

201-15901B

Substance Group: Group 1 – Alkyl Sulfides

Summary Prepared by: Petroleum Additives Panel
Health, Environmental and
Regulatory Task Group

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1.0 Physicochemical Properties

Robust Summary 1-Physchem-1 (Melting & Boiling Point)

CAS #	Value	Method *	Year	Remarks
67762-55-4	186.9 °C melting point	calculated by MPBPWIN (v1.31)	1999	y=2.5, x=1: melting point = 186.92 °C y=2.5, x=2: melting point = 213.83 °C
67762-55-4	> 300 °C boiling point	calculated by MPBPWIN (v1.31)	1999	y=2.5, x=1: boiling point = 504.54 °C y=2.5, x=2: boiling point = 537.80 °C
68511-50-2	147.5 °C melting point	calculated by MPBPWIN (v1.31)	1999	y=3: melting point = 147.52 °C y=8: melting point = 329.32 °C
68511-50-2	> 300 °C boiling point	calculated by MPBPWIN (v1.31)	1999	y=3: boiling point = 409.48 °C y=8: boiling point = 749.88 °C
68515-88-8	128.1 °C melting point	calculated by MPBPWIN (v1.31)	1999	y=1: melting point = 128.08 °C y=4: melting point = 186.87 °C
68515-88-8	> 300 °C boiling point	calculated by MPBPWIN (v1.31)	1999	y=1: boiling point = 377.79 °C y=4: boiling point = 477.56 °C
67124-09-8	68.15 °C melting point	calculated by MPBPWIN (v1.31)	1999	
67124-09-8	302.85 °C boiling point	calculated by MPBPWIN (v1.31)	1999	

This robust summary was prepared from modeled data by an HERTG member company representative. Reliability: (2) valid with restrictions

* Reference: Meylan W. and Howard P. 1999. EPIWin Modeling Program, Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510

Robust Summary 1-Physchem-2 (Water Solubility)

Test Substance*:	1-propene, 2-methyl-, sulfurized
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	2004
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: •Note: Concentration prep., vessel type, replication, test conditions.	Water Solubility calculated by WSKOWWIN subroutine, which is based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". Environ. Toxicol. Chem. 15:100-106. 1995.
Results: Units/Value: •Note: Deviations from protocol or guideline, analytical method.	Calculated Substance Component WS (mg/L) @ 25o C 68511-50-2 Molecular weight of 234 g (trimer) 1.29 Molecular weight of 406 g (pentamer) 3.94 x 10-4 Molecular weight of 498 g (hexamer) 6.32 x 10-6 The three molecular weights shown above represent the most common oligomers as stated by the manufacturer. The molecular weight of CAS # 68511-50-2 ranges from 160 – 1600 g with an approximate mean of 480 g. The oligmers in the molecular weight range of 160 – 560 g predominate. Distribution of the higher molecular weights is uniform with a steady decline to a molecular weight of approximately 1600 g. Additionally, the oligomers shown above possess only one sulfur between isobutylene moieties. Therefore, especially for the trimer, the modeled water solubility values shown above likely represent conservative estimates of each oligomer’s solubility.

Test Substance:	<ul style="list-style-type: none"> • CAS# 68511-50-2; 1-propene, 2-methyl-, sulfurized Commercial alkylsulfides are manufactured by reacting olefins (linear or branched) with sulfur in a controlled exothermic reaction and then sparged with nitrogen to remove hydrogen sulfide. More information on the Alkyl sulfide Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1). 1. Health, Environmental, Regulatory, Task Group (HERTG). 2000. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Alkyl sulfide Category. American Chemistry Council, Petroleum Additives Panel, HERTG.
Conclusion:	<p>Modeling data indicate that the water solubility range of CAS # 68511-50-2 is likely range from 1.39 to 6.32 x 10⁻⁶ mg/L at 25 °C. Because of the low solubility of the common 406 and 498 g derivatives, CAS # 68511-50-2 is likely to be very water insoluble. The expected water insolubility is supported by the lack of observed fish, daphnia, or algae toxicity at saturation (see American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for category 1) and also CAS # 50-2 is designed to be a hydrophobic surface acting agent (See corresponding IUCLID datasheet).</p>
Reliability:	<p>(2) Reliable with restrictions The results include calculated values based on chemical structure and represent a potential water solubility values for three molecular weight derivative of CAS # 68511-50-2.</p>
Reference:	<p>Water solubility values calculated by WSKOWWIN subroutine, which is contained in the computer program: EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.</p>
Other (source):	<p>American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group</p>

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

2.0 Environmental Fate

Category: Alkyl Sulfides

2.1 Biodegradation

Robust Summary 1-Biodeg-1

<i>Test Substance</i>	
CAS #	67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	<p>This substance is also referred to as propanol/dodecylthio derivative in HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
Method	
Method/Guideline followed	OECD 301F
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Yes
Year (Study Performed)	1998
Contact time (units)	28 days.
Inoculum	Return activated sludge from domestic waste water treatment plant.

Remarks for test conditions	<p>Inoculum: The sludge was aerated and stirred for 2-3 hours, homogenized for 2 minutes and allowed to stand for one-half to one hour. The supernatant was pipetted out and used for pre-adaptation. The inoculum was pre-adapted to the test material for 14 days during which the test substance was added incrementally at concentrations equivalent to 4, 8 and 8 mg carbon/L on days 0, 7, and 12, respectively. The targeted microbial level in the test mixture was 10,000 to 1,000,000 cells/mL.</p> <p>Conc of test chemical: Test substance concentration was approximately 100 mg/L mineral medium, giving at least 50 to 100 mg ThOD per L medium. No organic solvents were used to facilitate the dispersion of the test material. The test substance was weighed onto a teflon coupon and introduced into the medium.</p> <p>Temp of incubation: $23 \pm 1^\circ\text{C}$.</p> <p>Dosing procedure: A measured volume of the inoculated mineral medium containing approximately 100 mg/L test substance is continuously stirred in a closed system for 28 days.</p> <p>Sampling: The oxygen uptake were monitored continuously and recorded every 4 hours throughout the test.</p> <p>Controls: Yes, except abiotic and toxicity checks were not included.</p> <p>Analytical method: Oxygen uptake was measured using a BI-1000 electrolytic respirometer system.</p> <p>Method of calculating measured concentrations: Not applicable.</p> <p>Other: The inoculum was pre-adapted to the test substance for 14 days.</p>
Results	
Degradation % after time	5.9% after 28 days.
Kinetic (for sample, positive and negative controls)	% biodegradation (days) Reference (sodium benzoate) – 30.5% (1d), 76.4% (7d), 88.8% (28d). Test substance – 0% (1d), 1.6% (7d), 5.9% (28d).
Breakdown Products (Y/N) If yes describe breakdown products	Not monitored.
Conclusions	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.
Data Quality	Reliable without restrictions
References	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
Other	Updated: 12/27/99

Robust Summary 1-Biodeg-2

<i>Test Substance</i>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	<p>This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
Method	
Method/Guideline followed	OECD 301B, Ready Biodegradability, Modified Sturm Test
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1996
Contact time (units)	28 days
Inoculum	Domestic sewage sludge plus soil

Remarks for test conditions	<p>Inoculum: Sludge from domestic WWTP used at 30 mg dry solids/L; soil from forest area used at 0.1 g/L</p> <p>Conc of test chemical: Test chemical added directly to test vessels at 13.3 mg C/L (28.6 mg/L CAS# 68511-50-2). No preacclimation was used.</p> <p>Temp of incubation: 23 – 24 °C</p> <p>Dosing procedure: Neat test chemical added by micropipettor to culture medium in vessels immediately prior to addition of sewage and soil inocula</p> <p>Sampling: Days 1, 3, 6, 10, 14, 21, 29 (after acidification on d 28)</p> <p>Controls: Yes (blank and positive controls used per guideline); toxicity control not used. Positive Control was Benzoic acid (Na salt) at 20 mg C/L</p> <p>Analytical method: Titration of residual Ba(OH)₂ in trapping solution, using HCl</p> <p>Method of calculating measured concentrations: N/A; CO₂ evolution and % biodegradation were calculated using the average of duplicate blank-corrected titration volumes at each titration interval</p> <p>Other:</p> <ul style="list-style-type: none"> The % biodegradation value reported is slightly inflated by the use of zero titration volume rather than negative volume when corrected for blanks; however, comparison of titration volumes for the test chemical and blank show them to be very similar, so inhibition of inoculum is not suspected.
Results	Not Readily Biodegradable
Degradation % after time	0.3% in 28 days
Kinetic (for sample, positive and negative controls)	t _{1/2} for Positive Control was <10 d
Breakdown Products (Y/N) If yes describe breakdown products	N
Conclusions	Not Readily Biodegradable; biodegradation was essentially zero
Data Quality	Reliable without restrictions
References	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
Other	Updated: 12/29/99

2.2 Application of Environmental Fate Modeling to HERTG HPV Group 1 - Alkyl Sulfides Category

This section provides a short evaluation of the EQC computer model, which was used to assess the fate and distribution, and hence environmental concentrations, of selected members of the HERTG Group 1, alkyl sulfides.

The US EPA has agreed that computer modeling techniques are an appropriate approach to estimating chemical partitioning and distribution in the environment. Specifically, fugacity based, multimedia fate modeling can be applied to compare the relative distribution of chemicals between environmental compartments (i.e., air, soil, water, suspended sediment, sediment, biota). A widely used model for this approach is the EQC model (1). EPA cites the use of this model for this purpose in its document titled Determining the Adequacy of Existing Data, prepared for the HPVC program.

There are three "levels" of the EQC model. In its document, EPA states that it accepts Level I fugacity modeling to estimate transport/distribution values. In the same document EPA states that Level III model data are considered "more realistic and useful for estimating a chemical's fate in the environment on a regional basis". However, the selection and application of any one of the three models should not be done without considering their appropriateness for use with chemical(s) of interest. This includes a basic understanding of selected physical/chemical properties of the chemicals to be modeled, as well as the model.

The EQC Level I model utilizes input of the basic chemical properties of molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. The EQC Level II model also calculates the rates of transport (advection) and degradation within the environmental compartments. Application of the level II model requires data on the rates of biodegradation, hydrolysis, photolysis, and oxidation. EQC Levels I and II were used for this evaluation. EQC Level III evaluates the effects of discharge rates to air, water, and soil and intermedia transport rates. EQC Level III was not conducted for the present evaluation since the physical properties of the chemicals will not result in emissions or transport to air or water. Since many of the basic physical properties and degradation rates of this class of chemicals are likely to be unavailable, another model was needed to estimate physical/chemical properties from structure. The model used for this purpose was EPIWIN, version 3.02 (2), which is also used by the EPA and was developed jointly with Syracuse Research Corporation. EPIWIN includes algorithms for estimation of all properties and rates needed for the application of EQC.

