

File No: STD/1159

24 April 2006

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME  
(NICNAS)**

**FULL PUBLIC REPORT**

**1-Decene, sulfurized**

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**Director  
NICNAS**

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**FULL PUBLIC REPORT****1-Decene, sulfurized****1. APPLICANT AND NOTIFICATION DETAILS**

## APPLICANT(S)

Acheson A.N.Z Pty Ltd (89 000 563 002)  
Units 8-9, 12-14 Riverside Road  
Chipping Norton NSW 2170

## NOTIFICATION CATEGORY

Standard: Chemical other than polymer (more than 1 tonne per year).

## EXEMPT INFORMATION (SECTION 75 OF THE ACT)

Data items and details claimed exempt from publication:

- Chemical identity (Other names)
- Composition
- The specific use.
- Manufacture/Import volumes
- Identity of sites

## VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)

Variation to the schedule of data requirements is claimed as follows:

Spectral data

Purity of chemical

Physical and Chemical Properties

Acute toxicity

- Acute oral toxicity
- Acute dermal toxicity
- Acute inhalation toxicity
- Skin irritation
- Eye irritation
- Skin sensitisation

Repeat Dose Toxicity

Genetic Toxicity

- Induction of point mutations
- Induction of germ cell damage
- Chromosome damage

Ecotoxicity

- Fish, Acute Toxicity
- Daphnia sp. Acute Immobilisation/Reproduction
- Alga, Growth Inhibition Test

Biodegradation

- Ready biodegradation
- Bioaccumulation

## PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)

None.

## NOTIFICATION IN OTHER COUNTRIES

None.

**2. IDENTITY OF CHEMICAL**

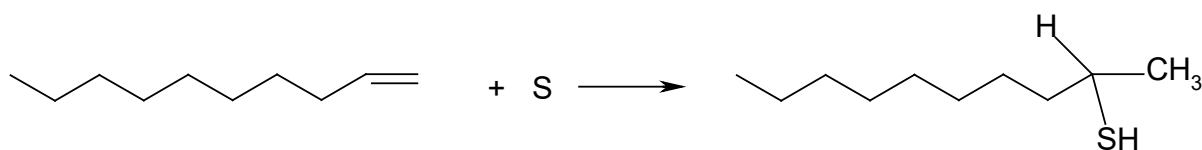
CHEMICAL NAME  
1-Decene, sulfurized

MARKETING NAME(S)  
1-Decene, sulfurized

CAS NUMBER  
72162-15-3

MOLECULAR FORMULA  
 $C_{10}H_{22}S$

STRUCTURAL FORMULA



MOLECULAR WEIGHT  
174.1

SPECTRAL DATA      Notifier unable to source data for the notified chemical from the formulators of the products to be imported. If the notified chemical is to be imported at > 6%, spectral data may need to be obtained in accordance with the Secondary notification condition.

### 3. COMPOSITION

DEGREE OF PURITY  
>90%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS  
None known.

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)  
None known.

ADDITIVES/ADJUVANTS  
None.

### 4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS  
The notified chemical will be imported as part of formulations at less than 5% in 200 kg steel drums.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	1	2	3	4	5
Tonnes	1 - 3	1 - 3	1 - 3	1 - 3	1 - 3

USE  
Used in production of glass manufacture.

## 5. PROCESS AND RELEASE INFORMATION

### 5.1. Distribution, transport and storage

#### PORT OF ENTRY

The notified chemical will be imported through Sydney by wharf.

#### IDENTITY OF MANUFACTURER/RECIPIENTS

Glass manufacturers

#### TRANSPORTATION AND PACKAGING

The notified chemical will be imported in the two products at < 3% concentration and at < 5% concentration. It will be imported in 200 kg steel drums. It will be transported by road from wharf to the notifier's warehouse (Acheson ANZ Pty Limited) and stored. No repackaging operations will be carried out at the notifier's site. Product containing the notified chemical will then be transported by road unopened to the glass manufacturing site.

### 5.2. Operation Description

#### *Transport and storage*

Product containing the notified chemical will be imported in 200 kg steel drums. Product containing the notified chemical will be stored in dry and well-ventilated area at the notifier's site and then on-sold and transported to glass manufacturers. After production of the glass bottles, they will be sold to various facets of the food and beverage industry. There will be no residue of the notified chemical in the final product, as it is destroyed by the high temperatures in the glass manufacturing process.

#### *Glass Bottle manufacture*

At the glass manufacturing site the following processes take place:

Step 1: Glass Melting. The furnace melts cullet (crushed, recycled glass), sand, soda ash, limestone, and other raw materials together. Molten glass usually ranges in temperature between 1260 and 1537°C. A Furnace Control Room houses the computer which monitors and controls furnace temperature.

Step 2: Container Forming. The Refiner distributes the molten glass to the fore hearth, which brings the temperature of the molten glass to a uniform level. The notified chemical will be automatically injected into the system at this stage. The notified chemical will be transferred to 200 L holding tanks and mixed with other ingredients. Laboratory staff are responsible for formulating the preparation and carrying out analysis of samples. A dedicated pump is used to transfer product containing the notified chemical to the holding tank. The transfer line is permanently connected to the pump. The notified chemical is added to the molten glass through a dedicated transfer line which is also permanently connected. The Shearing and Distribution System then cuts molten glass from the fore hearth into uniform gobs and sends them to an I.S. (Individual Section) Forming Machine that forces the molten gobs into the mold shape. The glass temperature drops further in the Forming Machine to below 1489°C. Formed glass containers leave the machine, crossing a cooling plate where they are cooled rapidly to below 482°C. The glass has now passed from liquid to solid form.

Step 3: Container Conditioning. The formed containers are loaded into an Annealing Lehr, where their temperature is brought back up close to the melting point, then reduced gradually to below 482°C. This reheating and slow cooling eliminates the stress in the containers making them stronger and shock resistant.

Step 4: Surface Treatment. The temperature of the containers is reduced to between 107 and 132°C. Cold End Sprays then apply an exterior coating to the bottles to increase line mobility, and reduce abrasions to maintain the inherent strength of the container

Step 5: Automatic Inspection. The Fast Cooling Section then brings container temperatures down to about 38°C - cool enough to touch by hand. The manufactured containers then pass through a series of instruments that physically and optically test the containers. Rejected containers are recycled back into the furnace.

Step 6: Product Handling & Packaging. A Case Packer then packs the containers in corrugated cases for shipment. The cases are then sent to the Case Palletizer, where they are stacked in a prearranged pattern to increase stability for shipment. A strapper fits plastic bands around the stacked boxes for added stability and, finally, the Stretch Wrap Unit covers the stacked boxes with plastic wrap. Containers can also be sent to a Bulk Palletizer that stacks the individual containers in 5 to 15 layers, depending upon the size of the container. These Bulk loads are also strapped for stability and sent through the Stretch Wrap Unit and covered with plastic wrap for shipment.

### 5.3. Occupational Exposure

#### *Number and Category of Workers*

<i>Category of Worker</i>	<i>Number</i>	<i>Exposure Duration</i>	<i>Exposure Frequency</i>
Transport and Warehouse	3-6	2 hours/day	241 days/year
Laboratory staff	2	3 hours/day	241 days/year
Process Operators	26-28	2 hours/day	241 days/year
Maintenance worker	2	1 hour/day	241 days/year

#### *Exposure Details*

##### *Transport and storage*

Dock workers will unload the 200 L drums from the ship and then load them onto trucks for road transport to the notifier's site. These workers are only likely to be exposed to the notified chemical in the case of an accidental spillage from damaged containers.

##### *Glass Manufacturing*

Laboratory workers: - Dermal and ocular exposure may occur from taking samples for analysis and formulating the notified chemical with other ingredients before it is introduced into the manufacturing process. Laboratory workers will wear wrap around safety goggles, laboratory coats, chemical resistant gloves and totally enclosed footwear to prevent exposure to the notified chemical. In addition to personal protective equipment, the whole system is enclosed and automated with exhaust ventilation in place.

Dermal and ocular exposure may be possible due to drips and spills when opening drums and connecting to a dedicated pump. This is carried out under local exhaust ventilation and workers wear overalls, goggles and impervious gloves. Therefore exposure is minimal. The rest of the glass manufacturing process is fully automated and computerised and therefore exposure to the notified chemical is not expected. Plant operators involved in the "cold end & finished products", were they check for any defective bottle and plant operators involved in the "despatch and storage" stage are not exposed to the notified chemical as it is destroyed by the high temperatures at the "forming stage".

Maintenance workers will only need to intervene in the manufacturing process when equipment malfunctions, or during routine maintenance. The process will be stopped prior to workers entering the enclosed system. Workers outside of the enclosure will wear protective coveralls, safety glasses and safety boots. Workers who will be entering the enclosure will also wear protective coveralls, safety glasses and safety boots.

##### *End-users*

End-users of the glass products are not exposure to the notified chemical as it is destroyed by the high temperatures in the glass manufacturing process.

### 5.4. Release

#### RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured in Australia, therefore there will no Australian release during this stage.

During transport and storage there is the possibility of accidental release due to spills. It is estimated that a maximum of 1% of the notified chemical (< 30 kg per year) would be lost due to spillage. Spills are contained and soaked up with inert absorbent material and placed in a sealable container and

disposed of to landfill.

#### RELEASE OF CHEMICAL FROM USE

The notified chemical will be destroyed during high temperature stage of glass manufacture, potentially releasing water and oxides of carbon and sulphur.

The only possible routes of environmental release during the use of the chemical are spills and in empty containers. Annually up to 1% (up to 30 kg) of the notified chemical used in Australia may be lost via spills during material transfers. The spilt material is contained via bunding and either pumped back into the storage containers or in the case of a minor spill, it is collected using an adsorbent material, placed in containers ready for disposal.

The empty 200 kg steel drums will be rinsed with solvent. The residue and the empty containers will be collected by licensed waste contractors, it is estimated that up to 1% of the notified chemical will be lost in this manner. The containers will be disposed off to landfill.

#### 5.5. Disposal

Any spilt material will be sent to landfill with the absorbent material. Rinsed containers will also be disposed of to landfill by the waste contractor.

#### 5.6. Public exposure

Exposure of the public as a result of manufacture, transport and disposal of glass products made using the notified chemical is negligible. The public may make dermal contact with finished glass product. However, public exposure to the notified chemical is unlikely since it is expected that the notified chemical is destroyed by the high temperatures in the glass manufacturing process and hence no residue is present in the final product.

### 6. PHYSICAL AND CHEMICAL PROPERTIES

Physicochemical properties for the notified chemical are not generally available. Where indicated these are based on analogues and may have been calculated rather than measured. This is accepted on the basis that the notified chemical is imported at 5% or less in two (mainly) petroleum oil formulations GM 900 A and GM 900 C for which the MSDS are attached to this report). If the notified chemical is to be imported at a concentration greater than 6% the missing data may need to be generated (see section on Secondary Notification).

<b>Appearance at 20°C and 101.3 kPa</b>	Black fluid (imported products containing the notified chemical)
<b>Melting Point/Freezing Point</b>	Not determined.
Remarks	Imported products are liquid under normal environmental conditions.
<b>Boiling Point</b>	Not determined
METHOD	Estimated by EPIWIN.
Remarks	Is expected to be between 505 - 538°C based on the analogue Alkenes, C15-18 alpha, sulfurized.
TEST FACILITY	Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide, page 4, Table 1: Physical Properties of Representative Structures of Alkyl Sulfides as Modeled by EPIWIN".
<b>Density</b>	Not determined.
Remarks	Cited in MSDS for Base 18-V as 1000 kg/m <sup>3</sup> .
<b>Vapour Pressure (1)</b>	3.90 x 10 <sup>-12</sup> to 5.69 x 10 <sup>-11</sup> kPa based on the analogue Alkenes, C15-18 alpha, sulfurized.
Remarks	Cited in "High Production Volume (HPV) Challenge Program – Robust



Summaries & Test Plans: Alkyl Sulfide, page 4, Table 1: Physical Properties of Representative Structures of Alkyl Sulfides as Modeled by EPIWIN".

**Vapour Pressure (2)** 8 to 140 kPa at 50°C for tert-dodecanethiol

Remarks Summary of data presented in IUCLID for tert-dodecanethiol.

**Water Solubility (1)**  $1.64 \times 10^{-11}$  to  $1.59 \times 10^{-10}$  mg/L based on the analogue Alkenes, C15-18 alpha, sulfurized.

Remarks Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide, page 4, Table 1: Physical Properties of Representative Structures of Alkyl Sulfides as Modeled by EPIWIN".

**Water Solubility (2)** 0.5096 mg/L (10 chain thiol)

METHOD ECOSAR v0.99

Remarks These results are calculated.

**Hydrolysis as a Function of pH** Not determined. The notified chemical does not contain any functional groups considered to be hydrolysable.

**Partition Coefficient (n-octanol/water) (1)** Not determined

Remarks log  $K_{ow}$  expected to be between 16 – 16.95 based on the analogue Alkenes, C15-18 alpha, sulfurized.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide, page 4, Table 1: Physical Properties of Representative Structures of Alkyl Sulfides as Modeled by EPIWIN".

**Partition Coefficient (n-octanol/water) (2)** log  $P_{ow}$  = 6.1 (calculated) for tert-dodecanethiol

REMARKS Summary of data presented in IUCLID for tert-dodecanethiol.

**Partition Coefficient (n-octanol/water) (3)** log  $K_{ow}$  = 5.12 (estimate) (10 chain thiol)

METHOD KowWin – ECOSAR v0.99

**Adsorption/Desorption** Not determined

Remarks log  $K_{oc}$  is expected to be between 9.50 – 9.77 based on the analogue Alkenes, C15-18 alpha, sulfurized.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide, page 4, Table 1: Physical Properties of Representative Structures of Alkyl Sulfides as Modeled by EPIWIN".

**Dissociation Constant** pKa = 9.0 – 11.0 (Aliphatic thiols)

METHOD Test reports were not provided.

