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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Antimony Triacetate

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Antimony Triacetate

1. APPLICANT

Leading Synthetics Pty Ltd of 2060 Hume Highway CAMPBELLFIELD VIC 3061 has submitted a standard notification statement in support of their application for an assessment certificate for Antimony Triacetate.

Details of the exact import volume and formulation of products containing the notified chemical have been exempted from publication in the Full Public Report and the Summary Report.

2. IDENTITY OF THE CHEMICAL

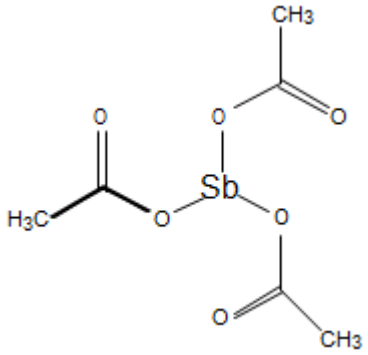
Chemical Name: antimony triacetate

Chemical Abstracts Service (CAS) Registry No.: 6923-52-0

Trade Name: Catalyst S-21

Molecular Formula: $C_6H_9O_6Sb$

Structural Formula:



Molecular Weight: 298.75

Spectral Data: an infrared spectrum was provided

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa: off-white hygroscopic crystals with a vinegar odour

Melting Point: 120 – 125°C

Density: 1 220 kg/m^3 at 20°C

Vapour Pressure: not determined - see comment below

Water Solubility: decomposes in the presence of water

Partition Co-efficient (n-octanol/water): not determined - see comment below

Hydrolysis as a Function of pH: not determined - see comment below

Adsorption/Desorption: not determined - see comment below

Dissociation Constant: not determined - see comment below

Flash Point: not determined; the substance decomposes slowly above 200°C to antimony trioxide and acetic acid

Autoignition Temperature: not determined

Explosive Properties: structure is not indicative that the notified chemical will be explosive

Particle Size: the particle size of 4 samples was determined with the following results:

Sample #	*Median Diameter (μm)*	*% with size greater than specified diameter*
1	434.6	90% > 204.5
2	387.1	90% > 95.2
3	414.0	90% > 145.3
4	433.5	90% > 112.4

Reactivity/Stability: reacts with water to form antimony trioxide and acetic acid

Comments on Physico-Chemical Properties

Decomposition commences at temperatures above 200°C.

The vapour pressure was not determined since, with > 99% purity, the volatile component of the notified substance is < 1%.

The chemical hydrolyses immediately with water according to equation (1). In air, it reacts with residual moisture and decomposition is most likely diffusion controlled. Due to this hydrolytic behaviour, water solubility, partition coefficient, absorption/desorption and dissociation constant were not determined.

$$2\ Sb(O_2CCH_3)_{3(s)} + 3\ H_2O_{(l)} \longrightarrow Sb_2O_{3(s)} + 6\ CH_3CO_2H_{(aq)} \qquad (1)$$

4. PURITY

Degree of Purity: > 99%

Toxic or Hazardous Impurities: < 0.1%

Non-hazardous Impurities (> 1% by weight): < 1%

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical is to be used as a catalyst in the manufacture of polyethylene terephthalate for the production of polyester fibre, yarn and/or chips. It will be imported as a pure powder at a rate of less than 100 tonnes per annum for the first five years. The concentration of the notified chemical in the imported product is greater than 99% (w/w).

6. OCCUPATIONAL EXPOSURE

The notified chemical is imported in small plastic pails, consolidated into a shrink wrapped pallet load. A container load of these pallets are transported to the notifier's site, where polyester is manufactured, on 10 days or less per year. Exposure will only occur in the event of accidental spillage. Transfer of the pallets to the plant store will be done by 4 operators,

requiring 5 hours per year per individual.

Three shift teams of 5 workers continuously operate the polyester production plant each day. One operator per shift takes 15 minutes to pour the contents of 4 pails per batch onto a vibrating screen. The filling point is enclosed in a hood with a dedicated local exhaust ventilation system and it is estimated that 125 g of the notified chemical will be extracted as dust for each batch operation. Any remaining lumps of the notified chemical will be broken up manually with a mallet, to fall through the screen into the vessel below. The extracted antimony triacetate will be hydrolysed in a water scrubber. The products of hydrolysis, namely, antimony trioxide and acetic acid will be discharged in the site wastewater system and into the metropolitan sewer after pH adjustment.

The notifier states that the operator is potentially exposed to the notified chemical by inhalation and eye contact during the loading operation and by skin and eye contact when the empty pails are washed out with water. The notifier recommends the use of personal protective equipment during these operations, namely, industrial clothing, footwear, respiratory protection, gloves and goggles.