Five basic chemical structures were utilized for this evaluation and these are shown in Figure 1 (JRC document). Not all possible structures were modeled since this is a scoping evaluation, but for a number of chemicals, the high and low ends of molecular weight range were evaluated in the models, as was the difference in results between mono- and di-sulfide links. In all, the basic physical properties of over a dozen structures were estimated using EPIWIN and 9 of these are shown in Table 1. The program worked with

the particular sulfur compounds and molecular weight ranges tested and produced estimates for each structure. Inspection of the results in Table 1 indicates that all of these compounds have very low water solubility and low volatility. They also have very high log Kow values. This is not unexpected, however, it should be cautioned that, at least for the high molecular weight compounds, these properties are likely to be outside the range of the training and validation data sets for which the model was developed. As a result, values like a log Kow of 20 are likely to be indicative, rather than quantitatively accurate. However, the results appear to be directionally correct; that is to say, it is expected that these compounds will be virtually in-soluble and non volatile, and strongly bound to organic carbon. The EPIWIN model also has a cut-off limit for the bioconcentration (BCF) of high molecular weight chemicals. Not shown in Table 1, but used in producing the EQC model, are rate estimates for photochemically catalyzed air oxidation and for aquatic biodegradation. Due to strong binding to soil, soil biodegradation rates were assumed to be negligible. In addition, the model predicts negligible hydrolysis for these chemicals.

Results of EQC Level I modeling are shown in Table 2. All of the structures evaluated have essentially the same environmental distribution: 100% goes to soil and sediment (the relative percentages merely reflect the relative available volumes of these compartments). Only the 2-propanol derivative (CAS# 67124-09-8) shows any significant water solubility, resulting in an aqueous distribution of 0.4%. That chemical was low enough in molecular weight to have any associated volatility, resulting in 0.2% partitioning to air. These results are not unexpected. Based on physicochemical properties, it is expected these chemicals will partition strongly to soil and sediment. Table 3 shows results of EQC Level II modeling. The linear molecule (CAS# 67762-55-4) had considerable predicted biodegradability. All of the chemicals were predicted to air oxidize rather quickly (half-lives of a few hours), however, for the higher molecular weight species this fate was limited due to low volatility. So, in general terms, the major (and only) effective removal mechanism for these chemicals is air oxidation. For the high molecular weight chemicals, e.g. MW ~ 400 and higher, this mechanism is slow and consequently the chemical is advected out of the region before more than a few percent are degraded.

In conclusion, it is evident that EQC modeling may be conducted on this class of additives. Additionally, the EPIWIN model may be used to estimate the physical properties and degradation rates of these chemicals which are needed for input into the EQC model. Results of fugacity modeling show that molecules that comprise the alkyl sulfides are expected to partition almost exclusively to soil and sediment. They also would not be expected to migrate appreciably as indicated by high log Koc values. Although the results of this modeling are consistent with the expected behavior of these chemicals, the exact values of the physical properties are somewhat suspect when applied to the very high molecular weight members of this group.

References

- 1 Mackay, D., A. Di Guardo, S. Paterson, and C. Cowan. 1996. Evaluating the Environmental fate of a Variety of Types of Chemicals using the EQC Model. *Environ. Toxicol. Chem.* 15:1627-1637.
- 2 EPIWIN. 1999. Estimation Program Interface for Windows, version 3.02. Syracuse Research Corporation, Syracuse, NY, USA.

Table 1: Physical Properties of Representative Structures of Alkyl Sulfides as Modeled by EPIWIN

CAS #	N	Molecular Weight	Log K _{ow}	Water Solubility (mg/L)	Vapor Pressure (Pa)	Log K _{oc}	Log Bio-concentration Factor	Melting Point (°C)	Boiling Point (°C)	Atmospheric Oxidation	
										OH Rate Constant (cm ³ /molec-sec)	Half-life (hrs)
67124-09-8	Monomer	260.5	5.43	0.475	5.89E-03	3.00	3.48	68.15	302.85	23.32	5.51
68511-50-2	y=3	410.8	7.99	3.94E-04	3.71E-05	6.12	3.45	147.52	409.48	35.69	3.60
68511-50-2	y=8	851.6	15.23	3.29E-18	3.63E-16	11.98	0.5	329.32	749.88	90.67	1.42
68515-88-8	y=1	402.8	10.65	2.35E-06	3.56E-04	6.49	0.5	128.08	377.79	18.94	6.78
68515-88-8	y=4	835.6	20.56	1.20E-17	4.40E-14	12.74	0.5	186.87	477.56	46.69	2.75
67762-55-4	y=2.5, x=1	497.0	16.00	1.64E-11	5.69E-08	9.50	0.5	186.92	504.54	77.22	1.66
67762-55-4	y=2.5 x=2	529.0	16.95	1.59E-10	3.90E-09	9.77	0.5	213.83	537.80	300.52	22.63

Table 2: Environmental Distribution of Representative Structures of Alkyl Sulfides as Modeled by EQC Level I

CAS#	N	Air (%)	Water (%)	Soil (%)	Sediment (%)	Suspended Sediment (%)	Biota (%)	Fugacity (μPa)
67124-09-8	Monomer	0.265	0.407	97.1	2.158	0.067	5.48E-03	0.025
68511-50-2	y=3	8.81E-03	1.13E-03	97.7	2.172	0.068	5.52E-03	5.32E-04
68511-50-2	y=8	1.31E-11	6.96E-11	97.8	2.172	0.068	5.52E-03	3.80E-13
68515-88-8	y=1	0.03	2.47E-06	97.7	2.172	0.068	5.52E-03	1.87E-03
68515-88-8	y=4	1.88E-10	3.04E-16	97.8	2.172	0.068	5.52E-03	5.57E-12
67762-55-4	y=2.5, x=1	3.84E-06	1.10E-11	97.8	2.172	0.068	5.52E-03	1.91E-07
67762-55-4	y=2.5 x=2	3.30E-07	1.24E-12	97.8	2.172	0.068	5.52E-03	1.55E-08

Table 3: Environmental Fate of Representative Structures of Alkyl Sulfides as Modeled by EQC Level II

CAS #	N	Air % degraded	Water % degraded	Soil % degraded	Sediment % degraded
67124-09-8	Monomer	91.5	nil	nil	nil
68511-50-2	Y=3	92.7	nil	nil	nil
68511-50-2	Y=8	nil	nil	nil	nil
68515-88-8	Y=1	89.7	nil	nil	nil
68515-88-8	Y=4	nil	nil	0.002	nil
67762-55-4	Y=2.5, x=1	3.47	nil	0.002	nil
67762-55-4	Y=2.5 x=2	1.04	nil	0.002	nil

3.0 AQUATIC ORGANISMS

Category: Alkyl Sulfides

3.1 Acute Toxicity to Fish

Robust Summary 1-FISH-1

Test Substance	
CAS #	67124-09-8
Chemical Name	2-Propanol, 1-(tert-dodecylthio)-
Remarks	<p>This substance is also referred to as propanol/dodecylthio derivative in HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
Method	
Method/Guideline followed	OECD Guideline for Testing of Chemicals #203 Fish Acute Toxicity Test
Test Type	Semi-Static acute toxicity test (renewal)
GLP (Y/N)	Y
Year (Study Performed)	2003
Species/Strain	Oncorhynchus mykiss
Analytical Monitoring	Test material concentrations of exposure solutions were not determined.
Exposure Period (unit)	96 hours
Statistical methods	The Lethal Loading Rate 50 (LL50) and confidence limits were calculated using the geometric mean method.
Remarks field for test conditions (fill as applicable)	<p>Fingerlings were obtained from a commercial breeder and were acclimated for twenty days. The fish had a mean length of 4.1 cm and a mean weight of 0.78 g.</p> <p>The water-accommodated fractions (WAF) were each prepared by weighing the appropriate amounts of test material into scintillation vials and adding approximately 15mL of dechlorinated tap water. The vials were gently swirled to bring the test material to the surface prior to adding to the surface of 21 liters of dechlorinated water. After the addition of the test material the dechlorinated tap water was stirred by magnetic stirrer using a stirring rate such that a vortex was formed to give a slight dimple at the media surface. The stirring was stopped after 48 hours and the mixtures allowed to stand for 1 hour prior to removing the aqueous phase (WAF) by siphon (first 75-100 mL discarded). Microscopic examination of each WAF confirmed that no undissolved test material was present.</p> <p>A sealed 96 hours semi-static test was carried out with daily renewal of the test WAF's. 20-liter glass exposure chambers were filed with each WAF or control. Ten fish were placed in each chamber and the chambers were sealed. The fish were not fed during the study. The test vessels were aerated via narrow bore glass tubes. WAF solutions were replaced daily.</p> <p>The fish were observed for toxicity at 3, 6, 24, 48, 72 and 96 hours.</p> <p>Dissolved oxygen, water temperature and pH were determined throughout the study. Vortex depth and mixing rates were recorded</p>

	periodically throughout the mixing period.																																																							
Test Concentrations (Nominal)	Initial evaluation: 1.0, 1.8, 3.2, 5.6 and 10 mg/L WAF Repeat evaluation: 0, 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L WAF																																																							
Range Finding Study	Concentrations of 0.1, 1.0, 10, 32 and 100 mg/L WAF																																																							
Results	The 96 hour LL ₅₀ 's (loading levels likely to cause 50% mortality) was 0.42 mg/L WAF. The 96 hour No observed effect level was 0.32 mg/L WAF																																																							
Remarks	<p>Several range finding studies were conducted using different ranges of the concentrations specified above. Neither mortality nor sublethal effects were observed at loading rates of 0.1 and 1.0 mg/L WAF. Mortality was observed at 24 hours at 10 mg/L WAF.</p> <p>During the initial main study mortality or sublethal effects were observed at all concentrations therefore a second definitive study was conducted at 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L WAF.</p> <p>During the second, definitive study, sub-lethal effects at 0.56 mg/L WAF and above included swimming at the bottom with increased pigmentation and loss of equilibrium. After 22 hours all of the fish at 1.8 and 3.2 mg/L WAF were moribund. After 46 hours all of the fish at 1.0 mg/L WAF were moribund. All moribund fish were killed.</p> <p>Cumulative immobilization data were as follows:</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">WAF mg/L</th> <th colspan="6">Cumulative Mortality (%)</th> </tr> <tr> <th>3 Hr</th> <th>6 Hr</th> <th>24 Hr</th> <th>48 Hr</th> <th>72 Hr</th> <th>96 Hr</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> </tr> <tr> <td>0.32</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> </tr> <tr> <td>0.56</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>100</td> </tr> <tr> <td>1.0</td> <td>0</td> <td>0</td> <td>0</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>1.8</td> <td>0</td> <td>0</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>3.2</td> <td>0</td> <td>0</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> </tbody> </table> <p>Temperature was maintained at 14.5-15.8°C throughout the test. No treatment related differences were observed in dissolved oxygen concentration or pH.</p> <p>After 48 hours stirring and a 1-hour standing period the WAFs were clear colorless water columns with oily globules of test material floating at the water surface. After siphoning and for the duration of the test, the WAFs were clear colorless solutions. No undissolved test material was present upon microscopic examination.</p> <p>Water chemistry: Temperature: 14.5-15.8°C; pH: 7.8-8.2; % Dissolved Oxygen Saturation: 79-102%</p>	WAF mg/L	Cumulative Mortality (%)						3 Hr	6 Hr	24 Hr	48 Hr	72 Hr	96 Hr	0	0	0	0	0	0	0	0.32	0	0	0	0	0	0	0.56	0	0	0	0	0	100	1.0	0	0	0	100	100	100	1.8	0	0	100	100	100	100	3.2	0	0	100	100	100	100
WAF mg/L	Cumulative Mortality (%)																																																							
	3 Hr	6 Hr	24 Hr	48 Hr	72 Hr	96 Hr																																																		
0	0	0	0	0	0	0																																																		
0.32	0	0	0	0	0	0																																																		
0.56	0	0	0	0	0	100																																																		
1.0	0	0	0	100	100	100																																																		
1.8	0	0	100	100	100	100																																																		
3.2	0	0	100	100	100	100																																																		
Conclusions	The 96 hour LL ₅₀ 's (loading levels likely to cause 50% mortality) was 0.42 mg/L WAF (0.32-0.56). The 96 hour No Observed Effect Level was 0.32 mg/L WAF																																																							
Data Quality	Reliable with restriction (Klimisch Code). Restriction due to the lack of analytical confirmation of test concentrations.																																																							
References	Acute Toxicity to Rainbow Trout SafePharm Laboratories Project No.: 1666/019 (May 2003)																																																							