**Particle Size** Not applicable as it is a liquid

**Flash Point** > 176.67°C

METHOD Cleveland

Remarks Cited in the MSDS for Base 18-V

**Flammability Limits** Not determined.

Remarks Not expected to be flammable based on use pattern.

**Autoignition Temperature** Not determined.

Remarks Not expected to autoignite based on use pattern.

**Explosive Properties** Not determined.

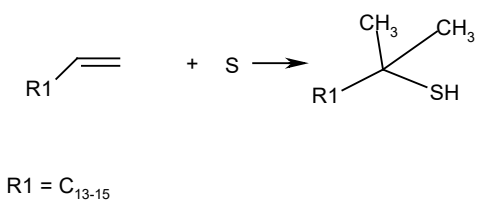
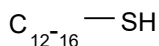
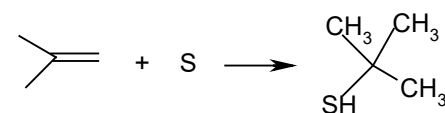
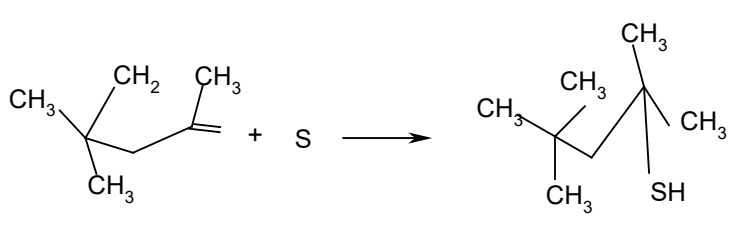
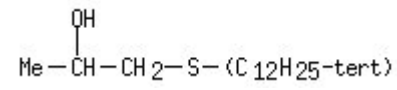
Remarks Not expected to be explosive based on use pattern.

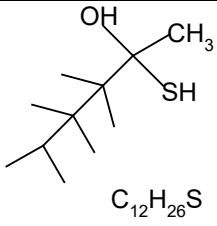
**Reactivity**

Remarks Expected to be stable under normal conditions of use. Avoid contact with strong oxidants.

## 7. TOXICOLOGICAL INVESTIGATIONS

No toxicology data are available for the notified chemical. The notifier has presented data for structurally similar analogues to the notified chemical. While these data are indicative, they are not fully acceptable. The US EPA (<http://www.epa.gov/chemrtk/alkylsul/c12549tc.htm>) is currently considering the alkyl sulfides as a chemical category. After reviewing the available data, they concluded that the data for acute toxicity and genotoxicity were adequate but the data for repeated dose toxicity did not warrant placing the chemicals in a category. However, as the notified chemical is to be imported at a concentration no greater than 5%, a secondary notification requirement has been included in this report stating that if a concentration greater than 6% is to be imported, the Director must be notified and will then decide what further data may be required. This is based on the particular use pattern and controls in place.

ANALOGUE NAME	CAS REGISTRY NUMBER	REFERENCE	STRUCTURE
Alkenes, C15-18 a-, sulfurized	67762-55-4	Robust Summaries & Test Plans: Alkyl Sulfide	 <p>R1 = C<sub>13-15</sub></p>
Alkyl (C12-C16) Sulfide	91770-97-4	Robust Summaries & Test Plans: Alkyl Sulfide	
*1-Propene, 2-methyl-, sulfurized	68511-50-2	Robust Summaries & Test Plans: Alkyl Sulfide & IUCLID Data Set (ID: 68511-50-2)	
Diisobutylene, sulfurized	68515-88-8	Robust Summaries & Test Plans: Alkyl Sulfide	
2-Propanol, 1-(tert-dodecylthio)-	67124-09-8	Robust Summaries & Test Plans: Alkyl Sulfide	

*Tert- Dodecanethiol	25103- 58-6	IUCLID Data Set (ID: 25103- 58-6)	 $C_{12}H_{26}S$
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\* Data extracted from IUCLID Data Set are presented in summary form at the end of this document. Data is presented in table format as information is limited for each of the studies.

These chemicals in the table above belong to the group alkyl sulfides. The molecular weights for these chemicals are all > 250 and have similar physical characteristics. They also share certain properties i.e. hydrophobic, lipid-like substances with low volatility and chemical reactivity.

The table below summarises the studies available on each of the analogues as cited in the “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide” and IUCLID Data Set for tert-Dodecanethiol (2000) and 1-Propene, 2-methyl-, sulfurized (2000)

Analogue/End point	Alkenes, C15-18 alpha, sulfurized CAS No. 67762-55-4	Alkyl (C12- C16) Sulfide CAS No. 91770- 97-4)	1-Propene, 2-methyl sulfurized CAS No. 68511-50-2	Pentene, 2,4,4- trimethyl sulfurized CAS No. 68515-88-8	2-Propanol 1- (tert- dodecylthio)- CAS No. 67124-09-8	Tert- Dodecanethiol CAS No. 25103-58-6
Acute Oral			✓	✓	✓	✓
Acute Dermal	✓			✓	✓	✓
Acute Inhalation			✓	✓		✓
Acute intraperitoneal						✓
Skin Irritation			✓			✓
Eye Irritation			✓			✓
Skin Sensitisation			✓			✓
Repeat Dose Toxicity			✓	✓	✓	✓
Genotoxicity <i>in vitro</i> – Bacterial Reverse Mutation	✓		✓	✓	✓	
Genotoxicity <i>in vitro</i>			✓		✓	✓
Genotoxicity <i>in vivo</i>		✓	✓	✓		
Development toxicity/Teratogenicity						✓

Endpoint and Result

Assessment Conclusion

Rat, acute oral LD50:

- 1-Propene, 2-methyl-, sulfurized:  
LD50 = 8600 mg/kg bw (male rats) Low toxicity
- 1-Propene, 2-methyl-, sulfurized:  
LD50 = 5.7 mL/kg (male rats) Low toxicity
- Pentene, 2,4,4-trimethyl-, sulfurized  
LD50 > 5000 mg/kg bw Low toxicity
- 2-Propanol, 1-(tert-dodecylthio)-  
LD50 > 5000g/kg bw (male and female) Low toxicity

Rat, acute dermal:

- Alkenes, C15-18 alpha, sulfurized:  
LD50 > 2000 mg/kg bw Low toxicity

Rabbit acute dermal:

- Pentene, 2,4,4-trimethyl-, sulfurized  
LD50 > 2000 mg/kg bw Low toxicity
- 2-Propanol, 1-(tert-dodecylthio)-  
LD50 > 2000 mg/kg bw Low toxicity

## Rat, acute inhalation LC50 ... mg/L/4 hour:

- 1-Propene, 2-methyl-, sulfurized:  
LC50 > 0.39 mg/L/4hours Low toxicity
- Pentene, 2,4,4-trimethyl-, sulfurized  
LC50 (mice) > 4.3 mg/L/4 hours; LC50  
(guinea pigs) > 4.3 mg/L/4 hours Ten of ten CD-1 mice and ten of ten Hartley guinea pigs received a single four-hour whole-body exposure to 4.3 mg/L test material as a respirable aerosol.
- Pentene, 2,4,4-trimethyl-, sulfurized  
LC50 (mice) > 4.3 mg/L/4 hours Low toxicity  
LC50 (rat) < 4.3 mg/L/4 hours  
LC50 (guinea pigs) > 4.3 mg/L/4 hours
- Pentene, 2,4,4-trimethyl-, sulfurized  
LC50 (males) > 5.0 mg/L/4 hours  
LC50 (females) = 2.17 mg/L/4 hours Following 4-hour whole-body exposure to a liquid droplet aerosol of the test material, the LC50 in male Sprague-Dawley rats is considered to be greater than 5.6 mg/L. The LC50 value in females was calculated to be 2.17 mg/L with upper and lower confidence limits of 3.69 and 0.64 mg/L.

Rabbit, skin irritation:

- 1-Propene, 2-methyl-, sulfurized  
(cited in IUCLID Data Set) Slightly irritating

Rabbit, eye irritation

- 1-Propane, 2-methyl-, sulfurized  
(cited in IUCLID Data Set) Slightly irritating

Guinea pig, skin sensitisation – Maximization test

- 1-Propane, 2-methyl-, sulfurized  
(cited in IUCLID Data Set) No evidence of sensitisation.

Rat, Dermal repeat dose toxicity - 21 days:

- 1-Propene, 2-methyl-, sulfurized

A NOAEL was not established in this study. The LOEL for clinical signs and systemic toxicity was 140 mg/kg/day dermal exposure for 3 weeks. No minimally irritating concentration was identified by this study.

Rabbits, Dermal repeat dose toxicity – 28 days

- 1-Propene, 2-methyl-, sulfurized

A NOAEL was not established in this study. A LOEL was not established in this study. No minimally irritating concentration was identified by this study.

Rats, Dermal repeat dose toxicity – 90 days

- 1-Propene, 2-methyl-, sulfurized

NOEL for systemic toxicity was 50 mg/kg/day dermal exposure for 13 weeks. The minimally irritating concentration of methyl propene derivative diluted in 100 mineral oil base stock is 10% (100, 50, 10 mg/kg/day).

Rabbits, Dermal repeat dose toxicity – 28 days

- Pentene, 2,4,4-trimethyl-, sulfurized

No NOAEL was assigned to this study. All animals survived throughout the study and physical examinations were generally unremarkable.

Rats, Inhalation repeat dose toxicity – 28 days

- Pentene, 2,4,4-trimethyl-, sulfurized

No NOAEL was assigned to this study.

Rats, Oral repeat dose toxicity – 28 days

- 2-Propanol, 1-(tert-dodecylthio)-

No NOAEL was assigned to this study. Although renal and hepatic changes were evident at all dose levels (100, 300, and 1000 mg/kg/day), the renal changes are species-specific and the hepatic changes are probably adaptive in nature. Therefore, little subchronic toxicity was observed over the range of doses administered in this study.

Genotoxicity - bacterial reverse mutation:

- Alkenes, C15-18 alpha, sulfurized

Non mutagenic

Genotoxicity - bacterial reverse mutation:

- 1-Propane, 2-methyl-sulfurized

Non mutagenic

Genotoxicity - bacterial reverse mutation:

- Pentene, 2,4,4-trimethyl-, sulfurized

Non mutagenic

Genotoxicity - bacterial reverse mutation:

- 2-Propanol, 1-(tert-dodecylthio)-

Non mutagenic

Genotoxicity – in vitro in Chinese hamster ovary CHO cells

- 2-Propanol, 1-(tert-dodecylthio)-

Non genotoxic

Genotoxicity – in vivo mouse micronucleus test:

- Alkyl (C12-C16) sulfide Non genotoxic

Genotoxicity – in vivo mammalian bone marrow erythrocyte micronucleus test:

- 1-propene, 2-methyl-, sulfurized Non- genotoxic
- Pentene, 2,4,4-trimethyl-, sulfurized Non clastogenic

Genotoxicity – in vivo mammalian bone marrow erythrocyte micronucleus test, adjunct to 13 week dermal subchronic toxicity test:

- 1-Propene, 2methyl-, sulfurized Non-genotoxic

**7.1. (a) Acute toxicity – oral**

TEST SUBSTANCE	1-Propene, 2-methyl-,sulfurized
METHOD	Litchfield and Wilcoxon (J. Pharm. & Exp. Therap. 96:99, 1949)
Species/Strain	Rat/Wistar (40 male rats, 4 groups of 10)
Vehicle	None: administered undiluted
Remarks – Method	Rats fasted for 24 hours prior to dosing; Test material administered by gavage in a single oral dose at concentrations of 5.0, 7.12, 10.14, and 14.43 g/kg. Animals observed 3-4 hours after dosing and once daily for 14 days post-dosing. Mortality, toxicity, and pharmacological effects were recorded for each animal. Body weights were recorded pretest. At the end of 14 days, all survivors were sacrificed and all animals, including those which died during the course of the study, were examined for gross pathology.
RESULTS	
LD50	8.6 g/kg (male rats)
Signs of Toxicity	At 5.0 g/kg 2/10 died (1 at day 1 post dose and 1 at day 13 post dose); at 7.12 g/kg 4/10 died (3 at day 2 post dose and 1 at day 6 post dose); at 10.14 g/kg 6/10 died at day 2 post dose; at 14.43 g/kg 10/10 died (1 at day 1 post dose and 9 at day 2 post dose). Toxicity was observed for the following doses: at 5.0 g/kg lethargy, ataxia, ptosis, piloerection and flaccid muscle tone were noted in 5 or more animals. Isolated instances of diarrhea, chromorhinorrhea, chromodacryorrhea, and tachypnea were also noted; at 7.12 g/kg lethargy, diarrhea, piloerection, ptosis, chromodacryorrhea, ataxia, and chromorhinorrhea were noted in 5 or more animals. Isolated instances of tachypnea, respiratory noise and prostration were also noted; At 10.14 g/kg lethargy, diarrhea, chromorhinorrhea, ptosis, piloerection, chromodacryorrhea and ataxia were noted in 5 or more animals. Isolated instances of emaciation, prostration and hyperactivity were also noted; at 14.43 g/kg lethargy, ataxia, ptosis, diarrhea, chromorhinorrhea and piloerection were noted in 5 or more animals. Overall body weights increased slightly in the 5.0, 7.12, and 10.14.
Effects in Organs	None noted.
CONCLUSION	The test substance is of low toxicity via the oral route.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.1. (b) Acute toxicity – oral**

TEST SUBSTANCE	1-Propene, 2-methyl-, sulfurized
METHOD	Not specified
Species/Strain	Rat/Sherman/Wistar
Vehicle	None, administered undiluted
Remarks – Method	Rats fasted 24 hours prior to dosing; Test material administered by gavage in a single oral dose at concentrations of 2.0, 4.0, 8.0, 16.0 or 32.0 ml/kg. Animals observed for 14 days postdosing for signs of toxicity or mortality. Body weights were not taken; gross necropsies and histopathology were not performed
RESULTS	
LD50	5.7 ml/kg (male rats) mg/kg bw
Signs of Toxicity	No deaths were observed at 2.0 or 4.0 ml/kg; at 8 ml/kg 4/5 dead at day 1 post dosing, 1/5 dead at day 2; 5/5 rats dead at day 1 in groups given 16.0 or 32.0 ml/kg. No data presented on parameters other than mortality.
CONCLUSION	The test substance is of low toxicity via the oral route.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.1. (c) Acute toxicity – oral**

TEST SUBSTANCE	Pentene, 2,4,4-trimethyl-, sulfurized
METHOD	OECD TG 401 Acute Oral Toxicity.
Species/Strain	Rat/Albino rats of the outbred Sprague-Dawley strain
Vehicle	Mineral oil-based material
Remarks – Method	Route of administration - Oral gavage with a syringe and Nelaton catheter. The animals were fasted overnight before dosing.
	The sample was administered as supplied at a limit dose of 5.0 mg/kg. Following administration, the animals were allowed food and water for the 15-day observation period. The animals were observed three times on the day of dosing and twice on study day two and daily thereafter. Individual weights were recorded on the day of dosage and on the day of termination (day 15). The animals were euthanized by carbon dioxide at the conclusion of the observation period. Gross autopsies were performed on all animals that died during the observation period and on all survivors after day 15.
RESULTS	
LD50	5000 mg/kg bw
Signs of Toxicity	All animals survived to termination of the experiment (day 15). Decreased activity (3/5 females), diarrhea (1/5 males), salivation (1/5 males and 1/5 females) and apparent urinary incontinence (3/5 females) were noted following dose administration. All animals appeared normal on study days 5-15. Test material did not cause an adverse effect on mean body weight in either sex.
CONCLUSION	The test substance is of low toxicity via the oral route.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.