The notified chemical is added to warm ethylene glycol to obtain a solution with a concentration of 0.8% (w/w) as antimony, and is then added to the reactants to obtain a final concentration of up to 200 ppm Antimony in Polyester. This is pumped through the reactor system where the polyester product is formed. After addition to the slurry, exposure to the notified chemical is unlikely as it is contained in a closed system.

If and when maintenance of the catalyst vessel is required, the vessel is taken out of service, cleaned with ethylene glycol to remove excess notified chemical, and decontaminated to remove the ethylene glycol.

Following production of the polyester, exposure to the notified chemical is unlikely given that it is irreversibly combined in a solid matrix and not separately available for exposure or absorption.

7. PUBLIC EXPOSURE

There is little potential for exposure of the public to the notified chemical, as it is irreversibly bound in the polyester. The public will only come into contact with the polyester materials where the notified chemical will be trapped inside the solid matrix of the polyester fibres, yarn or chips. While the potential for exposure is high, the risk to public health is very low and the notifier states that polyester has been used in the public marketplace for many years without reports of adverse health effects.

8. ENVIRONMENTAL EXPOSURE

Release

A small amount of the chemical is expected to be trapped as dust in a scrubbing unit or vented into the atmosphere during the polymerisation process, with effluent from the scrubbers going to the on-site wastewater system. The notifier estimates that 125 g per batch will be extracted as dust.

Residual catalyst in the pails (approximately 5 g per pail) will be washed out of the pail with water where it will enter the waste water system at an approximate concentration of 0.6 mg/L.

Total loss of the notified chemical to the environment is estimated at less than 0.3%. This produces antimony trioxide which is dissolved or suspended in the wastewater. The wastewater is discharged into the sewer as trade waste, after the pH is adjusted into the range 6-10. The notifier estimates an average concentration of antimony trioxide in the trade waste discharged from the site of 0.59 mg/L

In the event of a transport accident, the spilled chemical would be swept up, packaged and delivered to the notifier for assessment and disposal by treatment onsite or at a waste disposal site.

Fate

The chemical is expected to hydrolyse immediately on contact with water (*ie.* in wastewater streams, the atmosphere or the sediment/soil compartment). The hydrolysis product, antimony trioxide, is insoluble and will settle to sediments and be immobile in soils. Acetic acid will also be produced and acidify the immediate vicinity of the hydrolysis reaction. The degree of change of pH will depend on whether dilution occurs (*eg.* from other wastewater streams or receiving water) and the potential for buffering in the aquatic, sediment or soil compartment.

After conversion to textile fabrics or polyester padding, the fate of the notified substance is linked with the fate of the particular item. It is expected that a significant proportion of the manufactured polyester will be exported and the remainder distributed across Australia. Eventually the polyester will enter the waste disposal stream for recycling or ultimately for disposal as waste in landfill. During usage, fibre abrasion will lead to particles of the chemical entering the environment.

The cleaned empty pails will be disposed of as general waste into an approved landfill. Since the pails will have contained a hazardous substance, it is inadvisable for them to enter a recycling program.

9. EVALUATION OF TOXICOLOGICAL DATA

The notified chemical decomposes in the presence of water to antimony trioxide and acetic acid. Therefore, studies conducted with antimony trioxide are included in this section.

9.1 Acute Toxicity

Summary of the acute toxicity of antimony triacetate

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity			
study No. 1	rat	LD_{50} > 2.5 g/kg	(Heenehan et al., 1977b)
study No. 2	rat	LD_{50} = 7 g/kg	(Fegley, 1967b)
study No. 3	rat	LD_{50} >50 - < 5000 mg/kg	(Budd, 1967)
acute dermal toxicity			
study No. 1	rabbit	LD_{50} > 2 g/kg	(Budd, 1967)
study No. 2	rabbit	LD_{50} > 2 g/kg	(Heenehan et al., 1977a)
study No. 3	rabbit	LD_{50} > 12.8 g/kg	(Fegley, 1967a)
study No. 4	rabbit	LD_{50} > 8 g/kg	(Gabriel, undated)
skin irritation			
study No. 1	rabbit	Corrosive	(Stachowiak & Baker, 1975)
study No. 2	rabbit	slight irritant	(Edmonds, 1967b)
study No. 3	rabbit	moderate to severe irritant	(Budd, 1967)
study No. 4	rabbit	severe irritant	(Heenehan et al., 1977c)
study No. 5	rabbit	severe irritant	(Gabriel, undated)
study No. 6	rabbit	corrosive under humid conditions	(Chang, 1981)
eye irritation			
study No. 1	rabbit	severe irritant	(Edmonds, 1967a)
study No. 2	rabbit	severe irritant	(Budd, 1967)
study No. 3	rabbit	severe irritant	(Heenehan et al., 1977d)