Robust Summary 1-FISH-2

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	<p>This substance is referred to as methyl propene derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	Test protocol followed US EPA Toxic Substances Control Act Test Guideline #797.1400 (1985), OECD Guideline for Testing of Chemicals #203, Fish Acute Toxicity Test (1984).
Test Type	WAF static renewal test
GLP (Y/N)	Y
Year (Study Performed)	1993
Species/Strain	Fathead minnow (<i>Pimephales promelas</i>)
Analytical Monitoring	Total organic carbon (TOC) measurements of initial test solutions and control (0-hour) and after one day on test (24-h) before daily renewal of fresh test solution.
Exposure Period (unit)	96 hours
Statistical methods	Statistical analysis of survival data not warranted.
Remarks field for test conditions (fill as applicable)	<p>Test Organisms: source – Aquatic Research Organisms, Hampton, New Hampshire, age – juvenile, total length – 25 mm average (longest fish not more than twice the shortest fish), wet weight – 0.1 g average (no range reported). Loading - <0.5 g biomass/L, Pretreatment – none, fish held for a minimum of 14 days before testing. No feeding during the test.</p> <p>Test System: Individual WAFs were prepared for each test level and renewed daily. A measured weight of test material was added to a measured volume of dilution water (30-L) in a glass vessel and stirred for 24 hours. Stirring accomplished using a Telfon coated magnetic stir bar. Mixing speed adjusted such that a vortex formed between 30 to 50% of the distance to the bottom. Following the mixing period, the test solutions were allowed to stand for 1 hour before the water phase was removed. To avoid removing test material from the surface or bottom, a siphon was placed in the mixing vessel prior to addition of water and test substance with the lower end 1-2 inches off the bottom. The siphoned water phase (i.e., WAF) was used in the aquatic toxicity test. About 80% of the solution in each test level was renewed daily after 24, 48, and 72 hours. Two 15-L replicates per treatment, 10 fish per replicate (20 per treatment). Test vessels loosely covered to reduce entry of dust, etc.</p> <p>Dilution Water: Filtered well water collected at Hampton, New Hampshire and adjusted to the appropriate hardness of 176 mg/L as CaCO₃. The water was passed through activated carbon, a particle filter, and then an ultraviolet sterilizer, and then it was stored in a polyethylene tank where it was aerated. The water was characterized as moderately hard water. Alkalinity not reported. Dissolved oxygen – 7.1 to 8.7 mg/L, pH – 7.8 to 8.5, conductivity – 570 to 650 umhos/cm,</p>

	<p>temperature – 21.4 to 22.8 C. TOC levels were between 2 to 3 mg/L in the control, 3 mg/L at 100 mg/L test level, between 3 to 4 mg/L at 300 mg/L test level and 5 mg/L at 1,000 mg/L test concentration level.</p> <p>Test Levels: Control, 100, 300 & 1,000 mg/L WAF loading rates.</p> <p>Test Findings: No mortality was observed in all treatments and the control throughout the entire test and no signs of toxicity were noted in all treatments throughout 72 hours. At 96 hours, all 20 fish in the 1,000 mg/L test level were lethargic and exhibited erratic swimming, but no signs of toxicity were observed in the lower test levels and control.</p> <p>Calculation of LL₅₀s: Statistical analysis of survival data not warranted.</p> <p>Test Substance: No undissolved test material was seen on the surface of the test vessels during the entire aquatic toxicity test.</p> <p>Reference Substance: No</p>
<u>Results</u>	<p>Nominal concentrations: 96-h LL₅₀ >1,000 mg/L. 96-h LL₀ = 300 mg/L. No mortality at 1,000 mg/L but at 96 hours all fish were lethargic and exhibited erratic swimming. TOC measurements at 1,000 mg/L were 5 mg/L compared to 2 to 3 mg/L in the control.</p>
Remarks	<p>Measured concentration: n/a</p> <p>Unit: mg/L</p> <p>LC50, LC0, LL50 or LL0 at 48, 72, 96 hours: LL₅₀ and LL₀ reported as LC₅₀ and NOEC, respectively, although test results were based on WAF loading rates.</p> <p>Statistical results: Statistical analysis of survival data not warranted.</p> <p>Other:</p> <ul style="list-style-type: none"> The TOC in dilution water at the beginning and end of the test was greater than 2 mg/L rather than <2 mg/L. It could not be verified that water samples were passed through a 0.45 micron filter prior to TOC analysis, that the test vessels were covered, or that the continuous temperature measurement was made in a control vessel during the study. But, these deviations did not compromise the study.

<u>Conclusions</u>	No mortality was observed in all treatments and the control throughout the entire test and no signs of toxicity were noted in all treatments throughout 72 hours. At 96 hours, all 20 fish in the 1,000 mg/L test level were lethargic and exhibited erratic swimming, but no signs of toxicity were observed in the lower test levels and control.
<u>Data Quality</u>	Reliable without restrictions
<u>References</u>	<p>Chemical Manufacturers Association, HERTG</p> <p>Ward, T.J. (1993) Acute Toxicity of The Water Accommodated Fractions (WAFs) of CMA 613 to The Fathead Minnow, <i>Pimephales promelas</i>. T.R. Wilbury Study #9176-CMA/ESI-613.</p>

Robust Summary 1-FISH-3

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	<p>This substance is referred to as methyl propene derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	Test protocol followed OECD Guideline for Testing of Chemicals #203, Fish Acute Toxicity Test (1984).
Test Type	WSF static renewal test; a one level screening test
GLP (Y/N)	Y
Year (Study Performed)	1986
Species/Strain	Sheepshead minnow (<i>Cyprinodon variegatus</i>)
Analytical Monitoring	Total organic carbon (TOC) measurements of each freshly prepared test solution and control and after 24-h on test just before daily renewal with fresh test solution.
Exposure Period (unit)	96 hours
Statistical methods	Statistical analysis of survival data not warranted.
Remarks field for test conditions (fill as applicable)	<p>Test Organisms: source – a commercial supplier in New Hampshire, age – 24 to 29 days old, total length – 20.3 mm average (range 13 to 30 mm; n=18), wet weight – 0.16 g average (range 0.03 to 0.039 g; n = 18). Loading - 0.32 g biomass/L, Pretreatment – none, fish held for a minimum of 20 days before testing. No feeding during the test.</p> <p>Test System: Individual WSFs were prepared for each daily renewal of the 10,000 mg/L test level. A measured weight of test material was added to a measured volume of dilution water (15-L) in a glass vessel and stirred for 16 to 24 hours. Stirring accomplished using a Telfon coated magnetic stir bar. Mixing speed adjusted such that a vortex formed between 30 to 50% of the distance to the bottom. Following the mixing period, the test solutions were allowed to stand for 2 hours before the water phase was removed. To avoid removing test material from the surface or bottom, a siphon was placed in the mixing vessel prior to addition of water and test substance with the lower end approximately midway between bottom and surface. The siphoned water phase, designated water soluble fraction (WSF), was used for the aquatic toxicity test. About 90% of the test solution in each test vessel was renewed daily after 24, 48, and 72 hours. Two 5-L replicates per treatment, 10 fish per replicate (20 per treatment). Test vessels were loosely covered to reduce entry of dust, etc.</p> <p>Dilution Water: Natural seawater collected from Cape Cod Canal, Bourne, Massachusetts which derives water from Buzzards Bay or Massachusetts Bay. The water was filtered through 0.5-micron polypropylene core filter and activated carbon, then stored for 1 to 4 days prior to use while being constantly aerated. During storage the water had a salinity of 32 to 33 ppt and pH of 7.7 to 7.8. During the test: dissolved oxygen – 5.6 mg/L to above 100% saturation (7.5 mg/L), pH – 6.9 to 8.0, salinity – 32, temperature – 20 to 22 C. Mean</p>

	<p>measured TOC levels in the control and 1,000 mg/L WSF test level were 2.7 mg/L (range 1.2 to 6.0) and 4.5 mg/L (range 3.0 to 5.6), respectively</p> <p>Test Levels: Control & 10,000 mg/L WSF loading rate.</p> <p>Test Findings: No mortality or signs of toxicity were noted in the 10,000 WSF test level and the control throughout the entire test.</p> <p>Calculation of LL₅₀s: Statistical analysis of survival data not warranted.</p> <p>Test Substance: No undissolved test material was seen on the surface of the test vessels during the entire aquatic toxicity test.</p> <p>Reference Substance: Sodium lauryl sulfate (SLS). The 96-h LC₅₀ was 1.2 mg/L. No information provided on method of calculation.</p>
Results	<p>Nominal concentrations: 96-h LL₅₀ >10,000 mg/L. 96-h LL₀ = 10,000 mg/L (no mortality or toxic signs noted). Mean measured TOC in the 10,000 mg/L WSF test level was 4.5 mg/L compared to 2.7 mg/L in the control.</p>
Remarks	<p>Measured concentration: n/a</p> <p>Unit: mg/L</p> <p>LC50, LC0, LL50 or LL0 at 48, 72, 96 hours: LL₅₀ and LL₀ reported as LC₅₀ and NOEC, respectively, although test results were based on WSF loading rate.</p> <p>Statistical results: Statistical analysis of survival data not warranted.</p> <p>Other:</p> <ul style="list-style-type: none"> •
Conclusions	<p>No mortality or signs of toxicity were noted in the 10,000 WSF test level and the control throughout the entire test.</p>
Data Quality	<p>Reliable without restrictions</p>
References	<p>Chemical Manufacturers Association, HERTG</p> <p>Nicholson, R.B. (1986) Acute toxicity of CMA Test Material Code 525 to Sheepshead Minnow, <i>Cyprinodon variegatus</i>. Springborn Bionomics Study #10823-0186-6100-500-525, Report #BW-86-04-2004.</p>

3.2 Acute Toxicity to Aquatic Invertebrates (e.g. Daphnia)

Robust Summary 1-DAPH-1

<u>Test Substance</u>	
CAS #	67124-09-8
Chemical Name	2-Propanol, 1-(tert-dodecylthio)-
Remarks	<p>This substance is referred to as propanol dedocylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	OECD Guideline for Testing of Chemicals #202 <i>Daphnia</i> sp. Acute Immobilization Test and Reproduction Test (1984).
Test Type	Static acute toxicity test (Limit Test)
GLP (Y/N)	Y
Year (Study Performed)	2003
Species/Strain	<i>Daphnia magna</i>
Analytical Monitoring	Test material concentrations of exposure solutions were not determined.
Exposure Period (unit)	48 hours
Statistical methods	The Effective Loading Rate 50 (EL50) and confidence limits were calculated using the geometric mean method.
Remarks field for test conditions (fill as applicable)	<p>1st instar <i>Daphnia magna</i> derived from in house cultures were used for the study.</p> <p>The water-accommodated fractions (WAF) were each prepared by weighing the appropriate amounts of test material into scintillation vials and adding approximately 15mL of dechlorinated tap water. The vials were gently swirled to bring the test material to the surface prior to adding to the surface of 20 liters of dechlorinated water. After the addition of the test material the dechlorinated tap water was stirred by magnetic stirrer using a stirring rate such that a vortex was formed to give a slight dimple at the media surface. The stirring was stopped after 48 hours and the mixtures allowed to stand for 1 hour prior to removing the aqueous phase (WAF) by siphon (first 75-100 mL discarded). Microscopic examination of each WAF confirmed that no undissolved test material was present.</p> <p>The toxicity test was conducted in 300 ml ground glass stoppered conical flasks that contained approximately 300mL of test solution. Twenty daphnids were distributed into each concentration (10 daphnids/replicate) and control. Test vessels were maintained at 21°C with a photoperiod of 16 hours light and 8 hours dark with 20 minute dawn and dusk transition periods. <i>Daphnia</i> were not fed nor were cultures aerated during exposure. Test preparations were not renewed during the exposure period.</p> <p>Water temperature was recorded daily throughout the test. Dissolved oxygen concentration and pH were recorded at the start and end of the study. Vortex depth were recorded at the start and end of the mixing</p>