**7.1. (d) Acute toxicity – oral**

TEST SUBSTANCE	2-Propanol, 1-(tert-dodecylthio)-
METHOD	OECD TG 401 Acute Oral Toxicity.
Species/Strain	Rat/Sprague-Dawley
Vehicle	Mineral oil-based material dosed undiluted
Remarks – Method	The sample was administered by oral gavage with a syringe and dosing needle as supplied at a limit dose of 5.0 mg/kg. Following administration, the animals were allowed food and water for the 14-day observation period. The animals were observed frequently on the day of dosing and twice per day thereafter. Individual weights were recorded on the day of dosage, weekly thereafter and prior to sacrifice. The animals were euthanized by carbon dioxide at the conclusion of the observation period. Gross autopsies were performed on all animals that died during the observation period and on all survivors after 14 days.
RESULTS	
LD50	> 5000 mg/kg bw
Signs of Toxicity	The animals were ruffled after 3 hours. They appeared oily and dirty after 24 hours. One death occurred within 48 hours and the remaining animals exhibited a discharge around the eyes and nose. The remaining animals appeared to be recovered by 72 hours. They continued to appear normal throughout the remainder of the observation period.
Effects in Organs	Gross pathological examination reveals no remarkable findings.
CONCLUSION	The test substance is of low toxicity via the oral route.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.2. (a) Acute toxicity – dermal**

TEST SUBSTANCE	Alkenes, C15-18 alpha, sulfurized
METHOD	Not specified.
Species/Strain	Test Type: Acute dermal toxicity, single exposure New Zealand White Rabbit
Vehicle	None, test article was doses as received
Type of dressing	Semi-occlusive.
Remarks – Method	One dermal, semi-occluded patch of test article at 2,000 mg/kg was applied to clipped dorsal skin of each animal. The patches were removed after 24 hours. All animals were observed daily for 14 days following test article administration.
RESULTS	
LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	No clinical signs were observed during the study. Erythema and/or oedema of the skin at application site were observed on Day 1 in some animals. There was an increase in mean body weight during the study. None of the animals died during the study.
Effects in Organs	No visible lesions were observed in any animal at terminal necropsy.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust

## Summaries &amp; Test Plans: Alkyl Sulfide”.

**7.2. (b) Acute toxicity – dermal**

TEST SUBSTANCE	Pentene, 2,4,4-trimethyl-, sulfurized
METHOD	FHSA Regulations 16 CFR 1500.40
Species/Strain	Rabbits/New Zealand White
Vehicle	Mineral oil-based material dosed undiluted
Type of dressing	Occlusive
Remarks – Method	The sample was applied to unabraded shaved skin under impervious occlusion for 24 hours at a limit dose of 2.0 mg/kg. At the end of the 24-hour exposure period, the wrapping was removed any unabsorbed test material remaining on the skin was removed by gentle sponging using a paper towel moistened with mineral oil. The animals were observed for signs of toxicity or behavioral changes frequently on the day of treatment. Thereafter, all surviving rabbits were examined for outward signs of toxicity one per day, for the entire 14-day observation period. Individual weights were recorded on the day of dosage, weekly thereafter and prior to sacrifice. The surviving animals were euthanized at the conclusion of the observation period. Gross autopsies were performed on all animals after 14 days.
RESULTS	
LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	One rabbit died on day 14 of the study. No other deaths were observed during the 14-day observation period. In the male group, mild skin erythema and mild-to-moderate oedema were observed after unwrapping at 24 hours. Slight to mild skin irritation noted at 7 day was completely resolved by day 14. A loss of body weight was noted for 1/5 male animals at day 7. The same animal was found dead on day 14 after experiencing a bloated appearance. Signs of dehydration and no formed fecal material in the intestinal tract were noted for the one mortality. Other than the previous observation, all animals appeared normal throughout the 14-day observation period. In the females, skin reactions were typical of those observed with the male group. A loss of body weight was noted in one female at day 7.
Effects in Organs	Gross pathological examination of the female rabbits revealed no remarkable findings.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.2. (c) Acute toxicity – dermal**

TEST SUBSTANCE	2-Propanol, 1-(tert-dodecylthio)-
METHOD	FHSA Regulations 16 CFR 1500.40
Species/Strain	Rabbits/New Zealand White
Vehicle	Mineral oil-based material dosed undiluted
Type of dressing	Occlusive
Remarks – Method	The sample was applied to unabraded shaved skin under impervious occlusion for 24 hours at a limit dose of 2.0 mg/kg. At the end of the 24-hour exposure period, the wrapping was removed any unabsorbed test material remaining on the skin was removed by gentle sponging using a paper towel moistened with mineral oil. The animals were observed for signs of toxicity or behavioral changes frequently on the day of treatment. Thereafter, all surviving rabbits were examined for outward

signs of toxicity one per day, for the entire 14-day observation period. Individual weights were recorded on the day of dosage, weekly thereafter and prior to sacrifice. The surviving animals were euthanized at the conclusion of the observation period. Gross autopsies were performed on all animals after 14 days.

## RESULTS

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	No deaths were observed during the 14-day observation period. Nasal discharge and fecal staining was observed in 3 of 10 animals. In one animal, the test material cause blistering and blanching at the site of dermal application.
Effects in Organs	Gross pathological examination reveals no remarkable findings.

CONCLUSION The notified chemical is of low toxicity via the dermal route.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.3. (a) Acute toxicity – inhalation

TEST SUBSTANCE 1-Propene, 2-methyl-, sulfurized

METHOD OECD TG 403 Acute Inhalation Toxicity (Experimental; modified)

Species/Strain	Rat/Sprague-Dawley (10 animals per sex)
Vehicle	Not applicable
Method of Exposure	Whole-body exposure
Exposure Period	4 hours
Physical Form	vapour (from sample heated to 200°C)
Remarks – Method	Rats were exposed to 0.07 or 0.39 mg/L vapor for a single 4 hour whole body exposure. Sham control rats were placed in inhalation chambers in room air. One half of rats (5M, 5F) from each group were sacrificed 24 hour post exposure; others maintained for 2 weeks recovery. Vapors from the methyl propene derivative were generated in a counter current generator and delivered into the exposure chamber. Air samples were pulled through glass fiber filters to verify that particles were not present and animals were being exposed to pure vapor. Vapors were analyzed by GC to quantitate chamber concentrations using octane as a standard; qualitative analyses were performed by GC/MS. Animals were observed in the chambers and post exposure for clinical signs of toxicity. Body weights were taken and selected organs weighed at necropsy. Histopathology on liver, kidney lungs, nasal turbinates, tracheobronchial lymph nodes.

## RESULTS

LC50	> 0.39 mg/L/ 4 hours
Signs of Toxicity	No mortality and minimal toxicity was observed. Abnormal clinical signs occurring during and immediately post exposure included oral and ocular discharge, shallow respiration (some high dose rats only) and decreased response to stimuli. No abnormal treatment-related clinical signs were observed from 1 hour post exposure to the end of the recovery period

Effects in Organs	Group body weights were unaffected by exposure. Weights of liver, kidney and lungs were unaffected by exposure. No treatment related microscopic lesions were observed in the 5 organs examined.
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CONCLUSION The notified chemical is of low toxicity via inhalation.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.3. (b) Acute toxicity – inhalation

TEST SUBSTANCE	Pentene, 2,4,4-trimethyl-, sulfurized
METHOD	Consistent with EPA Health Effects Guideline OPPTS 870.1300
Species/Strain	Mouse/CD-1 Guinea pig/Hartley
Vehicle	Mineral oil-based material, dosed as supplied
Method of Exposure	Whole-body exposure (aerosol inhalation)
Exposure Period	hours
Physical Form	Solid aerosol (particulate).
Particle Size	1.6 $\mu\text{m}$ with a geometric standard deviation of 2.1 (estimated % of particles < 10 microns = 100%).
Remarks – Method	Two groups of five mice/sex and five guinea pigs/sex were exposed for 4 hours to the test material (nominal 5 mg/L) as a liquid droplet aerosol generated by a Laskin nebulizer apparatus delivered into a plexi-glass chamber. Also, control group of mice and guinea pigs was exposed to mineral oil in the same manner as the test-material-exposed group except that the test material was not administered. The details of the whole body exposure are consistent with those described in EPA Health Effects Guideline OPPTS 870.1300. The actual exposure concentration as measured by gravimetric analysis was 4.3 mg/L. Particle size analyses were performed once/hour from the test material chamber using a cascade impactor. Animal observations for toxicological signs and mortality were recorded every 15 minutes during the exposure, and twice daily for the 14-day observation period. Individual weights were recorded on the day prior to exposure and on days 2, 3, 5, 8 and 14. At the conclusion of the observation period, the surviving animals were euthanized by exsanguination under general anesthesia. All animals were subjected to gross necropsy (nasal passages, trachea, external surface, all orifices, the cranial cavity, the brain and spinal cord, and all viscera).
RESULTS	
LC50	LC50 (mice) > 4.3 mg/L/ 4 hours; LC50 (guinea pigs) > 4.3 mg/L/4 hours
Remarks – Results	The mass median aerodynamic diameter for the studies was 1.6 microns with a geometric standard deviation of 2.1 (estimated percent of particles < 10 microns = 100%). One female guinea pig was euthanized on study day 7 because of a broken leg, an effect thought to be unrelated to the administration to the test material. All other animals survived the duration of the study. Observations noted during the test material exposure included reduced activity and matted coat. Signs exhibited by the test animals upon removal from the chamber and during the two-hour post-exposure observation period on day 1 included matted coat, yellow fur, yellow ano-genital staining and nasal discharge. The control groups were generally unremarkable during the exposure and immediately thereafter. During week 1, the test mice exhibited few signs other than matted coat. The test guinea pigs exhibited matted coat and ano-genital staining. During week 2, ano-genital staining was the only remarkable sign in the guinea pigs. No significant difference was noted between the test and control group weights for either species. No gross lesions that could be attributable to the test material were observed in any of the mice or guinea pigs.
CONCLUSION	Ten of ten CD-1 mice and ten of ten Hartley guinea pigs received a single four-hour whole-body exposure to 4.3 mg/L test material as a respirable

aerosol. All animals survived the exposure and the 14-day post-exposure observation period with the exception of a single guinea pig that was euthanized for a broken limb. Signs of treatment included reduced activity and matted coat during the exposure. The treated animals were generally comparable to air-only control animals during the observation period. Body weight values and gross post mortem observations were generally unremarkable for differences between control and treated animals of either species.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.3. (c) Acute toxicity – inhalation

TEST SUBSTANCE	Pentene, 2,4,4-trimethyl-, sulfurized
METHOD	Consistent with EPA Health Effects Guideline OPPTS 870.1300
Species/Strain	Mouse /CD-1 Cobs Swiss Albino Rat /Sprague-Dawley CD Guinea pig/Hartley
Vehicle	Mineral oil-based material, dosed as supplied
Method of Exposure	Whole-body exposure
Exposure Period	4 hours
Physical Form	Solid aerosol (particulate).
Particle Size	Particle size distribution measurements showed an average mass median aerodynamic diameter of 3.8 microns with an average geometric standard deviation of 1.9 microns. Approximately 93 percent of the aerosol was 10 microns or less in size.
Remarks – Method	Group of five mice/sex, five rats/sex and five guinea pigs/sex were exposed for 4 hours to the test material as a liquid droplet aerosol generated by a Laskin nebulizer apparatus delivered into a plexi-glass chamber. Also, control groups of mice, rats and guinea pigs were exposed to mineral oil in the same manner as the test-material-exposed group except that the test material was not administered. The actual exposure concentration as measured by gravimetric analysis was 4.3 mg/L. Particle size analyses were performed once/hour from the test material chamber using a cascade impactor. Animal observations for toxicological signs and mortality were recorded every 15 minutes during the exposure, and twice daily for the 14-day observation period. Individual weights were recorded on the day prior to exposure and on days 2, 3, 5, 8 and 14. At the conclusion of the observation period, the surviving animals were euthanized by exsanguination under general anesthesia. All animals were subjected to gross necropsy (nasal passages, trachea, external surface, all orifices, the cranial cavity, the brain and spinal cord, and all viscera).
RESULTS	
LC50	LC50 (mice) > 4.3 mg/L/ 4 hours; LC50 (rat) < 4.3 mg/L/4 hours; LC50 (guinea pigs) > 4.3 mg/L/hours
Signs of Toxicity	Three female rats died within a day after exposure. A single male mouse and a single male guinea pig also died on test days 7 and 9, respectively. All other animals survived the duration of the study. Observations noted during exposure included nasal discharge, salivation, closed eyes and wet fur. Signs exhibited by the rats upon removal from the chamber and during the two-hour postexposure observation period on day included numerous secretory responses, labored breathing, rales and wet fur. Also, several of the females showed tremors. One of the female rats dies two hours after exposure. The mice and the guinea pigs were generally unremarkable except for contaminated fur. Two additional rats were found dead the morning after exposure. The surviving rats (both sexes) continued to show responses without a complete recovery during the 14-day postexposure