skin sensitisation	guinea pig	not done

9.1.1 Oral Toxicity

Study No. 1 **(Heenehan et al., 1977b)**

Species/strain:	rat/Wistar
Number/sex of animals:	1/sex/dose group
Observation period:	14 days
Method of administration:	doses of 0, 50, 250, 500, 2 500, 5 000 and 10 000 mg/kg by gavage; vehicle: corn oil
Clinical observations:	noted during the first 24 hours following dosing: at 50 mg/kg, piloerection in 1 of 2 animals; at 250 mg/kg, piloerection and soft stool in 1 of 2; at 500 mg/kg: muscle tremors, lethargy in 1 of 2, urinary staining of the abdomen, piloerection and soft stool in 2 of 2; at 2 500 mg/kg: piloerection in 2 of 2, lethargy in 1 of 2; 5 000 mg/kg: urinary staining of the abdomen, piloerection and lethargy in 1 of 1 animal with the exception of 1 animal at 2 500 mg/kg (clear on day 7) and one animal at 5 000 mg/kg (clear on day 7), all animals surviving the study were free of signs
Mortality:	1 of 2 animals at 5 000 mg/kg; 2 of 2 at 10 000 mg/kg
Morphological findings:	in the decedents, white patches on various organs including lungs, kidney, liver and lungs; brown or brown-white liquid in stomach
Test method:	Unspecified
LD_{50}:	> 2 500 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

Study No. 2 **(Fegley, 1967b)**

Species/strain:	rat/SD
Number/sex of animals:	5 males/dose group

Observation period:	14 days
Method of administration:	doses of 3.2 g/kg (low), 6.4 g/kg (mid) and 12.8 g/kg (high) by gavage as a suspension in corn oil
Clinical observations:	none at the low dose; animals appeared listless at the mid dose following dosing
Mortality:	1/5 at the low dose, 2/5 at the mid dose, 4/5 at the high dose
Morphological findings:	not done
Test method:	Unspecified
LD_{50}:	7.0 g/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

Study No. 3 **(Budd, 1967)**

Species/strain:	rat/SD
Number/sex of animals:	5/sex/dose group
Observation period:	28 days
Method of administration:	doses of 50 or 5 000 mg/kg by gavage as a suspension in corn oil/Tween 80
Clinical observations:	rats given 5 000 mg/kg test article were lethargic and weak prior to death within 24 hours; at 50 mg/kg there were no signs
Mortality:	10/10 at 5 000 mg/kg; 0/10 at 50 mg/kg
Morphological findings:	necropsy not conducted at the high dose due to extensive post-mortem changes; at the low dose small areas of haemorrhage in the lungs
Test method:	Unspecified
LD_{50}:	> 50 mg/kg and < 5000 mg/kg
Result:	the acute oral toxicity in rats was not determined

9.1.2 Dermal Toxicity

Study No. 1 **(Budd, 1967)**

Species/strain:	rabbit/albino
Number/sex of animals:	2/sex
Observation period:	28 days
Method of administration:	under polyethylene wrap for 24 hours
Clinical observations:	moderate erythema on the skin of all four rabbits and severe oedema, particularly in the abdominal areas; ulceration and inflammation in the most severely affected areas during the first 14 days after treatment; scar formation during the last 14 days
Mortality:	None
Morphological findings:	None
Test method:	as described in 16 CFR 1500.40
LD_{50}*:*	> 2 000 mg/kg
Result:	the notified chemical was of low acute dermal toxicity in rabbits and may be a severe skin irritant

Study No. 2 **(Heenehan et al., 1977a)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	1/sex/dose group
Observation period:	14 days
Method of administration:	under occlusive dressing for 24 hours; test substance as an aqueous slurry at 200 mg/kg, 500 mg/kg and 2 000 mg/kg on abraded and non abraded skin
Clinical observations:	slight erythema was observed in one animal (500 mg/kg) and severe erythema was observed in the remaining five animals following dressing removal; slight oedema was observed in one animal (500 mg/kg), moderate oedema was observed in 4 animals and severe oedema in one animal (2 000 mg/kg); lethargy was noted in one animal during the first 24 hours following compound

	administration; clear nasal discharge was noted in one animal at each dose level beginning in two animals on day 3 and one animal on day 7; these signs persisted to the end of the study; a notable weight loss was observed in one animal at 200 and 500 mg/kg, and two animals at 2 000 mg/kg
Mortality:	None
Morphological findings:	None
Test method:	Unspecified
LD_{50}:	> 2 000 mg/kg
Result:	the notified chemical was of low acute dermal toxicity in rabbits and may be a severe skin irritant

Study No. 3 **(Fegley, 1967a)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	2/sex
Observation period:	21 days
Method of administration:	test substance moistened with propylene glycol and applied under occlusive wrap for 24 hours
Test method:	Unspecified
LD_{50}:	> 12.8 g/kg
Result:	the test substance was of low dermal toxicity in rabbits and was a severe skin irritant

Study No. 4 **(Gabriel, not dated)**

Species/strain:	rabbit/albino
Number/sex of animals:	16
Observation period:	14 days
Method of administration:	test substance applied under occlusive wrap for 24 hours
Test method:	Unspecified

LD_{50}:	> 8 g/kg
Result:	the test substance was of low dermal toxicity in rabbits

9.1.3 Inhalation Toxicity

No data provided.