	<p>period.</p> <p>Any immobilization or adverse reactions to exposure were recorded at 24 and 48 hours after the start of exposure. Daphnia were considered to be immobilized if they were unable to swim for approximately 15 seconds after gentle agitation.</p> <p>The Effective Loading Rate 50 (EL50) and confidence limits were calculated using the geometric mean method.</p>																																				
<i>Test Concentrations</i>	1, 1.8, 3.2, 5.6, 10, 18, 32, 56 and 100 mg/L																																				
<i>Range Finding Study</i>	Concentrations of 1.0, 10 and 100 mg/L WAF																																				
Results	The 48-hour EL50 (Effective Loading rate) was determined to be 1.3mg/L WAF. The no observed effect loading rate at 48 hours was 1.0 mg/L WAF.																																				
Remarks	<p>Temperature was maintained at approximately 21°C throughout the test. No treatment related differences were observed in oxygen concentration or pH.</p> <p>After 48 hours stirring and a 1-hour standing period the WAFs were clear colorless water columns with globules of test material floating at the water surface. After siphoning and for the duration of the test, the WAFs were clear colorless solutions. No undissolved test material was present upon microscopic examination.</p> <p>Cumulative immobilization data were as follows:</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th colspan="3" style="text-align: center;">Cumulative Immobilization (%)</th> </tr> <tr> <th style="text-align: center;">Concentration mg/L</th> <th style="text-align: center;">24 Hours</th> <th style="text-align: center;">48 Hours</th> </tr> </thead> <tbody> <tr><td style="text-align: center;">0</td><td style="text-align: center;">0</td><td style="text-align: center;">0</td></tr> <tr><td style="text-align: center;">1.0</td><td style="text-align: center;">0</td><td style="text-align: center;">0</td></tr> <tr><td style="text-align: center;">1.8</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">3.2</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">5.6</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">10</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">18</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">32</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">56</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> <tr><td style="text-align: center;">100</td><td style="text-align: center;">100</td><td style="text-align: center;">100</td></tr> </tbody> </table> <p>The 24 and 48-hour EL50s (Effective Loading rate) were determined to be 1.3 mg/L WAF.</p> <p>The no observed effect loading rate at 24 and 48 hours was 1.0 mg/L WAF.</p> <p>pH at 0 and 48 hours: 7.8 Dissolved oxygen concentration: 98-99% saturation</p>	Cumulative Immobilization (%)			Concentration mg/L	24 Hours	48 Hours	0	0	0	1.0	0	0	1.8	100	100	3.2	100	100	5.6	100	100	10	100	100	18	100	100	32	100	100	56	100	100	100	100	100
Cumulative Immobilization (%)																																					
Concentration mg/L	24 Hours	48 Hours																																			
0	0	0																																			
1.0	0	0																																			
1.8	100	100																																			
3.2	100	100																																			
5.6	100	100																																			
10	100	100																																			
18	100	100																																			
32	100	100																																			
56	100	100																																			
100	100	100																																			

Conclusions	The 48-hour EL50 (Effective Loading rate) was determined to be 1.3mg/L WAF. The no observed effect loading rate at 48 hours was 1.0 mg/L WAF.
Data Quality	Reliable with restriction (Klimisch Code) Restriction due to the lack of analytical confirmation of dose level concentrations.
References	Acute Toxicity to <i>Daphnia Magna</i> SafePharm Laboratories Project No.: 1666/020 (May 2003)

Robust Summary 1-DAPH-2

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	<p>This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	U.S. EPA 797.1300 (1985, 1987), OECD 202 (1984)
Test Type	Static acute toxicity test
GLP (Y/N)	Yes
Year (Study Performed)	1993
Species/Strain	Daphnia magna
Test details (static, semi-static, dosing rate, flow-through rate, etc.)	A static non-renewal test was conducted using water accommodated fractions (WAF) of the test material at 100, 300 and 1,000 mg/L loading rates. WAFs were prepared by adding a measured weight of the test material to a measured volume of the dilution water and stirring for 24 hours with a magnetic stir bar. The test solutions were allowed to stand for 1 hour before the water phase (WAF) was siphoned off.
Statistical Methods	Not conducted because there was greater than 50% survival in all test vessels.
Remarks field for test conditions (fill as applicable)	<p>Test species: Juvenile daphnids, less than 24-hours old were produced from laboratory in-house culture</p> <p>Test conditions: Two 250-mL glass beakers that contained 200 ml of test solution were used per treatment. The 250-mL test vessels were loosely covered to reduce entry of dust, etc.</p> <p>Test temperature range: $20 \pm 1^\circ\text{C}$</p> <p>Exposure vessel type:</p> <p>Dilution water: Filtered well water collected at Hampton, New Hampshire and adjusted to the appropriate hardness 168 to 172 mg/L as CaCO_3. The water was passed through activated carbon, a particle filter, and then an ultraviolet sterilizer and stored in a polyethylene tank where it was aerated. TOC levels were 2 mg/L at the beginning and end of the test, and 10 mg/L TSS at the beginning and <10 mg/L at the end of the test.</p> <p>Lighting: A 16 hour light and 8 hour dark photoperiod was maintained with cool-whit fluorescent lights with an intensity of $20 \mu\text{Ein}^{-1}\text{m}^{-2}$.</p> <p>Water chemistry: Dissolved oxygen – 8.2 to 8.7 mg/L; pH – 7.8 to 8.2; conductivity – 570 to 640 umhos/cm; temperature – 20.5 to 20.9°C.</p> <p>Element: Immobilization</p> <p>Test design: Control, 100, 300 & 1,000 mg/L WAF loading rates. 10</p>

	<p>daphnids per replicate (20 per treatment).</p> <p>Method of calculating mean measured concentrations: not applicable</p> <p>Exposure period: 48 hours</p> <p>Analytical monitoring: Total organic carbon (TOC) measurements of initial test solutions and control (0-hour) and at test termination (48-h). TOC levels were 2 mg/L in the control, 3 mg/L at the 100 mg/L and 300 mg/L test levels; and 4 to 5 mg/L at the 1000 mg/L test vessel. TOC levels were not considered to be indicative of actual test material concentrations and results are therefore based on nominal loading rates</p>
<u>Results</u>	<p>Nominal concentrations: 48-hour and 24-hour EC50 = >1,000 mg/L (based on nominal loading rates). 48-hour and 24-hour NOEC = 1,000 mg/L</p>
Remarks	<p>Measured concentration: N/A</p> <p>Unit: mg/L</p> <p>EC50, EL50, LC0, LL0 at 24, 48 hours: 48-hour and 24-hour EC50 = >1,000 mg/L (based on nominal loading rates). 48-hour and 24-hour NOEC = 1,000 mg/L</p> <p>Statistical results: not applicable</p> <ul style="list-style-type: none"> • Effect concentrations based on nominal loading rates • No immobilization seen at the highest test concentration of 1,000 mg/L (WAF) • Control response was satisfactory.
<u>Conclusions</u>	<p>The WAFs of the test material were not toxic to daphnids at the concentrations tested. Ninety-five to 100% survival occurred at all test concentrations. No sublethal effects were noted during the test.</p>
<u>Data Quality</u>	<p>Reliable without restrictions</p>
<u>References</u>	<p>Chemical Manufacturers Association, HERTG</p> <p>Ward, T.J. (1993) Acute Toxicity of the Water Accommodated Fractions (WAFs) of CMA #613 to the Daphnid, <i>Daphnia magna</i>. T.R. Wilbury Study #9178-CMA/ESI-613.</p>

3.3 Toxicity to Aquatic Plants (e.g. Algae)

Robust Summary 1-ALG-1

<u>Test Substance</u>	
CAS #	67124-09-8
Chemical Name	2-Propanol, 1-(tert-dodecylthio)-
Remarks	This substance is referred to as propanol dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	OECD Guideline for Testing of Chemicals #201 Alga, Growth Inhibition Test (1984).
Test Type	Static acute toxicity test (Water Accommodated Fraction- WAF)
GLP (Y/N)	Y
Year (Study Performed)	2003
Species/Strain	<i>Freshwater algae, Scenedesmus subspicatus/CCAP 276/20</i>
Element basis (# of cells/mL)	Approximately 2.27×10^6 cells/mL, 5 mL used to inoculate 1 liter of medium for an initial cell density of 10^4 cells/mL.
Exposure period/duration	96 hours
Range find test	Yes
Analytical monitoring	Test material concentrations of exposure solutions were not determined.
Statistical methods	A Students t-test incorporating Bartlett's test for homogeneity of variance was used to compare the area under the growth curve data of the treated and control groups at 96 hours.
Remarks field for test conditions (fill as applicable)	<p>Test Species: Cultures obtained from the Culture Collection of Algae and Protozoa (CCAP), Institute of Freshwater Ecology, The Ferry House, Far Sawrey, Ambleside, Cumbria, U.K.</p> <p>Loading Concentration Ranges Find Study: 0, 10 and 100 mg/L loading rate WAF. Definitive Study: 0 and 100 mg/L loading rate WAF (Limit Test)</p> <p>Test System: The WAF was prepared only at the beginning of the test. Using a glass syringe a measured weight of test material was added to the surface of a measured volume of culture medium (20-L) in a glass vessel and stirred for 48 hours. Stirring was accomplished using a magnetic stirrer. Mixing speed was adjusted such that a slight vortex formed causing a slight dimple at the media surface. Following the mixing period, the test solution was allowed to stand for one hour. A small amount of the WAF was removed and examined microscopically for the presence of micro-dispersions or globules of test material. None were observed therefore the WAF was removed by siphoning (the first 75-100 mL discarded). The siphoned water phase (i.e., WAF) was used for the aquatic toxicity test.</p> <p>Test Conditions: A static test was conducted; i.e., there was no daily renewal of test solution. Six 100-mL replicates per treatment, inoculum ~10,000 cells/mL. The 250-mL conical flasks were plugged with polyurethane foam bungs. During the test all treatment (6 flasks) and control (3) flasks were randomly</p>

placed on an orbital shaker adjusted to approximately 150 cycles per minute under constant light (24 hours/day) and maintained at 24°C for 96 hours. Cell densities were determined using a Coulter Multisizer II Particle Counter at 0, 24, 48, 72 and 96 hours. pH was determined at 0 and 96 hours.

Light: Continuous illumination approximately 7000 lux.

Test temperature: 24.0° C.

Culture Media: As specified in the guideline.