Effects in Organs	observation period, including nasal discharge, labored breathing, rales, and contaminated fur leading to alopecia. Body weight: Significant body weight losses were observed following exposure among all three species. The surviving mice and rats began to recover weight within a week after exposure. However, guinea pigs continued to lose weight throughout the first week and did not show a weight gain until the end of the second week.
	Gross post mortem observations: Discoloration of the lungs and nasal turbinates was noted among the spontaneously dying animals.
CONCLUSION	The test substance is of low toxicity via inhalation.
TEST FACILITY	Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.3. (d) Acute toxicity – inhalation

TEST SUBSTANCE	Pentene, 2,4,4,4-trimethyl-, sulfurized
METHOD	OECD TG 403 Acute Inhalation Toxicity.
Species/Strain	Rats/Sprague-Dawley
Vehicle	Mineral oil-based material dosed undiluted
Method of Exposure	Whole-body exposure
Exposure Period	4 hours
Physical Form	Solid aerosol (particulate).
Particle Size	The mass median aerodynamic diameter for the studies was 3.15 microns with a geometric standard deviation of 2.45 (estimated percent of particles < 12 microns = 90.5%).
Remarks – Method	Three groups of five rats/sex were exposed for 4 hours to the test material as a liquid droplet aerosol generated by a pressure spray apparatus delivered into a plexi-glass chamber. The actual exposure concentrations as measured by gravimetric analysis were 1.5, 2.5 and 5.6 mg/L. Particle size analyses were performed twice/hour using a multi-stage cascade impactor. Animal observations for toxicological signs and mortality were recorded periodically during the exposure, and twice daily for the 14-day observation period. Individual weights were recorded on the day prior to exposure and on days 4, 8 and 14. At the conclusion of the observation period, the surviving animals were euthanized using pentobarbital as an anesthetic followed by exsanguination. All animals were subjected to gross necropsy (external body surface and orifices, major visceral organs, body cavities and carcass).
RESULTS	
LC50	LC50 (males) > 5.0 mg/L/4 hours LC50 (females) = 2.17 mg/L/4 hours
Signs of Toxicity	Observations during the studies include alopecia (noted at all dose levels during second week of observation), ataxia (noted prior to the death of one female in the 5.6 mg/L group), dark material around eye (noted in two animal/sex at the 5.6 mg/l dose), decreased activity (noted in all animals at the dose level of 2.5 and 5.6 mg/L; reversible by study day 5), respiratory irregularity (increased respiration noted in all groups during and immediately following exposure; reversible by study day 7), tremors (noted in one female during and immediately following exposure to 2.5 mg/L). No male deaths were recorded for any of the dose levels. Group mean body weights were decreased at day 4 among males exposed to 2.5 and 5.6 mg/L. This effect was reversible by study observation day 8 and 14. Three of 5 females in the 1.5 mg/L group died on day 2 following exposure. Four of 5 female rats exposed to 2.5 mg/L died on observation day 2. Three females in the high dose group died on day 2 following exposure, with an addition death on day 6. Body weights decreased at day

Effects in Organs	4 in the surviving females, an effect that was reversible by days 8 and 14. No internal lesions or abnormalities were noted in any animal sacrificed at study termination. Pathological findings among females which died during the course of the observation period include brain (prominent vascularization, and blood in the cranial cavity), nasal passages (reddening of the nasal passage, with the notation of clear fluid in the nasal passage), lungs (reddening of the lungs, with the observation of a 'puffy' lung in one female) and trachea (clear fluid noted in the trachea of one female).
CONCLUSION	Following 4-hour whole-body exposure to a liquid droplet aerosol of the test material, the LC50 in male Sprague-Dawley rats is considered to be greater than 5.6 mg/L. The LC50 value in females was calculated to be 2.17 mg/L with upper and lower confidence limits of 3.69 and 0.64 mg/L.
TEST FACILITY	Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

#### 7.4. Irritation – skin

TEST SUBSTANCE 1-propene, 2-methyl-, sulfurized

Three studies were listed in the IUCLID data set for the above chemical. None were known to be done to GLP standards. The results of the studies were as follows:

1. Six rabbits (strain not stated) were treated with the test substance on abraded or non-abraded (3 rabbits each) skin for 24 hours. Observations were made at 24 and 72 hours and all readings were negative. The study was conducted by Lubrizol Great Britain Limited, Belper, Derby.
2. Six New Zealand White rabbits were treated with 0.5 mL of the test substance for 4 hours. The observation period was 48 hours. An OSHA score of 1.33 was noted as was a defatting effect. The study was conducted by Ethyl Petroleum Additives International Bracknell, Berkshire.
3. Two male and 1 female New Zealand White rabbits were treated with 0.5 mL of the test substance for 24 hours with an observation time of 7 days. Scores were 2.23 (OECD score, 0, 24, 48 and 72 hours) and 1.3 (OSHA score, 0 and 48 hours). A defatting effect was noted. The study was conducted by Ethyl Petroleum Additives International Bracknell, Berkshire.

Overall conclusion: slight irritant.

#### 7.5. Irritation – eye

TEST SUBSTANCE 1-propene, 2-methyl-, sulfurized

Three studies were listed in the IUCLID data set for the above chemical. None were known to be done to GLP standards. The results of the studies were as follows:

1. Six rabbits (strain not stated) were treated with the test substance and observed at 1, 2, 3, 4, and 7 days following treatment. All readings were negative. The study was conducted by Lubrizol Great Britain Limited, Belper, Derby.
2. Six New Zealand White rabbits treated with an observation period of 72 hours. Conjunctival redness and swelling were resolved by 72 hours. The study was conducted by Ethyl Petroleum Additives International Bracknell, Berkshire.
3. Two female and 1 male New Zealand White rabbits were treated with the test substance with an observation time of 7 days. By day 7 all effects had disappeared. The study was conducted by Ethyl Petroleum Additives International Bracknell, Berkshire.

Overall conclusion: slight irritant.

#### 7.6. Skin sensitisation

TEST SUBSTANCE 1-propene, 2-methyl-, sulfurized

METHOD	Maximisation test.
Species/Strain	Guinea pig/Dunkin Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: topical:
MAIN STUDY	
Number of Animals	Test Group: 6
induction phase	Control Group: None 0.3 mL of undiluted test substance were applied for 24 hour every other day for 10 application.
Signs of Irritation	Not stated.
CHALLENGE PHASE	
1 <sup>st</sup> challenge	After a 2-week rest period challenge was made using a 24-hour exposure.
Remarks – Results	The responses of the test animals at challenge were no more severe than their reactions to the induction doses.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test. However, this conclusion is not very robust given the non-rigorous nature of the test.
TEST FACILITY	Ethyl Petroleum Additives International Bracknell, Berkshire.

#### 7.7. (a) Repeat dose toxicity

TEST SUBSTANCE	1-Propane, 2-methyl-, sulfurized
METHOD	Not specified (Test Type: 21 Day Repeated Dose Dermal Toxicity Study)
Species/Strain	Rabbit/New Zealand White
Route of Administration	Dermal to shaved skin of backs and sides
Exposure Information	21 days
Vehicle	None: administered undiluted
Remarks – Method	Study was designed to evaluate local and systemic effects of test material when applied dermally. Methyl propene derivative was applied to the shaved backs and sides (approximately 10% of the body surface) of 3 groups of 10 N.Z. White rabbits 5 days per week for 3 weeks at dose levels of 140, 560 or 2240 mg/kg/day of undiluted test material on the same test schedule. The animals were fitted with plastic collars to inhibit ingestion of the test material, which was left uncovered on the skin and not removed prior to the next dose. One untreated shaved control group of 10 animals was included in the study. Assessments for local and systemic effects included twice daily (morning and afternoon) clinical observations, skin irritation scoring 5 days per week, weekly body weights, hematology, serum chemistry and urinalysis at pretest and termination, and gross necropsy evaluations at study termination.

#### RESULTS

##### *Mortality and Time to Death*

All rabbits survived the duration of the test.

##### *Clinical Observations*

Body weight changes were within expected ranges and comparable for all groups. Rabbits in all groups had lethargy, ptosis, G.I. disturbances, nasal and ocular discharges and respiratory distress, all more often in the second and third weeks with no discernible pattern of response. Skin responses included slight to moderate erythema and very slight to slight edema during Week 1 for all treated groups. During Week 2 responses in all treated groups were moderate to severe erythema with additional signs of cracked skin, bleeding and discoloration. Oedema was slight at the lowest dose and slight to moderate at the higher doses. During Week 3 all treated groups had severe erythema with cracked and bleeding skin, eschar and discoloration and oedema



was slight to moderate. No irritation was observed in the control group.

*Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

Urinalysis values were normal in all groups. Several individual and isolated haematological and serum chemistry values were out of expected range but with no discernible treatment related changes in the mean values for all groups.

*Effects in Organs*

At necropsy, sporadic occurrences of dark lungs and liver, red and bloated intestines, pale kidney or small or gray spleen were noted with no relationship to treatment. Epithelial hyperplasia of the treated skin was observed in all rabbits with the treated groups exhibiting slightly more severe grades of hyperplasia than the control group.

*Remarks – Results*

The rabbits were grouped by sex at the start of the study. At necropsy six errors in sexing were discovered which resulted in uneven sex distribution within the groups. Since there were no apparent effect differences between the sexes, the study is not considered to be compromised. With no discernable pattern of response in both test and control groups, observed clinical signs are considered to be related to handling. The occurrence of hyperplasia in all groups suggests a relationship to clipping rather to test material administration.

However, *in-life* dermal observations revealed severe erythema responses in all treated rabbits and none in the sham treated control group.

**CONCLUSION**

A NOAEL was not established in this study. The LOEL for clinical signs and systemic toxicity was 140 mg/kg/day dermal exposure for 3 weeks. No minimally irritating concentration was identified by this study.

**TEST FACILITY**

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.7. (b) Repeat dose toxicity**

**TEST SUBSTANCE**

1-Propene, 2-methyl-, sulfurized

**METHOD**

Federal Register, Volume 43, Number 163 – 28 Day Subchronic Dermal Toxicity Study

**Species/Strain**

Albino Rabbits

**Route of Administration**

Dermal to shaved dorsal trunk area of abraded or intact skin

**Exposure Information**

Total exposure days: 28days

**Vehicle**

None

**Remarks – Method**

Study was designed to evaluate the subchronic toxicity of the test material when applied dermally. Methyl propene derivative was applied to the shaved dorsal trunk area (approximately 10% of the body surface) of 2 groups of 12 albino rabbits (6M,6F) 5 days per week for 4 weeks at dose levels of 200 or 2000 mg/kg/day of undiluted test material on the same test schedule. Half the animals in each group were abraded once per week throughout the study. The abrasion penetrated the stratum corneum but did not cause bleeding. The treated skin was occluded for at least 6 hours daily and the trunk of each animal covered with an impervious material. One untreated shaved control group of 6 animals (3 intact, 3 abraded) was included in the study. Assessments for local and systemic effects were carried out

**RESULTS**

*Mortality and Time to Death*

One male rabbit death at the higher dose level. Body weight gains in control (0.5 to 1.0 kg) and lower dose group (0.2 to 1.0 kg). A trend of weight loss and food consumption among the high dose males in the latter half of the study. Weight gain in 5 of 6 high dose females.

### *Clinical Observations*

Treatment with the test material caused severe skin irritation at both doses. Abrasion of skin increased the degree of irritation at the low dose level. No irritation was observed in the control group.

### *Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

Urinalysis values were normal for all groups. The low dose group showed an increase in chloride and a decrease in albumin. The high dose group showed decreased alkaline phosphatase and an increase in chloride and globulin. Hematology showed no trends in the control and low dose groups while monocyte determinations were significantly different (increased) in the high dose group.

### *Effects in Organs*

Gross and histopathological examination of tissues did not reveal any pattern of changes attributable to dermal contact with the test material. At autopsy one animal in the control group was found to be female instead of male and one animal in the low dose group was found to be male instead of female. Statistical evaluation including and excluding these two animals showed no significant differences. The hematological and clinical chemistry data do not suggest a consistent trend indicative of a response to the test compound

### CONCLUSION

A NOAEL was not established in this study. A LOEL was not established in this study. No minimally irritating concentration was identified by this study.

TEST FACILITY Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

## 7.7. (c) Repeat dose toxicity

TEST SUBSTANCE	1-Propene, 2-methyl-, sulfurized
METHOD	Similar to OPPTS 870.3250 – Thirteen week dermal subchronic toxicity study
Species/Strain	Rat/Sprague Dawley (Tac:N[SD]fBR)
Route of Administration	Dermal – to shaved skin of backs
Exposure Information	Duration of exposure (dermal): 90 day;
Vehicle	Mineral oil base stock
Remarks – Method	Study was designed to identify inherent toxicity of test material and to determine whether dilution in a mineral oil carrier would alter toxicity. Methyl propene derivative was applied to the clipped backs of groups of 20 Sprague Dawley rats (10M,10F) 5 days per week for 13 weeks at dose levels of 500 or 2000 mg/kg/day undiluted or diluted in 100” mineral oil at dose levels of 500, 250,100, 50 or 10 mg/kg/day on the same schedule. Rats were fitted with Elizabeth collars to minimize ingestion of test material, which was left uncovered on the skin. One vehicle and 2 untreated shaved control groups were included in the study. Assessments for toxic response included daily clinical observations, weekly skin irritation scoring, weekly body weights and terminal organ weights, hematology, serum chemistry and urinalysis at weeks 5 and 13, gross necropsy evaluations , sperm morphology, and histopathology at study termination.