9.1.4 Skin Irritation

Study No. 1 **(Stachowiak & Baker, 1975)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	6/unspecified
Observation period:	72 hours
Method of administration:	0.5 g of dry powder was applied under occlusive dressing for 4 hours
Test method:	Department of Transportation, Hazardous Materials Regulations (Department of Transportation, 1972)
Result:	third degree chemical burns were observed in all animals up to 72 hours the notified chemical was corrosive to the skin in rabbits

Study No. 2 **(Edmonds, 1967b)**

Species/strain:	rabbit/albino
Number/sex of animals:	3/sex
Observation period:	72 hours
Method of administration:	0.5 mL of the test material under a gauze patch for 24 hours on abraded and unabraded skin
Test method:	Unspecified
Result:	at 24 hours erythema and oedema were slight in all animals; at 72 hours no irritancy was detected; with abraded skin, at 24 hours 3 animals exhibited moderate erythema and 3 animals slight erythema but

	oedema was slight in all animals; at 72 hours, 1 animal exhibited slight erythema but no other signs of irritancy were observed in this or other animals the notified chemical was a slight irritant to the skin in rabbits

Study No. 3 **(Budd, 1967)**

Species/strain:	rabbit/albino
Number/sex of animals:	6 female for a standard test; 3/sex treated for 5 minutes followed by a 10 minute washing procedure
Observation period:	72 hours
Method of administration:	0.5 g of the test substance under semi-occlusive dressing for 24 hours in the standard test; 5 minutes in the test using wash-off; abraded and unabraded skin
Test method:	Unspecified
Result:	2 rabbits exhibited moderate and 1 rabbit slight erythema at 24, 48 and 72 hours after treatment; 1 rabbit exhibited severe erythema and slight oedema at the same time points; 1 rabbit exhibited moderate erythema at 24 and 48 hours but slight erythema at 72 hours and 1 rabbit exhibited moderate erythema at 24 hours and slight erythema thereafter; no other oedema was observed in any rabbit at any time point; on abraded skin mostly severe erythema was observed the notified chemical was a moderate to severe skin irritant in rabbits a five minute treatment with wash-off resulted in slight skin irritation in rabbits

Study No. 4 **(Heenehan et al., 1977c)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3/sex
Observation period:	72 hours
Method of administration:	0.5 mL of a 1g/mL aqueous slurry of the test substance was applied under an occluded gauze patch for 24 hours

Test method:	16 CFR 1500.41
Result:	severe erythema was observed in all animals at 24 and 72 hours post-treatment; slight oedema was observed in 3 animals at 24 hours and 5 animals at 72 hours with the remaining animals exhibiting moderate oedema the notified chemical was a severe skin irritant in rabbits

Study No. 5 **(Gabriel, undated)**

Species/strain:	rabbit/Albino
Number/sex of animals:	6
Observation period:	72 hours
Method of administration:	0.5 g of the test substance was applied under an occluded gauze patch for 24 hours
Test method:	Federal Hazardous Substances Amendment (US Government, 1964)
Result:	severe erythema was observed in all animals at 24 and 72 hours post-treatment the notified chemical was a severe skin irritant in rabbits

Study No. 6 **(Chang, 1981)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	6/test: 3 tests done
Observation period:	up to 48 hours
Method of administration:	in all tests 0.5 g of the test substance was applied under a patch for 4 hours; the patches were: 1. 25 cm^2 gauze patch under occlusive plastic sheet; 2. a "Coverlet Eye Occlusor" (6 in^2); 3. 25 cm^2 gauze patch loosely wrapped in a plastic sheet
Test method:	Unspecified
Result:	1. at 4 hours, blanching and oedema in two rabbits, 4

rabbits normal; by 48 hours, necrosis in one rabbit and a blanched area surrounded by erythema in another rabbit; it was concluded that the test substance was corrosive in two rabbits;
2. observations up to 48 hours revealed necrosis at the test site in all rabbits;
3. observations up to 48 hours revealed no necrosis at the test site and barely perceptible to slight erythema and oedema in 5 rabbits and no reaction in another rabbit

it was concluded that, under the "Coverlet" adhesive pad, the test material was held tightly against the skin with possibly enhanced humidity leading to hydrolysis and the production of acetic acid which is corrosive