Method of calculating mean measured concentrations: not applicable

Exposure period: 96 hours

<p><u>Results</u></p>	<p>During the range finding study cell counts and percentage inhibition of growth values were unaffected by exposure to the test material. A dose level of 100 mg/L WAF was selected for the definitive study.</p> <p>During the definitive study neither the growth rate nor the biomass of <i>Scenedesmus subspicatus</i> (CCAP 276/20) was affected by the presence of the test material over the 96-hour exposure period.</p> <p>Effective Loading Rate (EL50) (96 hrs) = >100 mg/L loading rate WAF [Loading rate that reduced the biomass by 50%].</p> <p>EL50 (0-96 hrs) = >100 mg/L loading rate WAF [Loading rate that reduced specific growth rate by 50%].</p> <p>There were no statistically significant differences in the area under the growth curve data between the control and 100 mg/L WAF test group. Therefore the No Observed Effect Loading Rate (NOEL) was 100 mg/L WAF.</p> <p>The cell concentrations of the control cultures increased by a factor of 150 after 72 hours and 358 after 96 hours meeting the guideline requirement of at least a factor of 16 after 72 hours.</p> <p>At both the start and end of the mixing period and after the 1-hour standing period the WAF was a clear colorless water column with oily globules of test material floating at the media surface. After siphoning and at the start of the test, the WAF was a clear colorless solution. After the 96-hour test period the 100 mg/L loading rate WAF was a very bright green dispersion.</p> <p>All test and control cultures were inspected microscopically at 96 hours. No abnormalities were observed in any cultures. Control culture pH increased from 7.3 at 0 hour to 8.6-8.7 at 96 hours. This is consistent with the guideline. In the test cultures pH increased over the 96 hour test period from 7.3 at 0 hour to 8.6-8.7 at 96 hours.</p>
<p><u>Conclusions</u></p>	<p>Neither the growth nor the biomass of <i>Scenedesmus subspicatus</i> (CCAP 276/20) was affected by the presence of the test material over the 96-hour exposure period.</p> <p>EL50 (96 hrs) = >100 mg/L loading rate WAF EL50 (0-96 hrs) = >100 mg/L loading rate WAF No Observed Effect Loading Rate (NOEL) = 100 mg/L loading rate WAF</p> <p>Control response was satisfactory.</p>
<p><u>Data Quality</u></p>	<p>Reliable with restriction (Klimisch). Restriction due to the lack of concentration analysis of the dose solution.</p>
<p><u>References</u></p>	<p>Acute Toxicity to <i>Daphnia Magna</i> SafePharm Laboratories Project No.: 1666/021 (May 2003)</p>

Robust Summary 1-ALG-2

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Test protocol followed US EPA Toxic Substances Control Act Test Guideline #797.1050 (1985, 1987), OECD Guideline for Testing of Chemicals #201 Alga, Growth Inhibition Test (1984).
Test Type	WAF static non-renewal test
GLP (Y/N)	Y
Year (Study Performed)	1994
Species/Strain	Freshwater algae, <i>Pseudokirchneriella subcapitata</i> formerly called <i>Selenastrum capricornutum</i>
Element basis (# of cells/ml)	~10,000 cells/ml
Exposure period/duration	96 hours
Analytical monitoring	Total organic carbon (TOC) measurements of initial test solutions and control (0-hour) and at test termination (96-h). EPA Method 415.1 (1979). Water samples were passed through 0.45 micron filter prior to TOC analysis.
Statistical Methods	
Remarks field for test conditions (fill as applicable)	<p>Test Organisms: source – T.R. Wilbury in-house culture originally purchased from the University of Texas at Austin algae collection.</p> <p>Test System: Individual WAFs were prepared for each test level and renewed daily. A measured weight of test material was added to a measured volume of dilution water (1-L) in a glass vessel and stirred for 24 hours. Stirring accomplished using a Teflon coated magnetic stir bar. Mixing speed adjusted such that a vortex formed between 30 to 50% of the distance to the bottom. Following the mixing period, the test solutions were allowed to stand for 1 hour before the water phase was removed. To avoid removing test material from the surface or bottom, a siphon was placed in the mixing vessel prior to addition of water and test substance with the lower end 1-2 inches off the bottom. The siphoned water phase (i.e., WAF) was used for the aquatic toxicity test. A static test was conducted; i.e., there was no daily renewal of test solution. Three 100-mL replicates per treatment, inoculum ~10,000 cells/mL. The 250-mL Erlenmeyer flasks were stoppered with foam plugs to reduce entry of dust, etc. During the test all treatment and control flasks were randomly placed on an orbital shaker adjusted to approximately 100 cycles per minute under constant light (24 hours/day). Daily cell counts were made visually by means of direct microscopic examination with a hemocytometer. Cool-white fluorescent lights provided a light intensity of 47 to 50 $\mu\text{Ein}/\text{m}^2\text{sec}$.</p> <p>At the conclusion of the 96-h test a 0.5 mL subsample of test media from each</p>

	<p>100 mg/L test flask was combined with 100 mL of fresh untreated alga media and incubated for up to 9 days or as soon as growth occurs. This was done to determine if growth inhibition was algistatic or algicidal.</p> <p>Dilution Water: Sterile enriched alga growth media (US EPA, 1978, T.R. Wilbury SOP #6) adjusted to pH 7.5. Measured TOC and total suspended solids in fresh untreated alga media were <1.0 and <10 mg/L, respectively. Test temperature – 23.4 to 23.6 C, pH – 7.0 to 7.1 at 0-hour and 8.6 to 10.2 after 96 hours. TOC measurements were only made on the lowest and highest test levels and control at the beginning and end of the test. TOC levels were <1.0 mg/L in the control and 1.0 mg/L WAF test level and 3 mg/L at 100 mg/L.</p> <p>Test Levels: Control, 1.0, 5.0, 10, 50, 100 mg/L WAF loading rates.</p> <p>Calculation of EL₅₀s and NOELRs: Moving average and probit methods (Stephan, 1983) were used to calculate EC₅₀s (i.e., EL₅₀s). A parametric one-way analysis of variance (ANOVA) and Dunnett’s test were used to calculate the no-observed effect concentration (i.e., EL₀s) when data were normally distributed and a non-parametric Kruskal and Wallis test was used if data were not normally distributed.</p> <p>Test Substance: No undissolved test material was seen on the surface of the test vessels during the entire aquatic toxicity test.</p> <p>Reference Substance: No</p>															
<p><u>Results</u></p>	<p>Measurements expressed as mg/L WAF loading rate:</p> <table border="1" data-bbox="673 1134 1339 1228"> <thead> <tr> <th></th> <th><u>72-h EL₅₀</u></th> <th><u>72-h NOELR^c</u></th> <th><u>96-h EL₅₀</u></th> <th><u>96-h NOELR^c</u></th> </tr> </thead> <tbody> <tr> <td>Cell Density:</td> <td>26^a (21-32)</td> <td>5.0</td> <td>34^b (29-39)</td> <td>10</td> </tr> <tr> <td>Growth Rate:</td> <td>>100</td> <td>5.0</td> <td>>100</td> <td>10</td> </tr> </tbody> </table> <p>^a Moving average method. ^b Probit method. Confidence limits in parentheses. ^c Hypothesis analysis tests were used to determine NOELRs.</p> <p>Re-growth of inhibited cultures from the 100 mg/L test level revealed the effect was algistatic rather than algicidal.</p>		<u>72-h EL₅₀</u>	<u>72-h NOELR^c</u>	<u>96-h EL₅₀</u>	<u>96-h NOELR^c</u>	Cell Density:	26 ^a (21-32)	5.0	34 ^b (29-39)	10	Growth Rate:	>100	5.0	>100	10
	<u>72-h EL₅₀</u>	<u>72-h NOELR^c</u>	<u>96-h EL₅₀</u>	<u>96-h NOELR^c</u>												
Cell Density:	26 ^a (21-32)	5.0	34 ^b (29-39)	10												
Growth Rate:	>100	5.0	>100	10												
<p>Remarks</p>	<p>Measured concentration: N/A</p> <p>Unit: mg/L WAF loading</p> <p>Element value: EL₅₀ and NOELR (i.e., no-observable effect loading rate).</p> <ul style="list-style-type: none"> • EL₅₀s and NOELRs reported as EC₅₀ and NOEC, respectively, although test results were based on WAF loading rates. • Test concentrations for the definitive test were not specified in a protocol amendment and the pH of the sterile media at the start of the test was 7.0 rather than 7.5. These deviations did not compromise the study. 															

<u>Conclusions</u>	Re-growth of inhibited cultures from the 100 mg/L test level revealed the effect was algistatic rather than algicidal.
<u>Data Quality</u>	Reliable without restrictions
<u>References</u>	Chemical Manufacturers Association, HERTG

4.0 Toxicity**Category: Alkyl Sulfides****4.1 Acute Toxicity****4.1.1 Acute Oral Toxicity****Robust Summary #: 1-Acute Oral-1**

<u>Test Substance</u>	
CAS #	CAS# 67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Consistent with guidelines outline in OECD 401
Test Type	Acute oral toxicity
GLP (Y/N)	Y
Year (Study Performed)	1982
Species/Strain	Albino rats of the outbred Sprague-Dawley strain
Sex	Male and female
No. of animals/sex/dose	5
Vehicle	Mineral oil-based material dosed undiluted
Route of administration	Oral gavage with a syringe and dosing needle. The animals were fasted overnight before dosing.
Remarks field for test conditions	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 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.
<u>Results</u>	
LD50	> 5.0 gm/kg
Remarks	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. Gross pathological examination reveals no remarkable findings.

<u><i>Conclusions</i></u>	LD50 > 5.0 gm/kg (males and females)
<u><i>Data Quality</i></u>	Reliable without restriction (Klimisch Code)
<u><i>References</i></u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary #: 1-Acute Oral-2

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Experimental
Test Type	Acute oral toxicity (LD50)
GLP (Y/N)	N
Year (Study Performed)	1970
Species/Strain	Rat; Sherman/Wistar
Sex	Male, young adult
No. of animals/sex/dose	5
Vehicle	None; administered undiluted
Route of administration	Oral gavage
Remarks field for test conditions	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
<u>Results</u>	
5.7 ml/kg; 19/20 confidence limits 4-8 ml/kg	
Remarks	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.
<u>Conclusions</u>	
LD50 = 5.7 ml/kg (male rats)	
<u>Data Quality</u>	
Reliable with restrictions State of the art LD50 oral toxicity study for 1970, multi-dose, calculated LD50 with confidence limits. Non-GLP, details of study design and observations during study not presented	
<u>References</u>	
This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).	

Robust Summary #: 1-Acute Oral-3

Robust Summary #: 1-Acute Oral-4

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Consistent with guidelines outline in OECD 401
Test Type	Acute oral toxicity
GLP (Y/N)	Y
Year (Study Performed)	1987
Species/Strain	Albino rats of the outbred Sprague-Dawley strain
Sex	Male and female
No. of animals/sex/dose	5
Vehicle	Mineral oil-based material
Route of administration	Oral gavage with a syringe and Nelaton catheter . The animals were fasted overnight before dosing.
Remarks field for test conditions	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.
<u>Results</u>	LD50 > 5.0 gm/kg
Remarks	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.
<u>Conclusions</u>	LD50 > 5.0 gm/kg (males and females)
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

4.1.2 Acute Dermal Toxicity

Robust Summary 1-Acute Dermal-1

<u>Test Substance</u>	
CAS #	CAS# 67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	FHSA Regulations 16 CFR 1500.40
Test Type	Acute dermal toxicity
GLP (Y/N)	Y
Year (Study Performed)	1991
Species/Strain	Young, adult New Zealand white rabbits
Sex	Male and female
No. of animals/sex/dose	5
Vehicle	Mineral oil-based material dosed undiluted
Route of administration	Dermal application
Remarks field for test conditions	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.
<u>Results</u>	
LD50	LD50 > 2.0 gm/kg
Remarks	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. Gross pathological examination reveals no remarkable findings.
<u>Conclusions</u>	
LD50	LD50 > 2.0 gm/kg (males and females)
<u>Data Quality</u>	
Reliable without restriction (Klimisch Code)	
<u>References</u>	
This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).	