### RESULTS

#### *Mortality and Time to Death*

Male rats treated with methyl propene derivative for 13 weeks at dose levels 250 mg/kg/day gained less weight (15% less at study termination) than controls. Female weights were unaffected.

#### *Clinical Observations*

Undiluted test material and dilutions at 25% (500 mg/kg, 250 mg/kg in Part 2) induced moderate to strong reaction in the skin, characterized by erythema, oedema , increased thickness and stiffness; these effects were more severe in the 500 mg/kg (diluted 50% w/v). Microscopically, hyperkeratosis, hyperplasia of sebaceous

gland, increased mitosis in epidermis and dermal abscesses were observed. Virtually no irritation was observed in the vehicle control group or in dose groups of 100, 50, 10 mg/kg/day where dilutions were made at 10% or 5 %w/v.

#### *Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

At doses 250 mg/kg/day, both sexes had decreased levels of red blood cells and increased levels of neutrophils in circulation, increased spleen size and increased pigment and red pulp in the spleen. At doses 100 mg/kg/day, there was increased production of WBC in spleen and bone marrow.

#### *Effects in Organs*

Mean liver to body weights were increased in male rats at dose levels 250 mg/kg and in female rats at 500 mg/kg/day. Male rats treated with undiluted test material at 500 or 2000 mg/kg/day had increased kidney weights correlated with dose-related increase in hyaline droplet formation indicative of light hydrocarbon nephropathy.

The relative weight increases in livers of higher dose animals of both sexes had no microscopic correlate and is considered an adaptive response to treatment. The increase in kidney weight and hyaline droplet formation in male rats is indicative of light hydrocarbon nephropathy, a condition considered by EPA to be specific to male rats and not predictive of comparable toxicity in humans. Although many changes in hematology parameters can be associated with infections which can occur with severe skin irritation, increased dose related neutrophil production was observed in animals with minimal skin irritation and can be considered a direct effect of the test material.

No effects on sperm motility or morphology were observed in rats treated with 2000 mg/kg/day.

#### CONCLUSION

NOEL for systemic toxicity was 50 mg/kg/day dermal exposure for 13 weeks. The minimally irritating concentration of methyl propene derivative diluted in 100 mineral oil base stock is 10% (100, 50, 10 mg/kg/day).

#### TEST FACILITY

Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.7. (d) Repeat dose toxicity

#### TEST SUBSTANCE

Pentene, 2,4,4-trimethyl-, sulfurized

#### METHOD

OECD TG 410 Repeated Dose Dermal Toxicity: 21/28-day Study and OPPTS 870.3200

##### Species/Strain

Rat/Sprague-Dawley CD

##### Route of Administration

Dermal – semi-occluded

##### Exposure Information

Total exposure days: 28 days; Dosage 1000 mg/kg bw/day (limit study).

##### Vehicle

Mineral oil

##### Remarks – Method

Exposure period - 6 hours/day, after which the test material was removed with mineral oil.

Frequency of treatment - 5 days/week, 4 weeks (total of 20 applications). Control group and treatment 5 male rats received topical application of test material, 5 male rats served as controls by receiving topical application of mineral oil.

Statistical methods - Continuous data including body weight, body weight gain and food consumption was analyzed by analysis of variance.

#### RESULTS

##### *Mortality and Time to Death*

All animals survived throughout the study and physical examinations were generally unremarkable. No difference between the test material treated animals and control animals was noted for the parameters of body weight, body weight gain or food consumption.

*Clinical Observations*

These responses were characterized by erythema, eschar and flaking of the skin that persisted over the majority of the 28-day treatment period.

*Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

Not performed.

*Effects in Organs*

Detail gross pathological examination of external and internal features of the animals revealed no remarkable findings with the exception of weak moderate irritation responses at the site of test material application.

## CONCLUSION

No NOAEL was assigned to this study. All animals survived throughout the study and physical examinations were generally unremarkable.

TEST FACILITY Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.7. (e) Repeat dose toxicity**

TEST SUBSTANCE	Pentene, 2,4,4-trimethyl-, sulfurized
METHOD	OECD TG 412 Repeated Dose Inhalation Toxicity: 28-day or 14-day Study.
Species/Strain	Rat/Sprague-Dawley CD
Route of Administration	Inhalation – whole body
Exposure Information	6 hours/day, 5 days/week for 4 weeks at the target concentrations
Vehicle	
Physical Form	Solid aerosol (particulate).
Particle Size	The mass median aerodynamic diameter for the studies ranged from 1.9 to 2.6 microns with a geometric standard deviation ranging from 1.8 to 2.2. This data indicated that the aerosol was of a respirable size in the rat, with at least 96% of the particles 10 microns or less in diameter.
Remarks – Method	The rats were exposed on each treatment day for 6 hours to the test material (target concentrations = 15, 50, 150 mg/m <sup>3</sup> ) as a liquid droplet aerosol generated by an air atomizing nozzle apparatus delivered into a plexi-glass chamber. Control rats were exposed to in the same manner as the test-material-exposed group except that mineral oil only was administered. The actual exposure concentrations as measured by gravimetric analysis were 15, 50 and 160 mg/m <sup>3</sup> . Particle size analyses were performed once/week from the test material chamber using a cascade impactor. Animal observations for toxicological signs and mortality were recorded twice daily, once in the morning and once in the afternoon. Over the course of the study. Individual weights were recorded twice pre-test and then weekly during the exposure and recovery periods, and at termination. At the conclusion of the observation period, the surviving animals were euthanized with carbon dioxide. Animals were fasted prior to sacrifice. Five rats/sex were subjected to post-exposure blood analysis (routine hematology and clinical chemistry parameters) on test day 1 for the control and high dose groups, at termination on 5 rats/sex for all dose groups, and on 5 rats/sex from the control and high dose group after three weeks of recovery. Complete gross post mortem examinations were performed on all animals (nasal passages, trachea, external surface, all orifices, the cranial cavity, the brain and spinal cord, and all viscera). Nine major organs were weighed to obtain organ/body weight calculations, 42 individual organs and/or tissues were preserved, and 10 major organs and/or tissues were examined for histopathology.

## RESULTS

*Mortality and Time to Death*

One high-dose female had convulsive behavior following the third day of exposure, and was found dead the next morning. The cause of death was unclear. There were no other unscheduled deaths in the study.

*Clinical Observations*

Physical observations: The animals were unremarkable during the exposure period. Weekly detailed observations included an increased incidence of nasal discharge or dried red material on the facial area among the high-dose animals. However, these findings were not temporally consistent nor were they apparent in the lowest two doses of test material. No significant respiratory sounds were noted. Body weights: Although there were no significant differences seen between control and treated groups, there was a trend toward lower body weight gains during the exposure period of the study at all dose levels in the males and with the two highest dose levels in the females. During the three-week recovery period, the high dose animals did not regain the difference in body weight compared to the controls.

*Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

The only significant difference from control values was increased hemoglobin concentration in the high-dose females sacrificed after 4 weeks of exposure. Clinical chemistry: There were several statistically significant differences from the control values at both the postexposure and post-recovery time intervals. However, these differences did not correlate with dose, with sex, with potential target organs or with sacrifice interval.

*Effects in Organs*

Terminal organ and body weights: Following 4 weeks of exposure to test material, increases in kidney weights were seen in the males at all three dose levels, and were statistically significant in the higher two levels. This effect was considered to renal effects seen microscopically in males. This difference in weight abated following 3 weeks of recovery. Following 4 weeks of exposure, statistically significant increases were seen in high-dose liver weights and liver/body ratio in both sexes. These differences abated following 3 weeks of recovery. Spleen and adrenal weights increased compared to controls in the high dose groups of both sexes. Post-recovery increases in testis, heart, lung and spleen weights were recorded. These effects were not accompanied by pathologic microscopic findings, and therefore, the biological significance was considered equivocal. A few visible gross changes, such as discolored lungs, were noticed in the sacrificed animals. Microscopically, treatment-related effects were seen in the kidneys in the males in a dose-related profile. Findings included globular casts at the corticomedullary junction, the cortex and medulla, as well as hyaline droplets in the proximal convoluted tubule cells. These responses were seen in males in all treatment groups following 4 weeks of exposure, and in the high-dose group after 3 weeks of recovery. All other microscopic tissue alterations observed in other organs were considered incidental findings.

## CONCLUSION

No NOAEL was assigned to this study.

## TEST FACILITY

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.7. (f) Repeat dose toxicity**

## TEST SUBSTANCE

2-Propanol, 1-(tert-dodecylthio)-

## METHOD

OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.

## Species/Strain

Rat/Sprague-Dawley

## Route of Administration

Oral – gavage

## Exposure Information

Total exposure days: 28 days

## Vehicle

Corn oil

## Remarks – Method

Significant deviations from the OECD 407 test guidelines include:

- A function observational battery for neurotoxicity was not performed since this test was not part of the OECD 407 guideline at the time the study was performed.

## RESULTS

*Mortality and Time to Death*

All animals survived throughout the study and physical examinations were generally unremarkable.

*Clinical Observations*

Other minor effects of the test material consisted of a transient decrease in food consumption and body weight gain in the high-dose male group during the first week of study.

*Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

Evaluation of clinical chemistry and urinalysis studies revealed no evidence of renal or hepatic functional alterations, or any other signs of systemic effects due to the test material. A slight decrease in hemoglobin and hematocrit values was observed in the high-dose female group at termination that was found to be reversible during the 2-week recovery period.

*Effects in Organs*

Test material administration produced alterations in the liver and kidneys of treated animals that were evident in the evaluation of organ weights as well as gross and microscopic pathological examinations. Dose-related elevations in mean liver weights and/or liver/body weight ratios were seen at study termination in males at all dose levels and in females at the mid- and high-dose levels. Recovery was apparent during the two-week recovery period for the high-dose group. Gross post mortem examination of the liver revealed an accentuated lobular pattern in the mid- and high-dose females at termination of the dosing period, which resolved during the recovery period. Microscopic examination of liver revealed hepatocyte hypertrophy in all dose groups at the termination of treatment. This effect continued through the recovery period. The effect on the liver was consistent with the adaptive induction of hepatic metabolic mechanisms in response to a xenobiotic challenge. Kidney alterations were seen only in males. Kidney weights and kidney/body weight ratios for high-dose males were significantly higher than control values at termination of dosing. These values were comparable following termination of the recovery period. Gross post mortem examination of the kidneys revealed pale or tan discoloration of increasing frequency with increased dose. Microscopic alterations consisted of increased incidences of globular casts and hyaline droplets in treated males. Hyaline droplets in the proximal tubules were seen at termination of dosing only, indicating that this change in renal morphology was reversible after cessation of test substance administration. The renal effects are consistent with previous reports in the scientific literature of male rat-specific hydrocarbon nephropathy.

## CONCLUSION

No NOAEL was assigned to this study. Although renal and hepatic changes were evident at all dose levels (100, 300, and 1000 mg/kg/day), the renal changes are species-specific and the hepatic changes are probably adaptive in nature. Therefore, little subchronic toxicity was observed over the range of doses administered in this study.

## TEST FACILITY

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.8. (a) Genotoxicity – bacteria**

## TEST SUBSTANCE

Alkenes, C15-18 alpha, sulfurized (CAS. No. 67762-55-4)

## METHOD

Designed to be in compliance with microbial mutagenicity testing as set forth by OECD 1981, EPA 1982, FDA 1993

## Species/Strain

*S. typhimurium*:  
TA1535, TA1537, TA98, TA100, TA102.  
*E. coli*: WP2 uvrA

Metabolic Activation System  
Concentration Range in  
Main Test

Liver fraction (S9 mix) from rats pre-treated with Aroclor 1254  
Prescreen, duplicate cultures: 50.0, 167, 500, 1670, and 5000 µg/plate,  
plus control

Triplicate cultures: 50.0, 167, 500, 1670, 5000 and 10,000 µg/plate

## Vehicle

Not specified

## Remarks – Method

Test article was first evaluated in a prescreen using both liquid

preoccupation and plate incorporation treatment conditions. Duplicate cultures of strains TA1537, TA100, an dWP2 uvrA were treated with article at doses of 50.0, 167, 500, 1670, and 5000 micrograms/plate, as well as the solvent control, in the absence of S9. The test article was found to be incompletely soluble (droplets were observed) at all doses. The article was next evaluated using both treatment conditions. Based upon the results of the prescreen, the article was evaluated in triplicate cultures in strains TA1535, TA1537, TA98, TA100, TA102, and WP2 uvrA in the presence and absence of S9 at doses of 50.0, 167, 500, 1670, 5000 and 10,000 micrograms/plate. Six doses of the article were evaluated in the event of unacceptable toxicity and/or insolubility at the highest dose levels evaluated in the mutation assay. The S9 mixture included 6% (v/v) Aroclor 1254-induced male Sprague-Dawley rat liver homogenate with the appropriate bugger and cofactors. The test article was again found to be incompletely soluble at all doses, under both treatment conditions. All positive and negative controls were within acceptable ranges.

## RESULTS

### Remarks – Results

In the prescreen, results indicated that the article was not toxic. In the following study, normal growth was observed in all tester strains at all doses evaluated with and without S9. Revertant frequencies for all doses of article in all tester strains, with and without S9 under both treatment conditions approximated or were less than those observed in the concurrent negative control cultures.

## CONCLUSION

The test substance was not mutagenic to bacteria under the conditions of the test.

## TEST FACILITY

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

## 7.8. (b) Genotoxicity – bacteria

### TEST SUBSTANCE

1-Propene, 2-methyl-sulfurized

### METHOD

OECD TG 471 Bacterial Reverse Mutation Test.

#### Species/Strain

*S. typhimurium*:

TA1538, TA1535, TA1537, TA98, TA100.

#### Metabolic Activation System

Test conducted with and without metabolic activation.

Adult male Sprague-Dawley rat liver S-9 fraction, induced with Aroclor 1254.

#### Concentration Range in

a) With metabolic activation: 0 – 1.0 µl/plate.