9.1.5 Eye Irritation

Study No. 1 **(Edmonds, 1967a)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3/sex
Observation period:	72 hours
Method of administration:	0.1 g of the test substance into the right eye of each animal
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	severe corneal, iridal and conjunctival effects were seen in all animals at all time points
	the notified chemical was a severe eye irritant in rabbits

Study No. 2 **(Budd, 1967)**

Species/strain:	rabbit/albino
Number/sex of animals:	3/sex for each of two tests, one with a 15 minute washout after 5 minutes
Observation period:	72 hours
Method of administration:	0.1 g of the test substance into the right eye of each animal

Test method:	Unspecified
Result:	severe corneal, iridal and conjunctival effects were seen in all animals at all time points the notified chemical was a severe eye irritant in rabbits washout did not appreciably reduce the severe eye irritation

Study No. 3 **(Heenehan et al., 1977d)**

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 animals for each of two tests, one with a washout of 1 mL distilled water after 15 seconds followed by 30 mL distilled water after 5 minutes
Observation period:	7 days
Method of administration:	0.1 mL of the test substance into the right eye of each animal
Test method:	Unspecified
Result:	severe corneal, iridal and conjunctival effects were seen in all animals at all time points the notified chemical was a severe eye irritant in rabbits and should be considered corrosive as extensive tissue damage was noted on day 7 washout did not reduce the severe eye irritation

9.1.6 Skin Sensitisation

Not performed due to the corrosive nature of the notified chemical itself and the known corrosivity of acetic acid, a breakdown product, when in contact with rabbit skin. In addition, sensitisation has not been reported with antimony trioxide, another breakdown product.

9.2 Developmental toxicity

A recent review (Leonard & Gerber, 1996) stated that there have been insufficient studies investigating the potential teratogenicity of antimony salts. Although some indications exist that antimony trioxide could interfere with embryonic and foetal development, the studies do not seem entirely conclusive.

9.3 Repeated Dose Toxicity/Carcinogenicity

No data were available for the notified chemical.

A literature search conducted for this assessment revealed a recent paper by Newton et al., (1994) on subchronic and chronic inhalation toxicity of the hydrolysis product antimony trioxide. Fisher 344 rats were exposed by inhalation at levels of 0, 0.25, 1.08, 4.92 or 23.46 mg/m^3 for 6 hours/day, 5 days/week, for 13 weeks followed by a 27-week observation period or to levels 0, 0.06, 0.51 or 4.50 mg/m^3 for 12 months followed by a 12-month observation period. The median particle size was 3.05 μm in the 13-week study and 3.76 μm in the 12-month study. The only non-neoplastic changes of significance were corneal irregularities in the 13-week study, a dose-related increase in the incidence of cataracts in the 12-month study and inflammation in the lungs in both studies. In the 12-month study there was no increase in tumour incidence, despite previous studies having shown an increased incidence of lung tumours in female rats.

The notifier summarised other health effects observed in humans following accidental or medicinal ingestion of antimony trioxide, and treatment in experimental animals. These include irritation of the skin on repeated or prolonged contact with antimony trioxide and irritation of the nose, throat and eyes. Over the longer term, transient skin lesions called 'antimony spots', heart damage, chronic emphysema and other lung effects may occur. Long term, low-level ingestion by humans may result in heart damage, impaired kidney and liver function and effects on the spleen and blood. Long term inhalation has caused chronic emphysema and pneumoconiosis. Short and long term treatment of laboratory animals with antimony trioxide resulted in changes in lung, liver, spleen, eye and blood components.

Oral administration of antimony compounds in rats for their lifetime did not result in carcinogenic effects, but some lifespan shortening was noted. As well as the data described above, increased lung tumours have been observed after long-term exposure to antimony trisulphide. Limited epidemiological studies suggest an increased incidence of lung cancers among antimony workers. However, IARC (International Agency for Research on Cancer, 1989) concluded that the evidence for the carcinogenicity of antimony trioxide in humans is inadequate and have assigned it as a Group 2B carcinogen.

The notifier summarised the likely health effects of acetic acid. On guinea pig skin, concentrations of 50 - 80% causes moderate to severe burns, less than 50%, minor skin damage and less than 10%, no injury. Mice exposed 5 – 10 minutes daily for 29 days to a 6.25% acetic acid aerosol at a concentration of 2 250 mg/m^3 developed bronchopneumonia. Rabbits treated with 4.5 g/kg/day orally for 30 days showed upper digestive tract injury and forestomach changes. Concentrations of 0.01 – 0.25% in drinking water of rats for 2 – 4 months caused no toxic effects. A concentration of 0.5% affected food consumption and growth. Repeated skin applications of acetic acid did not cause local tumours in mice. However, it weakly increased tumour production by a known carcinogen in the multi mouse skin model. No birth defects were noted in rabbits given apple cider vinegar by the oral route during pregnancy at 15.6 g/kg/day. Acetic acid produced no genetic changes in standard tests

using human lymphocytes or animal cells in culture. Both positive and negative responses were reported in bacterial cells and insects.