Robust Summary 1-Acute Dermal-2

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	97% purity This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	FHSA Regulations 16 CFR 1500.40
Test Type	Acute dermal toxicity
GLP (Y/N)	Y
Year (Study Performed)	1986
Species/Strain	Young, adult New Zealand white rabbits
Sex	Male and female
No. of animals/sex/dose	5
Vehicle	Mineral oil-based material dosed undiluted
Route of administration	Dermal application
Remarks field for test conditions	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.
<u>Results</u>	
Remarks	LD50 > 2.0 gm/kg 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 edema 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. Gross pathological examination of the female rabbits revealed no remarkable findings.

<u>Conclusions</u>	The test article, when dosed as supplied and studied in 5 males and 5 female albino rabbits, appears to have an acute dermal LD50 greater than 2.0 gm/kg.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-Acute Dermal-3

<u>Test Substance</u>	
CAS #	CAS# 67762-55-4
Chemical Name	Alkenes, C15-18 alpha, sulfurized
Remarks	This chemical is also referred to as C15-C18 alkene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	
Test Type	Acute dermal toxicity, single exposure
GLP (Y/N)	Y
Year (Study Performed)	1996
Species/Strain	New Zealand White rabbits
Sex	Male and female
No. of animals/sex/dose	10/dose (5M, 5F)
Vehicle	None, test article was doses as received.
Route of administration	Dermal, to clipped intact,dorsal skin
Remarks field for test conditions	One dermal, semi-occluded patch of test article at 2,000 mg/kg was applied to clipped dorsa skin of each animal. The patches were removed after 24 hours. All animals were observed daily for 14 days following test article administration.
<u>Results</u>	
Remarks	No clinical signs were observed during the study. Erythema and/or edema 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. No visible lesions were observed in any animal at terminal necropsy.
<u>Conclusions</u>	LD50 > 2000 mg/kg
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

4.1.3 Acute Inhalation Toxicity

Robust Summary 1 – Acute Inhalation -1

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Experimental; modified OECD guideline 403
Test Type	Acute inhalation toxicity (4 hours)
GLP (Y/N)	Y
Year (Study Performed)	1990
Species/Strain	Rat; Sprague-Dawley
Sex	Male & Female (9 weeks old at initiation of study)
No. of animals/sex/dose	20 (10M, 10F/group)
Vehicle	Not applicable
Route of administration	Whole body inhalation of vapor from sample heated to 200°C
Remarks field for test conditions	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.
<u>Results</u>	
LC50	> 0.39 mg/l
Remarks	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. Group body weights and weights of liver, kidney and lungs were unaffected by exposure. No treatment related microscopic lesions were observed in the 5 organs examined.

<u>Conclusions</u>	LC50 > 0.39 mg/l of a vapor generated from the starting material at 200°C, not from the whole methyl propene derivative. Vapor approximates conditions of workplace exposure.
<u>Data Quality</u>	Reliable with restrictions. GLP compliant Study performed with two dose groups and is not a limit test. Physical and chemical properties provided with exception of structural formula, purity of starting material.
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1 – Acute Inhalation -2

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	<p>This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	Consistent with EPA Health Effects Guideline OPPTS 870.1300
Test Type	Acute inhalation toxicity
GLP (Y/N)	Y
Year (Study Performed)	1988
Species/Strain	Mouse (CD-1 strain) Guinea pig (Hartley strain)
Sex	Male and female
No. of animals/sex/dose	5
Vehicle	Mineral oil-based material, dosed as supplied
Route of administration	Aerosol inhalation
Dose	4.3 mg/L (limit study)
Remarks field for test conditions	<p>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).</p>
<u>Results</u>	
LC50 (mice) > 4.3 mg/L; LC50 (guinea pigs) > 4.3 mg/L	
Remarks	<p>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</p>

	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.
<u>Conclusions</u>	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.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1 – Acute Inhalation -3

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	<p>This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	Consistent with EPA Health Effects Guideline OPPTS 870.1300
Test Type	Acute inhalation toxicity
GLP (Y/N)	Y
Year (Study Performed)	1988
Species/Strain	Mouse (CD-1 Cobs Swiss Albino) Rat (Sprague-Dawley CD) Guinea pig (Hartley)
Sex	Male and female
No. of animals/sex/dose	5 animals/sex/dose
Vehicle	Mineral oil-based material, dosed as supplied
Route of administration	Aerosol inhalation
Dose	4.3 mg/L (Limit study)
Remarks field for test conditions	<p>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 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).</p>
<u>Results</u>	LC50 (mice) > 4.3 mg/L; LC50 (rat) < 4.3 mg/L; LC50 (guinea pigs) > 4.3 mg/L
Remarks	<p>The test animals received an average analytical exposure concentration of 4.3 mg/L test material with a nominal exposure concentration of 100 mg/L. 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. Mortality and</p>

	<p>physical observations: Three female rats dies 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 post-exposure 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 post-exposure 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.</p>
<u>Conclusion</u>	LC50 (mice) > 4.3 mg/L; LC50 (rat) < 4.3 mg/L; LC50 (guinea pigs) > 4.3 mg/L
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1 – Acute Inhalation -4

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	OECD 403
Test Type	Acute inhalation toxicity
GLP (Y/N)	Y
Year (Study Performed)	1987
Species/Strain	Albino rats of the Sprague-Dawley strain
Sex	Male and female
No. of animals/sex/dose	5 rats/sex/dose
Vehicle	Mineral oil-based material dosed undiluted
Route of administration	Aerosol inhalation
Dose	1.5, 2.5 and 5.6 mg/L (actual concentration)
Remarks field for test conditions	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 details of the whole body exposure are consistent with those described in OECD guideline 403. 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). The LC50 with 95% confidence intervals was computed using the method of Miller and Tainter (1944).
<u>Results</u>	
	LC50 (males) > 5.0 mg/L; LC50 (females) = 2.17 mg/L
Remarks	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%). Remarkable animal 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

	<p>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 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).</p>
<u>Conclusion</u>	<p>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.</p>
<u>Data Quality</u>	<p>Reliable without restriction (Klimisch Code)</p>
<u>References</u>	<p>This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).</p>

4.2 Repeated Dose Toxicity

Robust Summary 1-Repeated Tox-1

<u>Test Substance</u>	
CAS #	CAS# 67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	<p>This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	OECD 407
Test Type	28-day oral toxicity study in rats
GLP (Y/N)	Y
Year (Study Performed)	1991
Species	Rat
Strain	Sprague-Dawley CD, 41 days old at initiation of treatment
Route of administration	Oral gavage (syringe and dosing tube)
Duration of test	28 days of treatment and 14 day recovery period in the control and high dose satellite recovery groups
Doses/concentration levels	0, 100, 300 and 1000 mg/kg/day
Sex	Males and females
Exposure period	28-day treatment duration with a 14 day recovery
Frequency of treatment	7 days/week
Control group and treatment	5 rats/sex/group for each dose, and satellite recovery groups of 5 animals/sex for the control and 1000 mg/kg/day dose. Control group received daily doses of corn oil at 2.0 ml/kg, and treatment groups received the indicated dose of test material diluted in corn oil in a volume not to exceed 2.0 ml/kg
Post exposure observation period	14-days
Statistical methods	Body weight, food consumption, hematology and clinical chemistry parameters, organ weights and organ/body weight ratios were analyzed. Mean values of all dose groups were compared to control at each time interval. Tests included parametric ANOVA with a Dunnett's <i>post-hoc</i> test, non-parametric Kruskal-Wallis and Dunn's rank sum test, Bartlett's test for equal variances, and Student's <i>t</i> -test.
Remarks field for test conditions	<p>Significant deviations from the OECD 407 test guidelines include:</p> <ul style="list-style-type: none"> 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
<u>Results</u>	
Remarks	<p>No NOAEL was assigned to this study.</p> <p>All animals survived throughout the study and physical examinations were generally unremarkable. 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.</p>

	<p>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.</p> <p>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. 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. 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. 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.</p>
<u>Conclusions</u>	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.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-Repeated Tox-2

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	comparable to OPPTS 870.3250
Test Type	Thirteen week dermal subchronic toxicity study
GLP (Y/N)	Y
Year (Study Performed)	1989
Species	Rat
Strain	Sprague Dawley (Tac:N[SD]fBR)
Route of administration	Dermal to shaved skin of backs
Duration of test	5 days/week for 13 weeks
Doses/concentration levels	Part 1:500 and 2000 mg/kg/day undiluted test material; 500 mg/kg/day diluted 50%w/v in 100" mineral oil base stock Part 2: 500, 250, 100, 50, 10 mg/kg/day diluted in mineral oil base stock at concentrations of 25, 10 and 5% w/v respectively 20 (10M,10F/group): 8 treatment groups,1 vehicle control,2 untreated controls
Sex	Male and Female
Exposure period	
Frequency of treatment	
Control group and treatment	1 vehicle control,2 untreated controls Vehicle: mineral oil (100" solvent refined naphthenic base stock) density 0.88 g/ml
Post exposure observation period	
Statistical methods	Analysis of Variance followed by multiple range tests, Serum chemistry and hematology data were evaluated using the F test for ANOVA and Student-Newman-Keuls multiple comparison test.
Remarks field for test conditions	Age at initiation: 7 weeks old following 2 weeks acclimation 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.
<u>Results</u>	
Remarks	<p>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. 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. 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. 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, edema, 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. No effects on sperm motility or morphology were observed in rats treated with 2000 mg/kg/day.</p> <p>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.^a 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.</p>
<u>Conclusions</u>	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)
<u>Data Quality</u>	Reliable without restrictions: Guideline based study performed in accordance with US GLPs.
<u>References</u>	<p>This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).</p> <p>United States Environmental Protection Agency (EPA) 1991. Alpha 2 microglobulin: association with chemically induced renal toxicity and neoplasia in the male rat. P.85 In Risk Assessment Forum, U.S. Govt. Printing Office, Washington, DC</p>

Robust Summary 1-Repeated Tox-3

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Reference for study design: Federal Register, Volume 43, Number 163
Test Type	28 Day Subchronic Dermal Toxicity Study
GLP (Y/N)	Y
Year (Study Performed)	1982
Species	Albino Rabbits
Strain	
Route of administration	Dermal to shaved dorsal trunk area of abraded or intact skin
Duration of test	
Doses/concentration levels	Group 1: 200 mg/kg/day undiluted test material Group 2: 2000 mg/kg/day undiluted test material 36 animals tested: (6M,6F/group): 2 treatment groups, 1 untreated control
Sex	Male and female
Exposure period	
Frequency of treatment	
Control group and treatment	1 untreated control group (6M/6F)
Post exposure observation period	
Statistical methods	All data was submitted to analysis of variance (method: Statistical Analysis System, SAS Statistical Institute 1979) followed by evaluation using the Newman-Keuls method for all significant dose differences.
Remarks field for test conditions	Age at initiation of treatment: Not specified following 1 week acclimation. 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 included clinical observations, skin irritation scoring 5 days per week, body weights (pretest, every 3 to 4 days during testing, termination), hematology ,

	serum chemistry and urinalysis at pretest and termination, and gross necropsy evaluations at study termination.
<u>Results</u>	
Remarks	<p>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. 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. 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. Gross and histopathological examination of tissues did not reveal any pattern of changes attributable to dermal contact with the test material.</p> <p>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</p>
<u>Conclusions</u>	<p>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.</p>
<u>Data Quality</u>	Reliable with restrictions. Animal ages were not included in the report. Uneven sex distribution. Clinical behavior determinations beyond that of morbidity were not included in the report.
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-Repeated Tox-4

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	None cited
Test Type	21 Day Repeated Dose Dermal Toxicity Study
GLP (Y/N)	N
Year (Study Performed)	1979
Species	Rabbit
Strain	New Zealand White
Route of administration	Dermal to shaved skin of backs and sides
Duration of test	21 days
Doses/concentration levels	40 animals tested: 3 treatment groups (7M/3F, 8M/2F, 6M/4F), 1 untreated control (5M/5F) Group 1: 140 mg/kg/day undiluted test material Group 2: 560 mg/kg/day undiluted test material Group 3: 2240 mg/kg/day undiluted test material
Sex	Male and female
Exposure period	
Frequency of treatment	
Control group and treatment	1 untreated control (5M/5F)
Post exposure observation period	
Statistical methods	None cited.
Remarks field for test conditions	Age of animals at initiation: Not specified following at least 2 weeks acclimation. 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.

