 50 and 15 mg/kg/day, the principal changes consisted of reduced APTT activity, increased albumin and albumin/globulin ratios, reduced thymus weights and microscopic changes in the liver, kidneys, thymus and thyroids. These changes followed a dose-related trend among the treated groups (both in degree and number of animals affected). However, the microscopic effects noted at 15 mg/kg/day group were considered to be minimal. It was not possible to establish a NOAEL for this study as treatment-related microscopic changes were observed among animals receiving the 15 mg/kg/day dose. Accordingly, a Lowest Observed Adverse Effect Level (LOAEL) is established at 15 mg/kg/day.

There was no evidence of mutagenic activity of the notified chemical in either the *Salmonella typhimurium* or *Escherichia coli* reversion assays, either in absence of S9, or when tested with both a 10% and a 20% S9 mix. Similarly, there was no evidence that the notified chemical has potential to induce micronuclei in the bone marrow of the mouse *in vivo*, even when tested at a sufficiently high concentration (250 mg/kg) to cause deaths in three animals.

The notified chemical showed evidence of clastogenicity in an *in vitro* chromosomal aberration assay in human peripheral lymphocytes where, in two independent experiments, there were statistically significant dose-related increases in the frequency of chromosomal aberrations, independent of whether gaps were included or excluded. However, in the absence of clastogenic activity *in vivo* as reported above, these results have diminished significance because of several reasons. It is known that false positive results can occur *in vitro* due to high ionic strength and osmolality of chemical test solutions. Chromosomal

damage can result from action on chromosomal protein structure rather than by a direct DNA damaging effect. Thus, in spite of the positive chromosomal aberration result *in vitro*, the negative activity in the bacterial mutagenicity assays and in the mouse micronucleus test *in vivo* has more relevance and provides adequate evidence that the notified chemical should not be a genotoxic hazard.

Hazard Classification

Based on the available toxicity data, AERO®5460 Promoter, is acutely toxic by the oral route, causes well defined, prolonged skin irritation and is skin sensitising. A 28 day oral gavage repeat dose study revealed treatment related changes at all doses may pose a danger of serious damage to health by prolonged exposure. An *in vitro* chromosome aberration assay using human lymphocytes gave evidence of weak clastogenicity. However, there was insufficient evidence to consider the notified chemical as mutagenic. Under the NOHSC *Approved Criteria for Classifying Hazardous Substances*, (NOHSC, 1999a) 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.

ASSESSMENT OF ENVIRONMENTAL EFFECTS

Tests were performed according to corresponding EEC and 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.

10.1 Summary of Ecotoxicity Test Results

Test	*Species*	*Test concentrations (nominal) mg/L*	*Results mg/L*
Acute Toxicity (Semi-Static Test) (OECD TG 203)	Rainbow trout (*oncorhynchus mykiss*)	0.48, 1.0, 2.2, 4.6 & 10	96 h LC_{50} = 3.1
Acute Toxicity - Immobilisation (Static Test) (OECD TG 202 part I)	Water Flea (*Daphnia magna*)	1.0, 2.2, 4.6, 22, 46 & 100	48 h EC_{50} = 6.5
Growth Inhibition - Growth (μ) & Biomass (b) (Static Test) (OECD TG 201)	Green Algae (*Selenastrum capricornutum*)	1.0, 2.2, 4.6, 10, 22 & 46	72 h $E\mu C_{50}$ = 12 72 h E_bC_{50} = 4.1 72 h NOEC = 0.74
Respiration Inhibition (OECD TG 209)	Activated Sludge-Aerobic Waste Water Bacteria	10, 100, 260, 520 & 988	3 h IC_{50} = 144.7

10.2 Fish Acute Toxicity (HLS, 1998a)

The acute toxicity of AERO®5640 Promoter to Rainbow trout was determined in a 96 hour semi-static test. To ensure the maintenance of satisfactory environmental conditions and near nominal exposure levels the test medium was renewed daily. Due to the volatility of the test substance the study was conducted in sealed vessels to minimise losses of the test compound. The analytically determined test substance concentrations in the test media samples varied from 51% to 74% of the nominal values. The arithmetic mean measured concentrations were determined by the notifier to be 0.27, 0.66, 1.6, 3.5 and 8.2 mg/L. The notifier indicates that loss of notified chemical is probably due to volatility, however, the notified chemical may also adhere to both the vessel surfaces and the test organisms.