9.4 Genotoxicity

The notifier reported that antimony trioxide produces genetic changes in bacterial and animal cells; however, no genotoxicity data were provided for the notified chemical.

A literature review conducted for this assessment revealed a review article by Leonard & Gerber (1996), of the mutagenicity of antimony compounds that were available at that time. The authors reported that recombination-deficient strains of *Bacillus subtilis* exhibited similar sensitivity to $SbCl_3$ and $SbCl_5$ in the streak test but were more sensitive than wild-type when non-growing cells were exposed to $SbCl_3$, $SbCl_5$ and Sb_2O_3 for prolonged periods. Positive results were also found in the spore-plate method using $SbCl_3$, Sb_2O_3 and Sb_2O_5. The same compounds gave negative results in reversion tests with *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 and *Escherichia coli* strains WP2 and WP2*uvr*. Antimony acetate caused increased transformation of Syrian Hamster cells by a simian adenovirus. An increase in the frequency of sister chromatid exchanges was observed in Chinese Hamster V79 cells treated with $SbCl_3$ and Sb_2O_3 but not with $SbCl_5$ and Sb_2O_5. Increased numbers of chromatid breaks were observed in cultured animal leukocytes with antimony sodium tartrate. Increased numbers of structural chromosomal aberrations were observed in mouse bone marrow cells *in vivo* with $SbCl_3$ after single dose and Sb_2O_3 after repeated dose. Human male patients treated with $C_7H_{18}NO_8Sb$ did not exhibit an increase in sister chromatid exchanges or structural chromosomal aberrations in cultured blood lymphocytes but showed up to a 9-fold enhancement of micronuclei. Leonard & Gerber concluded that a claim that antimony compounds could be mutagenic was based on insufficient and not particularly relevant data. They noted that additional experiments, particularly with organic antimony compounds, would be desirable, but from what was already known, it appeared that antimony had less mutagenic risk than many other metals, such as arsenic, chromium, nickel, among others. Copies of original studies were not sought for this assessment.

In an attempt to provide quality data to aid in resolving the uncertainty of the genotoxicity of antimony trioxide, Elliott *et al.* (1998) were commissioned by the Association of Plastics Manufacturers in Europe to undertake a full genetic toxicology package of the compound with current OECD protocols and on material of established (99.9%) purity. They found no genotoxic activity in the Salmonella and L5178Y mutation assays, the mouse bone marrow assay and the liver DNA repair assay. A positive response was seen with *in vitro* human lymphocytes, but only at the maximum testable dose. The authors speculated that the inconsistency between the negative L5178Y assay and the positive human lymphocyte *in vitro* might be due to antimony inducing chromosomal damage by an action on chromosomal protein structure rather than by a direct DNA damaging effect. What was probably more important was that the concentration of antimony giving rise to the increased number of aberrant human lymphocytes had precipitated from solution. Another argument for giving less weight to the human lymphocyte positive effect was that the clastogenicity seen in that

assay was not expressed in the whole animal i.e., the mouse bone marrow assay. This is further reinforced by the negative findings in the DNA repair (UDS) assay.

It is now commonly believed that the positive findings reported many years previously, of activity in the bacterial repair (rec) and sister chromatid exchange assays, are of little relevance to an assessment of genotoxic hazard. Thus, clastogenicity *in vitro* is of less importance than the negative effects *in vivo* and consequently antimony trioxide appears to pose no (or very little) genotoxic hazard to exposed humans.

Acetic acid has not been shown to be genotoxic in standard experimental tests.

9.5 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity in rats (LD_{50} approximately 7.0 g/kg) and low acute dermal toxicity in rabbits (LD_{50} > 12.8 g/kg). It was corrosive to rabbit skin and a severe eye irritant in rabbits. The corrosivity is most likely due to the formation of acetic acid by hydrolysis of the notified chemical during the treatment period. No skin sensitisation studies were conducted because firstly, when considering breakdown products, there is no evidence the substance will be a sensitiser and secondly, the corrosive effects on rabbit skin override the potential additional hazard of skin sensitisation.

Long term exposure to the two hydrolysis products antimony trioxide and acetic acid has revealed the following toxic effects for antimony trioxide: in humans, irritation of the skin, eyes, nose, throat and eyes; transient skin lesions called 'antimony spots', heart damage, chronic emphysema, pneumoconiosis, impaired kidney and liver function and effects on the spleen and blood; in animals, changes in lung, liver, spleen, eye and blood components. Acetic acid aerosols have caused bronchopneumonia in mice; oral dosing in rabbits revealed injury to the upper gastrointestinal tract and forestomach; drinking water containing acetic acid at 0.5% affected food consumption and growth; repeated skin applications of acetic acid did not cause local tumours in mice, however, it weakly increased tumour production by a known carcinogen in the multi mouse skin model; no birth defects were noted in rabbits given high doses of apple cider vinegar by the oral route during pregnancy.