#### Main Test

b) Without metabolic activation: 0 – 1.0 µl/plate.

#### Vehicle

DMSO

#### Remarks – Method

All stock and working solutions were stored at 4°C in glass screwcapped bottles; All sterility controls were negative for bacterial growth; Vehicle was tested as negative control;

Positive controls (9-aminoacridine and 2-nitrofluorene without activation and 9-aminoacridine, 2-nitrofluorene, aflatoxin, and 6- aminochrysene with activation) were at least 3 times the number of colonies as the control.

## RESULTS

### Remarks – Results

The test agent did not induce a significant increase in the number of point mutations in *Salmonella typhimurium* strains in the absence of the activating system for strains TA1535, TA100, TA1537, TA1538, and TA98. It also did not induce a significant increase in the number of point mutations with the addition of an exogenous source of liver enzymes for

metabolic activation in strains TA1535, TA100, TA1537, TA1538, and TA98.

CONCLUSION The test substance was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.8. (c) Genotoxicity – bacteria

TEST SUBSTANCE Pentene, 2,4,4-trimethyl-, sulfurized

METHOD OECD TG 471 Bacterial Reverse Mutation Test.  
 Species/Strain *S. typhimurium*:  
 TA1538, TA1535, TA1537, TA98, TA100.  
 Metabolic Activation System S9 microsomal fraction from Aroclor 1254-treated rats livers  
 Concentration Range in a) With metabolic activation: 0 - 1 µg/plate.  
 Main Test b) Without metabolic activation: 0 - 1 µg/plate.  
 Vehicle DMSO  
 Physical Form Gas/vapour.  
 Remarks – Method No significant deviations from guideline protocols.

### RESULTS

Remarks – Results The test material was tested without metabolic activation at 1, 0.3, 0.1, 0.03, and 0.01 microliters of test material/plate and found to be nonmutagenic to the bacterial strains tested. The number of revertant colonies as a result of treatment with the test material did not differ significantly from the number produced by the DMSO vehicle control. The test material was not toxic to any strain at any concentration. The positive controls, sodium azide, 2-nitrofluorene, and 9-aminoacridine at concentrations ranging from 2.5-100 microgram/plate produced more than a 10-fold greater incidence of his<sup>+</sup> revertants/plate with the bacterial strains used in this study. The test material was also tested in the presence of an S9 microsomal fraction from Aroclor 1254-treated rat livers. The concentrations tested (1, 0.3, 0.1, 0.03, and 0.01 microliters of test material/plate) in the activated system did not induce significant detectable mutagenic events with the bacterial strains used. The positive metabolic activated control, 2-anthramine (2.5 microgram/plate) produced positive mutagenic responses in the bacterial strains used in this study.

CONCLUSION The test substance was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

### 7.8. (d) Genotoxicity – bacteria

TEST SUBSTANCE 2-Propanol, 1-(tert-dodecylthio)-

METHOD OECD TG 471 Bacterial Reverse Mutation Test and OECD 472

Species/Strain *S. typhimurium*:  
 TA1535, TA1537, TA98, TA100  
*E. coli*: WP2.  
 Metabolic Activation System S9 microsomal fraction from Aroclor 1254-treated rat livers  
 Concentration Range in a) With metabolic activation: 0 - 5000 µg/plate.  
 Main Test b) Without metabolic activation: 0 - 5000 µg/plate.



Vehicle  
Physical Form  
Remarks – Method

Gas/vapour.  
No significant deviations from guideline protocols.

## RESULTS

Remarks – Results

The test material was tested without metabolic activation at 5000, 1500, 500, 150, 50 and 15 microgram/plate and found to be non- mutagenic to the bacterial strains tested. The test material was toxic to TA1537 at 5000, 1500, 500 and 150 microgram/plate. In the confirming assay, the test material was tested at the identical concentrations, and again, no mutagenic response was observed with any of the bacterial strains. The positive controls, sodium azide, 2-nitrofluorene, 9-aminoacridine, and ENNG at concentrations ranging from 1.0-80 microgram/plate, produced statistically significant positive responses in the bacterial strains used in this study. The test material was also tested in the presence of an S9 microsomal fraction from Aroclor 1254-treated rat livers. The concentrations tested (5000, 1500, 500, 150, 50 and 15 microgram/plate) in the activated system did not induce detectable mutagenic events with the bacterial strains used. The negative responses were reproduced in a second confirmatory assay. Incidentally, the S9 mix reduced the toxicity of the test material in the presence of TA1537. The positive metabolic activated control, 2- anthramine at concentrations ranging from 0.5-20 microgram/plate, produced statistically significant positive mutagenic responses in the bacterial strains used in this study

## CONCLUSION

The test substance was not mutagenic to bacteria under the conditions of the test.

## TEST FACILITY

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.9. Genotoxicity – in vitro**

## TEST SUBSTANCE

2-Propanol, 1-(tert-dodecylthio)-

## METHOD

Species/Strain  
Cell Type/Cell Line  
Metabolic Activation  
System  
Vehicle  
Physical Form  
Remarks – Method

Consistent with EPA guidelines outlined in OPPTS 870.5375  
Chinese Hamster  
Ovary (CHO) cells  
S9 fraction prepared from livers of Arochlor 1254-induced Sprague-Dawley  
DMSO  
Gas/vapour.  
No significant deviations from guideline protocols.  
Concentrations:  
Non-activated assay: 0, 0.05, 0.15, 0.5, 1.5, 5, 15, 50, 495, 1490, 4950 ug/ml  
Activated assay: 0, 0.05, 0.15, 0.5, 1.5, 15, 50 and 150 ug/ml

Remarks – Results

## CONCLUSION

The test substance was not clastogenic to Chinese hamster ovary (CHO) cells treated in vitro under the conditions of the test.

## TEST FACILITY

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.10. (a) Genotoxicity – in vivo**

TEST SUBSTANCE	Alkyl (C12-C16) sulphide (CAS. No. 91770-97-4)
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test and EPA OPPTS 870.5395
Species/Strain	Male Mice/B6C3F1
Route of Administration	Intraperitoneal
Vehicle	Corn oil
Remarks – Method	Doses and concentrations were: 0, 500, 1000, and 2000 mg/kg/day, plus negative control (vehicle = corn oil) and positive control (= cyclophosphamide). Exposure period: 3 consecutive days.  There was a range-finding phase of the study, which consisted of four groups of two male mice/group. Dose levels were 0, 500, 1000, and 2000.  Groups of five mice each were dosed intraperitoneally with 0, 500, 1000, and 2000 mg/kg/day for three consecutive days and then sacrificed one day after the last dose. The positive control was administered as a single oral dose approximately 24 hours prior to sacrifice.  Bone marrow cells were analyzed for the number of polychromatic erythrocytes (PCEs) which contained at least one micronucleus. A minimum of 2000 PCEs were analyzed from each animal from the vehicle control and from mice dosed with the test article. A minimum of 1000 PCEs was analyzed from each animal dosed with the positive control.
RESULTS	
Doses Producing Toxicity	There was a slight cytotoxic effect on developing erythrocytes at 2000 mg/kg/day, the maximum dose typically used in the mouse micronucleus phase.
Genotoxic Effects	The test article did not cause an increase in micronuclei in developing erythrocytes in bone marrow from male B6F3C1 mice at the doses tested
Remarks – Results	The test article, when dosed to mice at 500, 1000 and 2000 mg/kg/day for three consecutive days did not induce an increase in the number of micronuclei. There was an indication of slight bone marrow cytotoxicity at the highest dose in the micronucleus phase. The decrease was statistically different from the vehicle control. This decrease was due to the lower percentage of PCEs for two animals.  The responses obtained from the negative and positive control articles confirmed the reliability that the test system was capable of detecting compounds that induce micronuclei.
CONCLUSION	The test substance was not clastogenic in this in vivo mouse micronucleus test under the conditions of the test.
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

**7.10. (b) Genotoxicity – in vivo**

TEST SUBSTANCE	1-propene, 2-methyl-, sulfurized (CAS. No. 68511-50-2)
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
Species/Strain	Male and female, Mice/B6C3F1

Route of Administration	Intraperitoneal Injection
Vehicle	Hydroxypropyl methylcellulose (Methocel K4M Premium – Dow Chemical)
Remarks – Method	Young male and female mice were treated with a single intraperitoneal injection of 3.5 g/kg test material, 50 mg/kg cyclophosphamide in saline, or methylcellulose vehicle alone. Dose had been determined in a preliminary toxicity test to identified MTD for this study. Animals were sacrificed and femurs removed at 24, 48 or 72 hours post dosing (5M, 5F per interval) for test material and negative control, and at 24 hours postdosing only for cyclophosphamide. Bone marrow smears were prepared and immature red blood cells (polychromatic erythrocytes, PCEs) and mature red blood cells (normochromatic erythrocytes, NCEs) were evaluated for toxicity and the presence of micronuclei. Slides were stained with acridine orange and scored under a fluorescence microscope. Slides from all dose groups were sorted by a computerized random number system and the cytogeneticist was unaware of what dose group any individual slide was from. The ratio of PCE or NCE per the first 1000 erythrocytes counted was calculated to determine cytotoxicity if any.
<b>RESULTS</b>	
Remarks – Results	In the preliminary toxicity test (2M, 2F/group) all mice died at 5.0 g/kg and all survived at 3.5 g/kg with no cytotoxicity in bone marrow cells 24 hours after injection. Data from the full study demonstrate that the frequency of micronucleated PCEs in femoral bone marrow for males and females treated with the test material was not significantly elevated ( $p < 0.05$ ) when compared to negative controls for groups sampled at 24, 48 or 72 hours postinjection. Results from both sexes combined demonstrate the same results. Cyclophosphamide, the positive control material did induce statistically significant increases in micronucleated PCEs in all animals demonstrating that a valid study was performed.
<b>CONCLUSION</b>	The test substance was not clastogenic in this in vivo mammalian bone marrow erythrocyte micronucleus test under the conditions of the test.
<b>TEST FACILITY</b>	Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

#### 7.10. (c) Genotoxicity – in vivo

TEST SUBSTANCE	1-Propene, 2-methyl-, sulfurized
METHOD	Modified OPPTS 870.5395
Species/Strain	Rat/Sprague Dawley
Route of Administration	Dermal to shaved skin of backs
Vehicle	
Remarks – Method	Methyl propene derivative was applied to the clipped backs of groups of 20 Sprague Dawley rats (10M,10F) 5 days per week for 13 weeks at dose levels of 0, 500 or 2000 mg/kg/day undiluted or 500 mg/kg diluted (50% w/v) in 100” mineral oil base stock. Rats were fitted with Elizabeth collars to minimize ingestion of test material, which was left uncovered on the skin. At termination of the 13 week subchronic study, approximately 24 hours after the final dermal administration, bone marrow was harvested from femurs of the first 5 rats/sex/group necropsied. Three bone marrow slides were prepared for each animal. Slides were stained with acridine orange and scored under a fluorescence microscope. All slides were randomized by a computer generated random numbers table so that the cytogeneticist was unaware of what dose group any individual slide was from. Immature red blood cells (polychromatic erythrocytes, PCE) and mature red blood cells (normochromatic

erythrocytes, NCE) were evaluated for toxicity and the presence of micronuclei. The ratio of PCE to NCE per the first 1000 erythrocytes counted was calculated to determine cytotoxicity if any. At least 1000 PCE and 1000 NCE were scored for the presence of micronuclei.

#### RESULTS

Doses Producing Toxicity  
Genotoxic Effects  
Remarks – Results

Methyl propene derivative undiluted (500 or 2000 mg/kg/day) and methyl propene derivative (500 mg/kg/day) 50% w/v in 100” mineral oil base stock were not cytotoxic to red blood cell formation. These test materials did not induce any statistically significant increase in the formation of micronucleated PCEs or NCEs in bone marrow red blood cells of male or female rats exposed dermally for 13 weeks.

#### CONCLUSION

The test substance was not clastogenic in this in vivo mammalian bone marrow erythrocyte micronucleus test, adjunct to 13 week dermal subchronic toxicity study under the conditions of the test.

#### TEST FACILITY

Cited in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

### 7.10. (d) Genotoxicity – in vivo

#### TEST SUBSTANCE

Pentene, 2,4,4-trimethyl-sulfurized

#### METHOD

OECD TG 474 Mammalian Erythrocyte Micronucleus Test.

Species/Strain

Mouse/B6C3F1

Route of Administration

Oral – gavage

Vehicle

Physical Form

Gas/vapour/liquid aerosol/solid aerosol (particulate).

Particle Size

µm

Remarks – Method

Number of animals per dose: 5/sex/group

Control groups and treatment: 5/sex negative control (mineral oil); 5/sex positive control (cyclophosphamide, 50 mg/kg

Intraperitoneal injection). Mice were approximately 12 weeks old and 17-31 grams at study initiation. Animals were observed daily and body weights were recorded after 18, 24 and 48 hours. Test material and negative control groups were sacrificed after 18, 24 and 48 hours, whereas the positive control group was terminated after 24 hours.

#### RESULTS

Doses Producing Toxicity  
Genotoxic Effects  
Remarks – Results

The frequency of polychromatic erythrocytes (PCEs) with micronuclei ranged from 1.0 to 5.9/1000 PCEs in negative control mice with groups means of 2.6, 3.0 and 2.4 PCEs for the three time points. These averages and group means were within the expected range based on published data on the performing laboratory historical controls. In contrast, male animals dosed with cyclophosphamide had 9.0 to 24.0 micronucleated PCEs/1000 PCEs, with a mean of 14.5 for the group. The average frequencies of micronucleated PCEs obtained from male animals receiving the test material after the three time periods were 5.1, 3.0 and 5.7/1000 PCEs. These group means were not significantly higher than the negative control values. The mean PCE/normochromatic erythrocytes (NME) ratios in negative male group for the three time periods were 0.60, 0.60 and 0.69, respectively. The test material was not cytotoxic since the PCE/NME ratio at the three time points was 0.60, 0.59 and 0.66. The mean frequency of micronucleated PCEs/1000 PCEs for female mice was

1.9, 2.1 and 2.9, respectively. The average micronucleated PCEs value for the cyclophosphamide treated females was 20.5. Female mice treated with the test material were found to have mean micronucleated PCEs values of 1.1, 2.0 and 1.2 at the three time points, respectively. A comparison of the PCE/NME ratio between the negative control and test material treated female mice did not vary significantly.