The 96 hour LC_{50} of the notified chemical was determined by the notifier using the Thompson and Weil model to be 3.1 mg/L and the highest concentration tested without toxic effects was 0.27 mg/L. Marked reactions to exposure, other than death, included increased pigmentation, swollen abdomen, swimming at the bottom, loss of equilibrium and hyperactive swimming.

Probit analysis cannot be carried out on the available data since there is only one partial response between the zero and 100% mortality rates. Probit analysis requires at least two such partial responses.

10.3 Aquatic Invertebrate Acute Toxicity (HLS, 1999c)

The acute toxicity of AERO®5640 Promoter to *Daphnia magna* was determined in a 48 hour static test. Due to the volatility of the test substance the study was conducted in sealed vessels to minimise losses of the test compound. The analytically determined test substance concentrations in the test media samples varied from 59% to 99% of the nominal values. Again the notifier indicates that loss of notified chemical is probably due to volatility, however, the notified chemical may also adhere to the vessel surfaces. The arithmetic mean measured concentrations were determined by the notifier to be 0.67, 1.8, 3.9, 8.7, 21, 41 and 88 mg/L. The 24 and 48 hour EC_{50} of the notified dye were determined by the notifier using the Thompson and Weil model to be 14 mg/L and 6.5 mg/L, respectively, which indicates a sharp increase in toxicity over time and that equilibrium may not have been reached. The highest concentration tested without toxic effects was 1.8 mg/L.

It is unclear as to how the notifier determined the LC_{50} value of the notified chemical using the Thompson and Weil model. The notifier states that the pattern of immobilisation at 48 hours was atypical in that 70% immobilisation was observed at a nominal concentration of 4.6 mg/L, but only 35% immobilisation was observed at the higher nominal concentration of 10 mg/L. The notifier indicates that a brown precipitate was present in the test vessels at both concentrations, which is thought to have accounted for these unusual results. The environmental assessment notes that the LC_{50} value of the notified chemical can only be said to lie between the arithmetic mean measured concentrations of 1.8 and 21 mg/L.

10.4 Alga Growth Inhibition Test (HLS, 1999e)

The acute toxicity of AERO®5640 Promoter to alga was determined in a 72 hour static test. Due to the volatility of the test substance the study was conducted in sealed vessels to

minimise losses of the test compound. The analytically determined test substance concentrations in the test media samples varied from 70% to 78% of the nominal values. The arithmetic mean measured concentrations were determined by the notifier to be 0.74, 1.7, 3.4, 7.3, 17 and 32 mg/L. The 72 hour inhibition rates calculated for both algal biomass and growth rate were E_bC_{50} = 4.1 mg/L and $E\mu C_{50}$ = 12 mg/L, respectively. The no-observed effect concentration was determined using the Williams test to be 0.74 mg/L.

The 72 hour E_bC_{50} of the notified dye was determined in this assessment by Linear Interpolation ICp analysis to be 5.39 mg/L. It was calculated by applying Toxcalc 5.0 for Microsoft Excel (Tidepool,) to the measured concentrations.

10.5 Activated Sludge, Respiration Inhibition Test (HLS, 1999b)

The inhibitory effect of AERO®5640 Promoter on aerobic wastewater bacteria, activated sludge from a domestic wastewater treatment plant, was investigated in a respiration test. At the nominal concentration of 10 mg/L a respiratory inhibition of 3% was observed. At the highest nominal concentration of 988 mg/L a respiratory inhibition of 75% was observed. The final 3 hour IC_{50} was determined to be 144.7 mg/L. All reported results are related to the nominal concentrations of the test substance, thus the IC_{50} may be below 144.7 mg/L.

10.6 Conclusion

The ecotoxicity data for AERO®5640 Promoter indicates that it is moderately toxic to fish, aquatic invertebrates and algae, and practically non-toxic to sewage microorganisms.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

AERO®5640 Promoter disposed of with the tailings either attached to gangue particles or dissolved in the water from the flotation process is not expected to be released to the wider environment. AERO®5640 Promoter will be contained within the tailings dam and release to the environment is expected to be minimal.