No repeat dose data were provided for the notified chemical.

Previous studies on the oncogenicity of antimony trioxide were conducted in Fischer 344 rats at a dose of 5 mg/m^3 for 1 year (Watt, 1983) and in Wistar rats at a dose of 46 mg/m^3 for 1 year followed by a 1-year observation period (Groth *et al.,* 1986). In the former study only female rats were exposed and in the latter only female rats exhibited pulmonary neoplasms. Newton et al. (1994) could not produce lung tumours in rats. However, it was concluded from comparative histopathological investigations by Dr William Busey of Experimental Pathology Laboratories, VA, USA, that a higher lung burden existed in the earlier studies than occurred at the highest tested dose of 4.5 mg/m^3 in the study of Newton *et al.* (1994). The negative results in this study do not negate the conclusions from previous studies but suggest that very high respiratory exposures are needed to produce tumours in experimental animals.

No genotoxicity studies were performed on the notified chemical.

The most recent studies on the mutagenicity of antimony trioxide were conducted by Elliott *et al* (1998). They found no genotoxic activity in the Salmonella and L5178Y mutation assays, the mouse bone marrow assay and the liver DNA repair assay. A positive response was seen with *in vitro* human lymphocytes, but only at the maximum testable dose where there was precipitation of the test material. Another argument for giving less weight to the human lymphocyte positive effect was that the clastogenicity seen in that assay was not expressed in the whole animal i.e., the mouse bone marrow assay. This is further reinforced by the negative findings in the DNA repair (UDS) assay.

The NOHSC *List of Designated Hazardous Substances* (1999b) lists antimony trioxide (CAS No. 1309-64-4) as a carcinogen, category 3, with risk phrase R40 – Possible Risk of Irreversible Effects. The notified chemical should have the same carcinogen classification, and risk phrase. Category 3 substances are those for which there is some evidence from appropriate animal studies that human exposure can result in the development of cancer, but this evidence is insufficient to place the substance in Category 2. IARC (1989) concluded that the evidence for the carcinogenicity of antimony trioxide in humans is inadequate, classifying it in Group 2B. Acetic acid is included in NOHSC *List of Designated Hazardous Substances* (NOHSC, 1999b) and is classified as Corrosive, with risk phrase R35 – Causes Severe Burns.

On the basis of the data presented the notified chemical would be determined to be hazardous according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999a). The overall hazard classification is Corrosive, (in terms of skin and eye burns) and Carcinogen, category 3 (possible risk of irreversible effects). The relevant risk phrases are R34 – Causes Burns and R40 - Possible Risk of Irreversible Effects. Risk phrase, R34 rather than R35, is appropriate because of the low water solubility of antimony triacetate which would preclude the formation of greater than 90% acetic acid.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicology data were provided for the chemical. However, data were provided from various literature sources for the decomposition products – antimony trioxide and acetic acid. Physico-chemical details were not provided.

	Chemical			
Species	***Antimony trioxide***		***Acetic acid***	
Fish:				
Fathead minnow *Pimephales promela*	LC_{50} (96 h)	833 mg/L	LC_{50} (96 h)	79 mg/L
Sheepshead minnow *Cyprinodon varietegas*	LC_{50} (96 h)	>6.2 mg/L		
Bluegill sunfish *Lepomis macrochirus*	LC_{50} (96 h)	530 mg/L	LC_{50} (96 h)	79 mg/L
Invertebrates:				
Daphnia magna	LC_{50} (48 h)	423 – 530 mg/L		
Mysid shrimp	LC_{50} (48 h)	920 mg/L		
Tubiflex worms	LC_{50} (48 h)	>4.2 mg/L		
Brine shrimp			TLm (24-48 h)	32-42 mg/L
Water fleas			TLm (24 h)	47 mg/L
Algae	EC_{50} (96 h)	0.61 to >4.2 mg/L	EC_{50}	90 mg/L

Embryo-larval bioassays with the fathead minnows produced chronic values greater than 7.5 mg/L, while no mortality was observed in rainbow trout exposed to 100-200 mg/L of antimony trioxide for 7 days.
The above data suggests that the hydrolysis products have slight to moderate toxicity for the majority of organisms included in the above table. However, this assessment concludes that pH changes *per se* (*eg.* if the pH change was sudden and large) might lead to some detrimental effects.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The majority of the notified chemical will share the fate of the end use polyester products disposed of to landfill at the end of their useful lifetime. Antimony triacetate waste from the manufacture process (53.5 kg per year) will be dissolved or suspended in wastewater or disposed of to landfill. Exposure to water or moisture results in the hydrolysis of antimony triacetate into antimony trioxide and acetic acid. Antimony trioxide is expected to be immobile in soils and sediments and not to become bioavailable. Any acetic acid produced may cause a change of pH in, at least, the immediate vicinity of the hydrolysis. While low pH or sudden change in pH could be expected to affect organisms, dilution effects and the low levels of antimony triacetate being released are expected to limit this impact.