<u>Results</u>	
Remarks	<p>All rabbits survived the duration of the test. 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. Edema 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 edema was slight to moderate. No irritation was observed in the control group. Urinalysis values were normal in all groups. Several individual and isolated hematological and serum chemistry values were out of expected range but with no discernible treatment related changes in the mean values for all groups. 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.</p> <p>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, <i>in-life</i> dermal observations revealed severe erythema responses in all treated rabbits and none in the sham treated control group.</p>
<u>Conclusions</u>	<p>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.</p>
<u>Data Quality</u>	<p>Reliable with restrictions. Animal age and organ weight data were not included in the report. The test site was not occluded following test material application.</p>
<u>References</u>	<p>This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).</p>

Robust Summary 1-Repeated Tox-5

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	OECD 412
Test Type	4-week inhalation toxicity study in rats
GLP (Y/N)	Y
Year (Study Performed)	1989
Species	Rat
Strain	Sprague-Dawley CD, 7 weeks old at initiation of treatment
Route of administration	Aerosol inhalation
Duration of test	4 weeks of treatment for all doses, and a 3 week recovery period in the control and high dose satellite recovery groups
Doses/concentration levels	0, 15, 50 and 150 mg/m ³
Sex	Males and females
Exposure period	4 weeks of inhalation treatments followed by a 3 week recovery period
Frequency of treatment	Inhalation treatment for 6 hours/day, 5 days/week for 4 weeks at the target concentrations
Control group and treatment	10 rats/sex/group for the low and mid dose levels, 15 male and 20 female rats for the high dose level group. Control rats (15 males and 20 females) received mineral oil only at a level of 150 mg/m ³ , while in the exposure chamber.
Post exposure observation period	
Statistical methods	Body weight, food consumption, hematology and clinical chemistry parameters, organ weights and organ/body weight ratios were analyzed. Mean values of all dose groups were compared to control at each time interval. Tests included parametric ANOVA with a Dunnett's <i>post-hoc</i> test, non-parametric Kruskal-Wallis and Dunn's rank sum test, Bartlett's test for equal variances, and Student's <i>t</i> -test.
Remarks field for test conditions	The rats were exposed on each treatment day for 6 hours to the test material (target concentrations = 15, 50, 150 mg/m ³) 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 details of the whole body exposure are consistent with those described in OECD guideline 412. The actual exposure concentrations as measured by gravimetric analysis were 15, 50 and 160 mg/m ³ . 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

	<p>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.</p>
<p><u>Results</u></p>	
<p>Remarks</p>	<p>No NOAEL was assigned to this study.</p> <p>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. Mortality: 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. 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. Hematology: 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 post-exposure and post-recovery time intervals. However, these differences did not correlate with dose, with sex, with potential target organs or with sacrifice interval. 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 (see below). 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 teste, heart, lung and spleen weights were recorded. These effects were not accompanied by pathologic microscopic findings, and therefore, the biological significance was</p>

	<p>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 cortico-medullary 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.</p>
<u>Conclusions</u>	No NOAEL was assigned to this study.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-Repeated Tox-6

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	<p>This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	Consistent with OECD 410 and OPPTS 870.3200
Test Type	28-day dermal toxicity study in rats
GLP (Y/N)	Y
Year (Study Performed)	1988
Species	Rat
Strain	Sprague-Dawley CD, 21 days old at initiation of treatment
Route of administration	Test material applied topically to shaved, unabraded skin (semi-occluded dressing)
Duration of test	28 days
Doses/concentration levels	1000 mg/kg/day (limit study)
Sex	Males
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.
Post exposure observation period	
Statistical methods	Continuous data including body weight, body weight gain and food consumption was analyzed by analysis of variance.
Remarks field for test conditions	
<u>Results</u>	
Remarks	<p>No NOAEL was assigned to this study.</p> <p>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. 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. These responses were characterized by erythema, eschar and flaking of the skin that persisted over the majority of the 28-day treatment period.</p>

<u>Conclusions</u>	No NOAEL was assigned to this study. All animals survived throughout the study and physical examinations were generally unremarkable.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

4.3 Toxicity to Reproduction

Robust Summary 1-ReproTox-1

<u>Test Substance</u>	
CAS #	<u>CAS# 67124-09-8</u>
Chemical Name	2-Propanol, 1-(tert-dodecylthio)-
Remarks	This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	OECD 415
Test Type	Oral (Gavage) One-Generation Reproductive Toxicity Study
GLP (Y/N)	Y
Year (Study Performed)	2001
Species	Rat
Strain	Sprague-Dawley Crl: CD®(SD) IGS BR rats, 71 days of age at initiation of treatment
Route of administration	Orally by gastric intubation
Duration of test	F ₀ males- 70 days pre-mating; mating period through completion of parturition. F ₀ females- 14 days pre-mating; mating; 25 days of gestation and 20 days of lactation. F ₁ pups- gestation through day 20 of lactation.
Doses/concentration levels	0, 50, 167 and 500 mg/kg/day
Vehicle control	<u>Corn Oil</u>
Dose volume	2.5 mL/kg
Sex	<u>Males and females</u>
Frequency of treatment	Once/day, 7 days/week
Analytical confirmation of concentration.	Homogeneity, stability and weekly dose concentration confirmation.
Control and treatment groups	28 F ₀ rats/sex/group in the control, low, mid and high dose groups.
Mating	1 male mated to 1 female from the same group until evidence of mating (presence of copulatory plug or sperm) was observed. If evidence of mating was not observed mating was discontinued after three weeks.
Post exposure observation period	<u>None</u>
Statistical methods	Pup ratios, pup survival indices, mean number stillborn and dead pups and parental fertility indices were evaluated using the Chi-square test. F ₀ body weights and gains, gestation and lactation body weights and gains, parenteral food consumption, mean litter weights, length of gestation, live litter size and organ weights were evaluated using ANOVA (two-tailed) with Dunnett's test. Histopathological findings were evaluated using the Kolmogorov-Smirnov (one-tailed) test. Post implantation loss was analyzed using the Mann-Whitney U Test.
Dose rangefinding study	None

Remarks field for test conditions

F₀ Generation:

All F₀ males were dosed for 70 days prior to mating and through the completion of parturition. All F₀ females were dosed for 14 days prior to mating and through day 20 of lactation. All F₀ animals were examined twice daily for appearance and behavior. Detailed clinical observations were performed weekly and cage side observations were performed daily approximately thirty to ninety minutes post dosing. Body weights were recorded weekly for both sexes prior to mating; maternal body weights were recorded on gestation days 0, 7, 14 and 21 as well as on lactation days 1, 4, 7, 14 and 21. Food consumption was recorded on the same days as body weights except during mating the period and during lactation. Animals were paired 1:1 for mating. Positive evidence of mating was confirmed by the presence of sperm or a vaginal copulatory plug (day 0 of gestation). If evidence of mating was not present after three weeks, mating was discontinued. All of the surviving F₀ females were allowed to deliver and rear their pups to lactation day 21. The offspring were potentially exposed to the test substance *in utero* and through nursing during lactation days 1-21 until euthanization on post-natal day 21. Hematology evaluations were performed on 10 males and 10 females /group prior to their scheduled termination. The surviving F₀ dams were necropsied on lactation day 21, following a minimum of 60 days of dosing. The surviving F₀ males were necropsied at the conclusion of parturition following a minimum of 96 days of dosing. The F₀ females with total litter loss were necropsied within 24 hours. F₀ females that failed to deliver were necropsied on post-mating day 25 (with evidence of mating) or 25 days following the termination of the mating period (with no evidence of mating).

Organ weights were determined and microscopic examinations were conducted for all surviving control and high dose F₀ animals. Tissues examined microscopically included the liver, kidney, brain, right epididymides, cervix, coagulation gland, ovaries, pituitary, prostate, seminal vesicles, testes, uterus, vagina and gross lesions.

F₀ animals from all groups found dead or sacrificed early were subjected to a gross necropsy and the microscopic evaluation of all tissues.

Sperm was collected from all surviving F₀ males and evaluated for sperm count, concentration, motility and morphology assessment.

F₁ Generation:

On lactation day 4 each litter was randomly culled to a maximum of eight pups, 4/sex/litter, when possible. Detailed pup examinations were performed on lactation days 0, 4, 7, 14 and 21. Pup sex was determined on lactation day 0 and verified on lactation days 4, 7, 14 and 21. Individual pup weights were determined on lactation days 1, 4, 7 14 and 21. Pups that were stillborn, cannibalized or found dead were subjected to a gross necropsy with emphasis on developmental morphology. Pups culled on day 4 were subjected to an abbreviated gross necropsy with emphasis on the reproductive system. All surviving pups