Based on an annual maximum import volume of 50 tonnes, approximately 3.75 tonnes of the notified chemical will be released to tailings dams per annum. The notifier assumes that the entire notified chemical may be used at the Mt. Keith mine in WA where the tailings dam is reported to be 10 km^2 in area and approximately three metres in depth. The dam, therefore, has a total capacity of 30 000 ML. The notifier also assumes that the mine uses approximately 40 ML of processing water per day and that AERO®5640 Promoter is used 365 days per year. Total tailings effluent for one year would be 14 600 ML and concentration of the notified chemical in the process effluent would be 0.26 mg/L. The notifier indicates that this will be further diluted within the tailings dam and assumes a dilution factor of 1:10, so the concentration of the notified chemical in the tailing dam would be 0.026 mg/L. The environmental safety margin for exposure of most sensitive aquatic organism, Rainbow trout 96 hour LC_{50} = 3.1 mg/L, would be 120.

However, noting that the assumed volume of the mine process effluent per year is approximately half of the assumed volume of the tailing dam, the dilution factor assumed by the notifier of 1:10 seems high and the environmental safety margin may be expected to be lower than 120. With a dilution factor of only 1:2, since the process effluent per year is half of the volume of the tailing dam, the concentration of the notified chemical in the tailing dam would be 0.13 mg/L. The environmental safety margin would, therefore, only be 24.

Presumably, when taking into account a high rate of evaporation due to the large surface area of the dam, the actual volume of the dam water would remain constant. The concentration of the notified chemical, however, would not be expected to increase as adsorption to sediment and hydrolytic degradation are likely to occur in the highly acidic effluent contained within the tailings dam. In the event of a dam breach, due to heavy rainfall, high dilution of the dam contents would be expected. Also, the major environmental concern of liberated dam water from a breach would likely be the high acidity of the water as well as any dissolved metals contained within the water.

The notifier has stated that tailings storage dams are designed to reduce "substantially" the potential for seepage as well as cope with a one-a-in-a hundred year flood. However, as noted above, 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 moderate toxicity to aquatic organisms and expected low environmental safety margins, suggest that the notified chemical may pose a significant environmental risk if accidentally released through seepage 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.

Given the above, environmental exposure and the overall environmental hazard is expected to be acceptable.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Based on the available toxicity data, AERO®5640 Promoter, is acutely toxic by the oral route, causes well defined, prolonged skin irritation and is skin sensitising. In a 28 day oral (gavage) repeat dose study a NOEL could not be established as the chemical caused treatment related changes at all doses. Hence, the notified chemical may pose a danger of serious damage to health by prolonged exposure. An *in vitro* chromosome aberration assay using human lymphocytes showed evidence of weak clastogenicity. However, there was insufficient evidence to consider the notified chemical as mutagenic. 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. The

notified chemical is used as a flotation agent in mining. 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 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 0.00375% in the slurry, however, as the slurry becomes more concentrated, the reagent concentration will increase. Therefore any worker who may potentially come in contact with the slurry should wear the personal protective equipment specified above.

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

1. To minimise occupational exposure to AERO®5640 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;

- Respiratory protection to conform to Australian/New Zealand Standard 1715-1994 (Standards Australia/Standards New Zealand, 1994a): *Use and Maintenance of Respiratory Protective Devices* and Australian/New Zealand Standard 1716-1991 (Standards Australia/Standards New Zealand, 1994b): *Respiratory Protective Devices*;

- 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, 1994c);
- 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.

2. 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.

3. 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 either fish or aquatic invertebrates should be conducted.

4. AERO®5640 Promoter 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 AERO®5640 Promoter 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

EPA. (1995). Best Practice Environmental Management in Mining Tailings Containment. US EPA.

European Commission. (1992). European Commission Directive 92/69/EC, Annex V: Brussels.

HLA. (1990). Mutagenicity Test on CT-429-90 *in vivo* Mouse Micronucleus Assay, Study No: 12148-0-455. Hazelton Laboratories America (HLA) Inc: Kensington.