The overall environmental hazard of the notified chemical is therefore expected to be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Toxicological data were provided on acute oral and dermal toxicity in rats and rabbits, respectively, and on skin and eye irritancy in rabbits. These studies suggest that the notified chemical is not likely to be acutely toxic by the dermal and oral routes in humans. However, the notified chemical is likely to be corrosive to skin and eyes, probably due to the hydrolysis product acetic acid, which carries the hazardous substances risk phrase R35. Elliott *et al*. (1998) have conducted the most recent studies on the mutagenicity of antimony trioxide. They found no genotoxic activity in the Salmonella and L5178Y mutation assays, the mouse bone marrow assay and the liver DNA repair assay and a positive response with *in vitro* human lymphocytes at the maximum testable dose. The authors concluded that antimony trioxide was not a genotoxic hazard to humans at low exposures.

Earlier reports of lung tumours caused by antimony trioxide have been attributed subsequently to the very high lung burden and other confounding variables, and lung tumours could not be reproduced in a recent study (Newton *et al.,* 1994). According to NOHSC *Exposure Standards for Atmospheric Contaminants in the Occupational Environment* (NOHSC, 1995) it is a probable human carcinogen during manufacture (NOHSC category 2) but not during handling and use. There is a NOHSC exposure standard for antimony trioxide (as antimony) of 0.5 mg/m^3 (time weighted average – TWA). The notifier has stated that this standard will be applied in the workplace.

NOHSC (1999b) lists antimony trioxide as Carcinogen, category 3 with risk phrase, R40 – Possible Risk of Irreversible Effects. On the basis of this assessment, the notified chemical is given the same carcinogen classification.

In summary, the notified chemical is determined to be a hazardous substance in terms of skin and eye corrosivity and the risk of irreversible effects and carries the overall hazard classification of Corrosive, with risk phrase R34 – Causes burns, and Carcinogen, category 3, R40 - Possible risk of irreversible effects. The risk phrases "Causes Burns" and "Possible Risk of Irreversible Effects" should be included on labels and in the MSDS.

Due to the use of sturdy packaging, exposure of transport and storage workers to the notified chemical is unlikely except in the event of accidental spillage. During cleanup, personal protective equipment as specified in the recommendations section (see below) should be employed.

The notifier states that workers emptying the antimony triacetate powder into the mixing vessel where it is dissolved in warm ethylene glycol may be exposed by inhalation and eye contact despite the use of local exhaust ventilation. However, since 90% of the particles have a size greater than 95 μm, the dust may be inspirable but not respirable. The notifier states that workers don personal protective equipment during this operation, namely, respiratory protection, gloves, goggles and industrial clothing. This is essential given the systemic and possible long term health effects. Following addition of the notified chemical to the reactor,

the system is enclosed and exposure is unlikely. However, exposure may be possible when the plastic pails in which the notified chemical is imported are washed out with water, and during maintenance operations when the mixing vessel containing residual notified chemical is cleaned with ethylene glycol. These workers will also need to wear the personal protective equipment specified above.

There is a NOHSC exposure standard for antimony trioxide and acetic acid (NOHSC, 1995). The exposure standard for antimony trioxide (handling and use: 0.5 mg/m^3 TWA) should be employed in workplaces using antimony triacetate. The exposure standard for acetic acid is 25 mg/m^3 (TWA) and 37 mg/m^3 (STEL). Employers are responsible for ensuring that the exposure standards are not exceeded in the workplace.

The public will only be exposed to the notified chemical when it is entrapped in the polyester material it is used to manufacture. Although this exposure will be high, the public health risk is low as the chemical is unlikely to be bioavailable.

13. MATERIAL SAFETY DATA SHEET

The MSDS for Catalyst S-21 containing the notified chemcial was provided in accordance 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.

14. RECOMMENDATIONS

To minimise occupational exposure to Antimony Triacetate the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);
- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987);
- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia/ Standards New Zealand, 1998);
- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/ Standards New Zealand, 1994c);
- Respiratory protection should conform to AS/NZS 1715 and 1716 (Standards Australia/Standards New Zealand, 1994a; Standards Australia/Standards New Zealand, 1994b);
- Spillage of the notified chemical should be avoided. Spillage should be cleaned up promptly with absorbents which should then 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.
- Employers need to ensure that the NOHSC exposure standards for antimony trioxide and acetic acid are not exceeded in the workplace.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

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

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Attachment 1

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

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

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

CORNEA

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

CONJUNCTIVAE

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

IRIS

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