**CONCLUSION**

The test substance was not clastogenic in this in vivo mammalian erythrocyte micronucleus test under the conditions of the test.

**TEST FACILITY**

Cited in "High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide".

SUMMARY OF INFORMATION FROM IUCLID DATA SET FOR TERT-DODECANETHIOL (CAS No. 25103-58-6) AND 1-PROPENE, 2-METHYL-, SULFURIZED (CAS No. 68511-50-2).

Summary as cited in "IUCLID Data Set for tert-Dodecanethiol (CAS. No. 25103-58-6)"

End point	Species	Result	Remarks
<i>Acute oral toxicity</i>	Rat	LD50 = 6800 mg/kg bw	
	Rat	LD50 ~ 15,000 mg/kg bw	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS-Nr. 93002-38-1)
	Rat	LD50 = 4380 mg/kg bw	other Test Substance: For the test material the structure of 1-Pentanethiol, 1,1,2,2,3,3,4-heptamethyl
	Rat	LD50 = 6800 mg/kg bw	Gross toxic signs consisted of moderate sedation, ataxia, mild tremors and diuresis. At necropsy, no gross pathological finding were noted.
	Rat	LD50 > 2150 mg/kg bw	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS-Nr. 93002-38-1)
	Rat	LD50 > 5000 mg/kg bw	other Test Substance: the test material is called tert. Dodecylmercaptane.
	Rabbit	= 860 mg/kg bw	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS-Nr. 93002-38-1).  Number of animals: 1; dose: 1 ccm/kg; examination of the liver function: no effect.
<i>Acute inhalation toxicity</i>	Rat	LC50 > 12 mg/L/4 hours	Gross toxic signs consisted of labored breathings, exophthalmus and signs of semi-consciousness. No deaths or other abnormalities were recorded.
	Rat	LC50 > 0.202 mg/L/4 hours	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No.: 93002-38-1)
	Rat	LC50 > 0.487 mg/L/6 hours	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No.: 93002-38-1)
	Mouse	Other: = 0.16 mg/L/6 hours	
	Mouse	LC50 > 0.202 mg/L/4 hours	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No.: 93002-38-1)
	Mouse	LC50 > 0.05 mg/L/8 hours	other Test Substance: the test material is called tert. Dodecylmercaptan
<i>Acute Dermal Toxicity</i>	Rabbit	LD50 = 12600	Gross toxic signs consisted of inactivity, loss of appetite and weakness. Local skin reactions at the applications side consisted of moderate erythema and discolorations. At negropsy, no gross pathological findings were noted.
<i>Skin Irritation</i>	Rabbit	Corrosive	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No.: 93002-38-1). 0.5 ml (on gauze) were applied into the ear and fixed for 1 or 2 hours (post exposure period = 7 d, 2 animals).
	Rabbit	-	Dose: 20 mg/24 h; effect moderate
	Rabbit	Method: Draize Test	Primary irritation index: 1.0

			Result: Slightly irritating Classification: Not irritating
	Human		other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No.: 93002-38-1).  After the dermal application (occlusive) of the substance on the lower arm of individuals for 4 h erythema and oedema were observed.
<i>Eye Irritation</i>	Rabbit	0.1 ml was applied into the conjunctival sac of 2 rabbits (observation time: 1, 24 and 48 h).	other Test Substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No.: 93002-38-1).  Slightly irritating.
	Rabbit	1-2- drops into the conjunctival sac	Effect: conjunctivitis in 2-4 days
	Rabbit	Dose: 500 mg/24h	effect: mild
	Rabbit	Method: Draize Test	Slight conjunctival irritancy was noted through 72 hours post-installation. No other abnormal findings were noted.  Result: Slightly irritating Classification: Not irritating
<i>Sensitisation</i>	Human	Allergic dermatitis is described in workers exposed to tert. dodecylmercaptan (no further information from the abstract).	
<i>Inhalation, Repeat dose toxicity, 28 days</i>	Rat (male/female) CD-1		LOAEL: 26 ppm  Rats exhibited dark red or black material around eyes and nose in both dose groups. Male rats showed a statistically significant decrease in body weight gain and a corresponding depression in food consumption at the high dose. High dose male rats showed a statistically significant increase in creatinine. Liver weights showed exposure related increase. Since no macroscopic or microscopic changes in rat livers were noted these weight increases cannot be clearly related to exposure. Male rats both levels exhibited mild renal tubular degeneration and granular cysts which were consistent with hydrocarbon necropathy.  High dose female rats exhibited hydronephrosis.
<i>Inhalation repeat dose toxicity, 28 days</i>	Mouse/CD-1 Male/female		LOAEL: 25 ppm  On day 23 of the study, 1 male and 1 female mouse at the high dose level died. No cause of death could be determined. Mice in the high dose group showed signs of alopecia and dried peeling in the high dose group. Mice exhibited statistically significant reductions in erythrocyte counts and hematocrit plus statistically significant

			elevation in MCH and MCHC after 4 weeks of exposure at high dose. High dose female mice showed a statistically significant elevation in alanine aminotransferase and blood urea nitrogen. High dose female mice exhibited depressed alkaline phosphatase values which were statistically significant. Low dose female mice showed a statistically significant elevation in blood glucose. Liver weights showed exposure related increases. Both sexes of mice showed liver enlargement, discolouration plus hepatocellular hypertrophy for the low dose and the high dose. High dose mouse ovary weights were statistically significantly depressed. Histopathologically the ovaries exhibited absent or few corpora lutea. High dose mice also exhibited dermal inflammation, acanthosis and hyperkeratosis.
<i>Inhalation repeat dose toxicity, 28 days</i>	Dog/Beagle Male/female		High dose female dog showed statistically significant increases in alanine aminotransferase and statistically significant reduction in blood urea nitrogen. Both sexes in dogs showed statistically significant increases in alkaline phosphatase. Liver weights showed exposure related increases. Dogs showed microscopic hepatocellular hypertrophy at the high dose for both sexes.
<i>Genotoxicity "in vitro"</i>	Ames Test <i>S. typhimurium</i> : TA 98, TA 100, TA 1535, TA 1537	Negative	Test substance: main component is 2,2,4,6,6-pentamethyl-4-heptanethiol (CAS No. 93002-38-1)
	Ames test <i>S. typhimurium</i> :	Negative	
	Ames test <i>S. typhimurium</i> : TA 98, TA 100, TA 1535, TA 1537, TA 1538	Negative	Test concentration: up to 10000 mug/plate. Metabolic activation: with and without
	Mouse lymphoma assay L5178Y	Negative	Test concentration: up to 75 mug/L Metabolic activation: with and without
	Sister chromatid exchange assay CHO	Negative	Test concentration: up to 100 mug/L Metabolic activation: with and without
<i>Developmental Toxicity/Teratogenicity: Inhalation</i>	Rat Female	NOAEL teratogen: = 88.6 ppm	Exposure period: 6 hours Frequency of treatment: 7 days a week Duration of test: 14 days
	Rat/CD-1 Female	NOAEL teratogen: = 88.6 ppm	Doses: 22.7 ppm; 88.6 ppm Frequency of treatment: 6 hours/day
	Mouse/CD-1 Female	NOAEL teratogen: = 88.6 ppm	Doses: 22.6 ppm; 88.6 ppm Frequency of treatment: 7 days a week Duration of test: 10 days



Toxicity Summary as cited in "TUCALID Data Set for 1-Propene, 2-methyl-, sulfurized (CAS No. 68511-50-2)"

End point	Species/Sex	Result	Remarks
<i>Acute oral toxicity</i>	Rat	LD50 = 5000-10,000mg/kg bw	The following dose levels were administered: 5 g/kg (6 rats), 10 g/kg (2 rats), and 20 g/kg (2 rats). There were no deaths at the 5 g/kg level. All animals at the 10 and 20 g/kg levels died.
	Rat/Wistar Male	LD50 = 8600 mg/kg bw	Observations were made over 14 days. Toxic signs included lethargy, ataxia, ptosis and piloerection at all dose levels. Isolated instances of diarrhoea, chromorhinorrhea, chromodacryorrhea, tachypnea, respiratory noise, emaciation, prostration, lethargy and hyperactivity seen at the lower dose levels became more common at higher dose levels.  Pathological findings included red exudate from nose and mouth, discolouration of intestines, stomach, lungs, kidney and spleen.
	Rat/Sprague-Dawley 5 per sex	LDLo > 1760 mg/kg bw	Observations were made over 14 days.  Toxic signs included reduced appetite and activity, increasing weakness, collapse and death.  Pathological findings included haemorrhagic lungs, liver discolouration and acute gastrointestinal inflammation.
<i>Acute inhalation toxicity</i>	Rat/Wistar male	LCLo > 2 mg/L	Exposure duration was 1 hour. Observations were made over 2 days.  There were no deaths.  Toxic signs included oily bodies and isolated instances of lethargy.  Pathological findings included mottled and dark kidneys.
	Rat 6 male	LCLo > 1.76 mg/L	Exposure duration was 6 hours. Observations were made over 14 days.  There were no deaths. No toxic signs or pathological observations were recorded.
	Rat 6 male	LCLo > 2 mg/L	Exposure duration was 6 hours. Observations were made over 14 days.  There were no deaths. No toxic signs or pathological observations were recorded.
	Rat 6 male	LCLo > 2.6 mg/L	Exposure duration was 6 hours. Observations were made over 10 days.  There were no deaths. No toxic signs or pathological observations were recorded.
<i>Acute dermal toxicity</i>	Rabbits/New Zealand White	LDLo > 2000 mg/kg bw	The dose used was 20 g/kg, with an exposure time of 24 hours.

			<p>None of the animals died.</p> <p>Toxic signs were isolated instances of bloodshot eyes, mucous in stools, lethargy, bloated abdomen and diarrhoea.</p>
	Rabbits/New Zealand White	LDLo = 3160 – 5010 mg/kg bw	<p>The doses used were 1.26, 2.00, 3.16, 5.01 and 7.95 g/kg, with an exposure time of 24 hours.</p> <p>The two test animals at the highest doses died.</p> <p>Toxic signs were reduced appetite and activity, increasing weakness, collapse and death.</p> <p>Pathology showed discolouration in the liver, enlarged gall bladder and gastrointestinal inflammation in the animals that died. Survivors killed at 14 days were normal.</p>
<i>Skin irritation</i>	Six Rabbit	Not irritating	<p>The skin of 3 animals was abraded; the skin of the remaining 3 animals was not. The duration of exposure was 24 hours. Animals were observed at 24 and 72 hours following dosing. All readings were negative. Material does not meet the Annex VI (R38) criteria for irritation.</p>
	Rabbits/ Six New Zealand White	Not irritating	<p>The dose used was 0.5 ml, with an exposure time of 4 hours. The observation period was 48 hours.</p> <p>Results: OSHA score (0 and 48 hours) = 1.33</p> <p>A defatting effect was noted.</p>
	Rabbits/ Six New Zealand White Two male and one female	Not irritating	<p>The dose used was 0.5 ml, with an exposure of 24 hours. The observation period was 7 days.</p> <p>Results: OECD score (0, 24, 48 and 72 hours) = 2.23 OSHA score (0 and 48 hours) = 1.3 A defatting effect was noted.</p>
<i>Eye irritation</i>	Rabbit Six animals	Not irritating	<p>The undiluted test article was administered. Animals were observed at 1, 2, 3, 4 and 7 days following treatment. Eyes were scored according to Draize scale. All readings were negative. Material does not meet the Annex VI (R36) criteria for irritation.</p>
	Rabbits/ Six New Zealand White	Not irritating	<p>The dose used was 0.1 ml, with an observation period of 72 hours.</p> <p>Conjunctival redness and swelling were scored. There were no observed effects on the cornea or iris.</p>

			After 72 hours all effects had disappeared.
	Rabbits/New Zealand White One male and 2 females	Not irritating	The dose used was 0.1 ml, with an observation period of 7 days.  By day 7 effects had disappeared.
<i>Sensitization – Guinea pig maximization test</i>	Guinea pig/Hartley Albino 3 per sex	Not sensitising	Two male and 2 female animals in the positive control group. There was no negative control group.  The dose was 0.3 ml of undiluted test material applied for 24 hours every other day for 10 applications. After a two week rest period, the challenge was made using a 24-hour exposure.  The responses of the test animals at challenge were no more severe than their reactions to the induction doses.
<i>Dermal Repeat Dose Toxicity, 21 days</i>	Rabbits/New Zealand White 5 per sex		Doses used: 0.14, 0.56 and 2.24 g/kg Frequency of treatment: 5 days per week for 3 weeks.  Dermal responses to all dose levels were severe erythema and slight to moderate oedema. Histomorphologically, skin responses could not be distinguished from controls. All other measured or observed parameters, including body weight, haematology, clinical chemistry, urinalysis and histopathology, were considered to be within the expected range for laboratory rabbits.
<i>Dermal Repeat Dose Toxicity, 28 days</i>	Rabbits/New Zealand White 3 per sex		Doses used: 0, 200 and 2000 mg/kg. Frequency of treatment: 6 hours per day, 5 days per week for 4 weeks. Doses were tested on both abrasions and intact sites. The test sites were wiped with corn oil between applications.  The test material caused severe skin irritation. The food consumption and body weights of the male rabbits in the high dose group were reduced. Examination of other data did not reveal any trends indicative of an adverse response to the test material. Clinical chemistry and haematology did not indicate a consistent trend indicative of a response to the material. Gross and histopathological examination of tissues did not reveal any pattern of changes attributable to dermal contact with the test material.
<i>Genotoxicity “in vitro” – Ames Test</i>	Ames Test S. typhimurium: TA 98, TA 100, TA 1535, TA 1537, TA 1538	Negative	Test concentration: 0.01, 0.05, 0.1. 0.5 and 1.0 µL/plate. Assays were performed on all samples with and without activation using Aroclor 1254-induced hamster liver S-9. Three replicates were carried out at each

			dose level. Positive controls were also evaluated.
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### 8.1. Environmental fate

No environmental fate data is available for the notified chemical. However, results for the analogues (2-Propanol, 1-(tert-dodecylthio)- and tert-docecaneethiol) with a 12 carbon chain rather than a 10 chain has been provided and is presented below.