HLS. (1998a). AERO 5460 Promoter Acute Toxicity To Rainbow Trout *(Oncorhynchus mykiss)* Report No: CTI077/992376. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998b). AERO 5460 Promoter Physico-Chemical Properties Report No: CTI1085/983446. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998c). AERO 5460 Promoter Acute Dermal Toxicity to the Rat Report No: CTI 069/983288/AC. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998d). AERO 5460 Promoter Acute Oral Toxicity to the Rat (Fixed Dose Method) Report No: CTI 068/983518/AC. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998e). AERO 5460 Promoter Bacterial Mutation Assay Report No: CTI 075/983527. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998f). AERO 5460 Promoter Eye Irritation to the Rabbit Report No: CTI 071/983253/SE. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998g). AERO 5460 Promoter *in vitro* Mammalian Chromosome Aberration Test in Human Lymphocytes Report No: CTI076/983879. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998h). AERO 5460 Promoter Skin Irritation to the Rabbit Report No: CTI 070/983228/SE. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998i). AERO 5460 Promoter Skin Sensitisation to the Guinea Pig Report No: CTI 072/983632/SS. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1998j). AERO 5460 Promoter Toxicity Study by Oral Administration to CD Rats for 4 Weeks Report No: CTI 074/983460. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1999a). AERO 5460 Promoter Abiotic Degradation - Hydrolysis as a Function of pH Report No: CTI082/993046. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1999b). AERO 5460 Promoter Activated Sludge - Respiration Inhibition Test Report No: CTI108/985061. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1999c). AERO 5460 Promoter Acute Toxicity To *Daphnia magna* Report No: CTI078/992375. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1999d). AERO 5460 Promoter Adsorption/Desorption Report No: CTI09/992309. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1999e). AERO 5460 Promoter Alga Growth Inhibition Report No: CTI080/992374. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

HLS. (1999f). AERO 5460 Promoter Biotic Degradation - Closed Bottle Test Report No: CTI079/985176. Huntingdon Life Sciences (HLS) Ltd: Huntingdon.

NOHSC. (1994). National Code of Practice for the Preparation of Material Safety Data Sheets [NOHSC:2011(1994)]. Australian Government Publishing Service: Canberra.

NOHSC. (1995). Adopted National Exposure Standards for Atmospheric Contaminants in the Occupational Environment, [NOHSC:1003(1995)]. In Exposure Standards for Atmospheric Contaminants in the Occupational Environment: Guidance Note and National Exposure Standards. Australian Government Publishing Service: Canberra.

NOHSC. (1999a). Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(1999)]. AusInfo.: Canberra.

NOHSC. (1999b). List of Designated Hazardous Substances [NOHSC:10005(1999)]. AusInfo.: Canberra.

Normandy Mining Limited. (1998). Environmental Report for Mt Leyshon Operations.
North Limited. (1998). Environment, Safety and Health Report.

OECD. (1995-1996). OECD Guidelines for the Testing of Chemicals on CD-Rom. OECD: Paris.

Standards Australia. (1987). AS 2919-1987, Australian Standard Industrial Clothing. Standards Australia: Sydney.

Standards Australia. (1990). AS 3765.1-1990, Australian Standard Clothing for Protection against Hazardous Chemicals Part 1 Protection Against General or Specific Chemicals. Standards Australia: Sydney.

Standards Australia. (1994). AS 1336-1994, Australian Standard Eye protection in the Industrial Environment. Standards Australia: Sydney.

Standards Australia. (1998). AS/NZS 2161.2:1998, Australian/New Zealand Standard Occupational Protective Gloves Part 2: General Requirements. Standards Australia and Standards New Zealand: Sydney/Wellington.

Standards Australia/Standards New Zealand. (1992). AS/NZS 1337-1992, Australian/New Zealand Standard Eye Protectors for Industrial Applications. Standards Australia and Standards New Zealand: Sydney/Wellington.

Standards Australia/Standards New Zealand. (1994a). AS/NZS 1715-1994, Australian/New Zealand Standard Selection, Use and Maintenance of Respiratory Protective Devices. Standards Australia and Standards New Zealand: Sydney/Wellington.

Standards Australia/Standards New Zealand. (1994b). AS/NZS 1716-1994, Australian/New Zealand Standard Respiratory Protective Devices. Standards Australia and Standards New Zealand: Sydney/Wellington.

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

Tidepool. Toxcalc 5.0 for Microsoft Excel, Vol. 1992-1994. Tidepool Scientific Software.

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