#### 8.1.1. (A) Ready biodegradability

TEST SUBSTANCE	2-Propanol, 1-(tert-dodecylthio)-			
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.			
Inoculum	Return activated sludge from domestic waste water treatment plant			
Exposure Period	28 days			
Auxiliary Solvent	Sodium benzoate			
Analytical Monitoring	Oxygen uptake was measured using a BI-1000 electrolytic respirometer system.			
Remarks – Method				
RESULTS				
	TEST SUBSTANCE		Sodium benzoate	
	Day	% degradation	Day	% degradation
	1	0	1	30.5
	7	1.6	7	76.4
	28	5.9	28	88.8
Remarks – Results	The test substance showed a low biodegradation rate (5.9%) in 28 days. The reference substance, sodium benzoate, reached a level of 88.8% in the same test period.			
CONCLUSION	The notified chemical cannot be classed as ready biodegradable.			
TEST FACILITY	Cited in “High Production Volume (HPV) Challenge Program; Robust Summaries & Test Plans: Alkyl Sulfide.”			

#### 8.1.1. Ready biodegradability (B)

TEST SUBSTANCE	tert-docecaneethiol
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Predominantly domestic sewage
Exposure Period	20 days
Auxiliary Solvent	Not specified
Analytical Monitoring	Not specified
Remarks – Method	
RESULTS	
Remarks – Results	
CONCLUSION	0 ± % after 20 days
TEST FACILITY	IUCLID Data Set for tert – Dodecanethiol, 2000

#### 8.1.2. Bioaccumulation

CONCLUSION	No data is available. The high estimated log P <sub>ow</sub> values indicate a high potential for bioaccumulation.
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## 8.2. Ecotoxicological investigations

No ecotoxicity data is available for the notified chemical. However, data for an unacceptable analogue (3 chain) were provided. The water solubility and ecotoxicity data for the proposed analogue differs with the modelling undertaken by DEH based on the chemical structure of the notified chemical. This modelling indicates a greater toxicity than the notifier has suggested. Therefore, the findings of the modelling are presented below but data for the unacceptable analogue are not included.

Data for a second acceptable analogue (tert-docecaneethiol) from IUCLID was also provided. However, it should be noted that in IUCLID the reliability of these reports has not been classified and they have not been sighted by DEH.

End point	Species	Result	Remarks
Acute toxicity to fish (96 hours) -Static	<i>Brachydanio rerio</i> (Fish, freshwater)	LC0 = $\geq$ 10000	
Acute toxicity to fish – (48 hours) -Static	<i>Leuciscus idus</i> (Fish, freshwater)	LC0 = 50 mg/L LC100 = 100 mg/L	
Static	<i>Salmo salar</i> (Fish, freshwater, marine)	LC50 = 0.9 mg/L	
Acute toxicity to aquatic invertebrates	<i>Daphnia magna</i> (crustacean)	EC0 = 1.4 mg/L EC50 = 3.9 mg/L EC100 = 11 mg/L	24 hour exposure period
	<i>Daphnia magna</i> (crustacean)	EC50 = 1.4-24 mg/L	24 hour exposure period
Toxicity to aquatic plants	<i>Scenedesmus subspicatus</i> (Algae)	EC50 = 81 mg/L	72 hour exposure No analytical monitoring
	<i>Scenedesmus subspicatus</i> (Algae)	EC10 = 52 mg/L EC50 > 100 mg/L	72 hour exposure period
Toxicity to microorganisms	<i>Pseudomonas fluorescens</i> (bacteria)	EC50 = 10000 mg/L	24 hours exposure period

### 8.2.1. Acute toxicity to fish

TEST SUBSTANCE                      Thiol (10 chain)

METHOD                              ECOSAR v0.99  
Exposure Period                      96 hours

RESULTS  
LC50                                      0.085 mg/L at 96 hours.  
Remarks – Results                      The calculated water solubility was 0.5093 mg/L.

CONCLUSION                              This modelled result indicates that the chemical may be highly toxic to fish.

### 8.2.1. Acute toxicity to aquatic invertebrates (Daphnia)

TEST SUBSTANCE                      Thiol (10 chain)

METHOD                              ECOSAR v0.99  
Exposure Period                      48 hours

RESULTS

LC50

0.035 mg/L at 48 hours.

Remarks – Results

The calculated water solubility was 0.5093 mg/L.

CONCLUSION

This modelled result indicates that the chemical may be highly toxic to daphnia.

## 9. RISK ASSESSMENT

### 9.1. Environment

#### 9.1.1. Environment – exposure assessment

Up to 60 kg of the notified polymer yearly will be released to the environment due to spills during transport, storage and use and up to 30 kg due to residues in empty containers. All this material will be disposed of via licensed waste contractors to landfill.

The ECOSAR modelling done by the Department of the Environment and Heritage (DEH) using the thiols class indicates that the notified chemical will have an estimated water solubility of 0.5093 mg/L (i.e. low water solubility) and an estimated log  $K_{ow}$  of 5.12 (i.e. low mobility in soil/sediments). Therefore in landfill the notified chemical will be immobile.

The notified chemical is not expected to be readily biodegradable. However, in landfill it will gradually degrade by abiotic and biotic processes to water and oxides of carbon and sulphur.

Due to the way the notified polymer is used the majority will be destroyed during use, whereby releasing water and oxides of carbon and sulphur.

A Predicted Environmental Concentration (PEC) calculation is not possible.

#### 9.1.2. Environment – effects assessment

Ecotoxicity data for an unacceptable analogue and one acceptable analogue were provided. The data for the tert-dodecanethiol indicates some toxicity to daphnia and algae. The results of the ECOSAR modelling undertaken by DEH indicated high toxicity to fish ( $LC_{50}$  = 0.085 mg/L) and daphnia ( $LC_{50}$  = 0.035 mg/L).

A valid PNEC could not be estimated.

#### 9.1.3. Environment – risk characterisation

The aquatic risk quotient ( $RQ = PEC/PNEC$ ) cannot be determined. However, the notified chemical is not expected to be released to the aquatic compartment. Therefore the proposed use does not represent a risk to the aquatic environment.

Overall, the environmental risk from the proposed use of the notified polymer is expected to be low. However, due to the uncertainty of toxic effects to fish and other aquatic organisms the notified polymer should be prevented from entering waterways.

### 9.2. Human health

#### 9.2.1. Occupational health and safety – exposure assessment

Exposure to workers is primarily limited by the fact that the notified chemical is to be imported at < 5%. Furthermore, once the drums are connected to the glass manufacturing equipment, the process is automated and exposure is unlikely. Therefore, the most likely site of exposure is drips and spills setting up transfer of the imported formulation to the glass manufacturing equipment and cleaning and maintenance of pumps and lines. Control of exposure at these points is said by the notifier to be controlled by the use of personal protective equipment (PPE). Some limited exposure of laboratory staff is also controlled by the use of PPE.

#### 9.2.2. Public health – exposure assessment

Exposure of the public as a result of manufacture, transport and disposal of glass products made using the notified chemical is negligible. The public may make dermal contact with finished glass product. However, public exposure to the notified chemical is unlikely since it is expected that the notified chemical is destroyed by the high temperatures in the glass manufacturing process and hence no residue is present in the final product. Exposure in the event of the transport accident is limited by the low concentration (< 5%) of the notified chemical in the imported formulation.



### 9.2.3. Human health – effects assessment

A range of analogues in the alkyl sulfide category have been studied for a range of toxicological endpoints. From these data it can be reasonably predicted from animal studies that the notified chemical is likely to be of low acute toxicity via oral, dermal and inhalation routes. It can also be reasonably predicted from a range of genotoxicity studies that the notified chemical is not genotoxic.

The data on irritation and skin sensitisation do not suggest the notified chemical is irritant or sensitising although the detail of the studies is lacking.

There were a number of studies on analogues for repeat dose toxicity described in “High Production Volume (HPV) Challenge Program – Robust Summaries & Test Plans: Alkyl Sulfide”.

For 1-propene, 2-methyl-, sulfurized, no significant systemic effects were seen in a 21-day dermal repeat dose study in New Zealand White rabbits up to 2240 mg/kg bw/day. A Low Effect Level (LOEL) of 140 mg/kg bw/day was given. In a similar 28-day study no NOAEL was established up to 2000 mg/kg bw/day. A 90-day repeat dose dermal study in rats up to 2000 mg/kg bw/day found effects that were adaptive or male rat-specific.

For pentene, 2,4,4-trimethyl-, sulfurized, a 28-day repeat dose dermal toxicity study in rats at 1000 mg/kg bw/day produced no notable systemic effects. In a repeat dose inhalation study in rats doses up to 150 mg/m<sup>3</sup> administered as an aerosol for 28 days only produced species-specific effects in the kidneys of male rats.

For 2-propanol, 1-(tert-dodecylthio)- an oral repeat dose toxicity study in rats up to 1000 mg/kg bw/day showed only adaptive effects in the liver and species specific effects in the kidneys of male rats.

The results described above for 1-propene, 2-methyl-, sulfurized were also summarised in a IUCLID data set (see above table).

A IUCLID data set is also available for tert-dodecanethiol although it appears that data for other related chemicals have been included as indicated in the above table. Tert-dodecanethiol appears to be of low acute toxicity via the oral, dermal and inhalation routes in rats. It was a slight skin irritant in rabbits and a slight eye irritant in rabbits. There was one report of a negative Buehler skin sensitisation test in Guinea pigs and a report of sensitisation with no details. In a 28-day repeat dose study a LOAEL of 26 ppm was noted with male rats exhibiting mild renal effects and high dose (98 ppm) females exhibiting hydronephrosis. In mice a 28-day inhalation study was conducted. The LOAEL was 25 ppm, adaptive effects were seen in the livers and at the high dose (109 ppm) there were effects on the ovaries. In Beagle dogs a 28-day inhalation study showed liver effects with possible adaptive effects. In a developmental toxicity study the NOAEL for teratogenesis was 88.6 ppm for inhalation given from gestation days 6 to 16. A range of genotoxicity tests were negative.

In the IUCLID data set there is also data for other related compounds which also exhibit low acute oral toxicity in rats (2,2,4,6,6-pentamethyl-4-heptanethiol (CAS-Nr. 93002-38-1), 1-pentanethiol, 1,1,2,2,3,3,4-heptamethyl), and tert-dodecylmercaptane). 2,2,4,6,6-pentamethyl-4-heptanethiol was skin corrosive in rabbits and irritant in humans but was a slight eye irritant in rabbits. Tert-dodecylmercaptan was shown to cause allergic dermatitis in workers. 2,2,4,6,6-pentamethyl-4-heptanethiol was negative in an Ames test for bacterial mutagenesis.

Based on the available data, the notified chemical is **not classified** as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004).

### 9.2.4. Occupational health and safety – risk characterisation

From studies on a range of analogues, it appears that the notified chemical is not likely to be acutely toxic or genotoxic. Although the US EPA does not regard the alkyl sulfides as a category on the basis of repeat dose toxicity data, significant systemic effects were not observed in a

number of studies. The data on irritation and sensitisation are weak. Slight irritation seems most likely. The skin sensitisation studies revealed negative and positive results, the positive result with tert-dodecylmercaptan.

The likelihood of significant worker exposure is expected to be low and this, combined with the predicted toxicological profile of the notified chemical suggests a low risk to workers. In the event that the notified chemical was sensitising, the fact that there is limited opportunity for repeated exposure suggests a low probability of workers developing allergic conditions.

#### 9.2.5. Public health – risk characterisation

The low concentration of notified chemical to be imported together with the limited opportunity for exposure suggests a low risk of health effects to the public.

## 10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

### 10.1. Hazard classification

Based on the available data the notified chemical is not classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

As a comparison only, the classification of notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes. Noting that the environmental fate and ecotoxicity data provided are for analogues or have been estimated, the notified chemical could not be given an environmental classification.

### 10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

### 10.3. Human health risk assessment

#### 10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

#### 10.3.2. Public health

There is Negligible Concern to public health when used as described.

## 11. MATERIAL SAFETY DATA SHEET

### 11.1. Material Safety Data Sheet

The MSDS of products containing the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003). It is (They are) published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

### 11.2. Label

The label for products containing the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994). The accuracy of the information on the label remains the responsibility of the applicant.

## 12. RECOMMENDATIONS

## CONTROL MEASURES

## Occupational Health and Safety

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced, as:
  - protective coveralls, safety glasses, impervious gloves and safety boots.

Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the MSDS should be easily accessible to employees.
- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

## Environment

- The following control measures should be implemented by reformulator to minimise environmental exposure during formulation of the cleaning products:
  - All storage and process areas should be bunded with only process drains going to a onsite collection point or treatment plant.

## Disposal

- The notified chemical should be disposed of by licensed waste contractors or secure landfill or preferably incineration, where possible, in line with State and Territory Authorities.

## Emergency procedures

- Spills/release of the notified chemical should be handled by containment, collected with appropriate absorbent material (eg vermiculite) then placed in labelled containers ready for disposal.

**12.1. Secondary notification**

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

- (1) Under Section 64(1) of the Act; if
  - The concentration of the notified chemical in the imported product is likely to exceed 6%
  - use of the chemical changes in such a manner as to significantly increase discharge of the notified chemical to the aquatic environment, the hazard should be reassessed and full results and reports on the physico-chemical properties and aquatic toxicity of the notified chemical may be required in order to conduct a more comprehensive environmental assessment.

or

- (2) Under Section 64(2) of the Act:
  - if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

**13. BIBLIOGRAPHY**

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