	<p>were euthanized on lactation day 21 and examined macroscopically. All internal gross lesions were preserved for possible future microscopic examination.</p>
<p><u>Results</u></p>	<p>Results of the homogeneity analysis indicate that the test article was homogeneous in the vehicle and stable for more than one week when stored under ambient conditions. Concentration analysis confirmed that the test article was at the appropriate concentration in the dosing solutions.</p> <p><i>F₀ Generation:</i></p> <p>F₀ males exhibited a significant increase in post dosing salivation in the mid and high dose groups and lower mean body weights (5-7% compared to controls) in the high dose group. The remaining F₀ male parameters were unremarkable including: mean food consumption, mating and fertility indices, hematology data, absolute and relative organ weights, sperm evaluation parameters and macro and microscopic pathology.</p> <p>F₀ females in the low, mid and high dose groups exhibited a low incidence of reddish vaginal discharge, mammary gland swelling and dark material around the eyes and nose. The mid and high dose females exhibited a low incidence of salivation prior to dosing, an increased incidence of urine stain and a dose related increase in post dosing salivation. The high dose females also exhibited a low incidence of ocular discharge. Two females in the low dose group delivered all stillborn pups. The number of females with live born pups was 25, 24, 27 and 26 in the control, low, mid and high dose groups respectively. There were no toxicologically meaningful differences between the control low, mid and high dose groups with respect to F₀ female mean body weights, body weight change, food consumption, mating and fertility indices, pre-coital intervals, gestation length or mean hematology values. Macroscopic findings observed in one high dose female sacrificed on post breeding day 25 included dark red/brown fluid in the uterus and vagina, and one small placenta and two nonviable pups in the vagina. No other remarkable findings were noted in the F₀ females at necropsy and no meaningful microscopic lesions were observed in any of the treated F₀ females.</p> <p><i>F₁ Generation:</i></p> <p>The total and mean number of F₁ pups delivered was comparable between the control and treated groups. However the number of F₁ liveborn pups in the low dose group was statistically lower than control. This was attributed to the higher number of still born pups, primarily from two females in this group that experienced total litter losses. The number of live pups/litter was comparable between the control and treated groups throughout lactation. Sex ratios were comparable to control in all treated groups on lactation days 0 and 21. Mean pup weights were statistically lower than control in the mid dose group on lactation day 14 and in the high dose group on lactation days 14 and 21, however, the mean pup weights of these groups remained within the range of the test facilities historical control data. With the exception of a slight increase in the incidence of pups that were cool to the touch, no remarkable pup observations were noted during lactation.. No significant necropsy</p>

	findings were noted for stillborn pups, pups found dead, pups culled on day 4 or pups sacrificed on lactation day 21.
<u>Conclusions</u>	Based on the results of this study the Study Director concluded that the 50 mg/kg/day dose level was the no observed adverse effect level (NOAEL) for parental F ₀ toxicity. There were no indications of impaired fertility or other reproductive effects in the parental males or females at doses up to 500 mg/kg/day. A dose level of 50 mg/kg/day was considered the (NOAEL) for developmental effects, as a result of decreased pup weights in the mid and high dose groups during the latter half of gestation.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	Unpublished confidential business information

4.4 Genetic Toxicity

Robust Summary 1-GenTox-1

<u>Test Substance</u>	
CAS #	CAS# 67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Consistent with guidelines outlined in OECD 471 and 472
Test Type	Reverse mutation assay
System of testing	Bacterial
GLP (Y/N)	Y
Year (Study Performed)	1988
Species/Strain	Salmonella typhimurium TA98, TA100, TA1535, TA1537 Escherichia coli WP-2
Metabolic activation	With and without
Concentrations	0 , 15, 50, 150, 500, 1500 and 5000 microgram/plate (DMSO vehicle)
Statistical methods	Revertant colonies were scored using an electronic colony counter. The mean number of revertants/plate and the standard deviation was calculated for each concentration and strain. A significant effect was considered to be a two-fold increase in revertants when the background was 50 revertant/plate or greater; a three-fold increase when the background was between 10 and 49 revertants/plate; and a four-fold increase when the background was less than 10 revertants/plate.
Remarks field for test conditions	No significant deviations from guideline protocols
<u>Results</u>	
Remarks	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.
<u>Conclusions</u>	The test material was assayed for its ability to induce mutations in Salmonella typhimurium and Escherichia coli in the presence and absence of a metabolic activation system. At the concentrations tested and under the conditions of the assay, the test material was considered to be non-mutagenic.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-GenTox-2

<u>Test Substance</u>	
CAS#	68511-50-2
Chemical name	1-propene, 2-methyl- sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for the Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/guideline followed	Consistent with guidelines outlined in OECD 471
Test Type	Reverse Mutation Assay
System of testing	Bacterial
GLP (Y/N)	No
Year (study performed)	1978
Species/Strain	<i>Salmonella typhimurium</i> strains TA1535, TA100, TA1537, TA1538, and TA98
Metabolic activation	Test conducted with and without metabolic activation Adult male Sprague-Dawley rat liver S-9 fraction, induced with Aroclor 1254 100 ul/plate
Concentrations	0, 0.01, 0.05, 0.1, 0.5, 1.0 ul of test agent per plate with and without metabolic activation
Statistical Methods	Determination of mean \pm S.D. of replicate plate counts
Remarks Field for Test Conditions	The vehicle was DMSO; All stock and working solutions were stored at 4°C in glass screw-capped 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.
<u>Results</u>	
Remarks	For all strains and dose levels with and without metabolic activation, the criteria for a positive mutagens (at least 3 times the number of colonies as the controls for spontaneous reversion) was not met.

Robust Summary 1-GenTox-3

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	97% purity This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Consistent with guidelines outlined in OECD 471
Test Type	Reverse mutation assay
System of testing	Bacterial
GLP (Y/N)	Y
Year (Study Performed)	1982
Species/Strain	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538
Metabolic activation	With and without
Concentrations	0, 0.01, 0.03, 0.1, 0.3, and 1 microliter/plate (DMSO vehicle)
Statistical methods	The mean number of his ⁺ revertants/plate for three replicate assay plates was calculated for each concentration and strain.
Remarks field for test conditions	No significant deviations from guideline protocols
<u>Results</u>	
Remarks	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 non-mutagenic 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 ⁺ 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.
<u>Conclusions</u>	The test material did not produce significant mutation in any of the Salmonella strains in the quantitative mutagenesis assay, either in the presence or absence of metabolic activation. Thus, under the conditions of the assay employed, the test material was determined to be non-mutagenic in the Salmonella/microsome mutagenesis assay.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-GenTox-4

<u>Test Substance</u>	
CAS #	CAS# 67762-55-4
Chemical Name	Alkenes, C15-18 alpha, sulfurized
Remarks	This chemical is also referred to as C15-C18 alkene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Designed to be in compliance with microbial mutagenicity testing as set forth by OECD 1981, EPA 1982, FDA 1993
Test Type	Reverse mutation assay
System of testing	Bacterial
GLP (Y/N)	Y, except analyses were not performed to verify the homogeneity, stability or accuracy of the test/control article preparation
Year (Study Performed)	1996
Species/Strain	Salmonella typhimurium – TA1535, TA1537, TA98, TA100 and TA102 Escherichia coli – WP2 uvrA
Metabolic activation	With and without
Concentrations	Prescreen, duplicate cultures: 50.0, 167, 500, 1670, and 5000 microgram/plate, plus control Triplicate cultures: 50.0, 167, 500, 1670, 5000 and 10,000 micrograms/plate
Statistical methods	Statistical analyses are performed using the program developed by Snee and Irr (1981), with significance established at the 95% confidence limit.
Remarks field for test conditions	Test article was first evaluated in a prescreen using both liquid pre-incubation 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.
<u>Results</u>	
Remarks	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.
<u>Conclusions</u>	The results were negative in this study, using liquid pre-incubation and plate incorporation treatments.
<u>Data Quality</u>	Reliable with restriction (Klimisch Code). No analyses to verify test article preparation.
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-GenTox-5

<u>Test Substance</u>	
CAS #	CAS# 67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	100% purity This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	Consistent with EPA guidelines outlined in OPPTS 870.5375
Test Type	In vitro chromosomal aberration assay
System of testing	Non-bacterial
GLP (Y/N)	Yes
Year (Study Performed)	1989
Species/Strain	Chinese hamster ovary (CHO) cells
Metabolic activation	S9 fraction prepared from livers of Aroclor 1254-induced Sprague-Dawley rats
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
Statistical methods	Metaphase cells were analyzed for chromosomal aberrations by 100x objective microscopy. The mitotic index was determined by counting a minimum of 500 total cells. Coordinates of cells with aberrations were recorded. The data were analyzed statistically using the method described in Margolin et al., Statistical analysis for in vitro cytogenetic assay using Chinese hamster ovary cells, Environ Mutagen 8:183-204, 1986.
Remarks field for test conditions	No significant deviations from guideline protocols
<u>Results</u>	
Remarks	The test material was investigated for its ability to induce chromosomal aberrations in Chinese hamster ovary (CHO) cells in the presence and absence of a rat liver homogenate metabolic activation system. CHO cells were seeded at a density of 0.5 or 0.75 x 10 ⁶ and maintained in essential culture medium in tissue culture flasks. Twenty-four hours later, the cells were exposed to test material, positive or negative controls. The compound was dissolved in DMSO, which served also as the negative control. The test concentrations that were tested for the induction of aberrations ranged from 0.05 to 4950 ug/ml in the non-activated assays, and from 0.05 to 150 ug/ml in the activated assays. All test sample concentration and controls were tested in duplicate flasks. Two assay periods were used, 10 and 20 hours, which totaled four independent experiments. The data were analyzed using two methods. Two hours prior to harvest, vinblastine sulfate was added to arrest the cells in metaphase. At the end of the incubation period, metaphase cells were collected by treatment with trypsin, concentrated by centrifugation, lysed in hypotonic solution, fixed in methanol: acetic acid and stained with Giemsa. The first used the traditional method in which gaps were not counted as chromosomal aberrations while the second method counted gaps as chromosomal aberrations. One hundred cell were scored from each duplicate flask for each concentration tested. The test substance was toxic to the CHO cells in

	<p>the non-activated assays at concentrations higher than 15 ug/ml for the 20-hour exposure period (86% reduction in the mitotic index), and at 50 ug/ml for the 10-hour exposure period (.90% reduction of the mitotic index). There was no significant increase in the percentages of aberrant cells in the 10 (4% vs. 4.5% vehicle control) and 20-hour (4% vs 3% vehicle control) non-activated assays. In contrast, the positive control mitomycin C (0.3 ug/ml) caused a significant increase in the percentage of cells with aberrations (approximately 85%). In the activated assays, cells were exposed simultaneously to test material and S9 microsomal fraction with isocitrate cofactors for 10-20 hours. After this period the cells were washed, re-incubated for 8 hours prior to metaphase arrest and chromosomal staining. Concentrations greater than 50 ug/ml for the 20-hour period and 15 ug/ml for the 10-hour exposure period were toxic (> 90% reduction in mitotic index for each incubation period). There was no increase in the percentage of aberrant cells in the 20-hour activated experiment (4.6% vs 4.5% vehicle control). A slight increase in aberrant cells was observed at 5 ug/ml in the 10-hour activated assay, however, this increase was not statistically significant (17.8% vs 14.5 % vehicle control). The positive control (benzo[a]pyrene; 15 ug/ml) caused aberration in nearly 100% of CHO cells in the 20-hour activated assay and 46% in the 10-hour activated assay, thus, demonstrating the efficacy of the metabolic activation system.</p>
<u>Conclusions</u>	<p>The test material was assayed for its ability to induce chromosomal aberrations in in vitro culture of Chinese hamster ovary cells in the presence and absence of a metabolic activation system. At the concentrations tested and under the conditions of the assay, the test material was considered to be non-clastogenic.</p>
<u>Data Quality</u>	<p>Reliable without restriction (Klimisch Code)</p>
<u>References</u>	<p>This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).</p>

Robust Summary 1-GenTox-6

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	OECD 474.
Test Type	Mammalian bone marrow erythrocyte micronucleus test
GLP (Y/N)	Y
Year (Study Performed)	1989
Species	Mouse
Strain	B6C3F1
Sex	Male and female
Route of administration	Intraperitoneal
Doses/concentrations	Single injection of 3.5 g/kg test material, 50 mg/kg cyclophosphamide in saline, or methylcellulose vehicle alone (vehicle = hydroxypropyl methylcellulose (Methocel K4M Premium - Dow Chemical)) 15 animals (5M, 5F/dose/sample interval); Positive control (5M,5F)
Exposure Period	Single dose
Statistical methods	Normal test for equality of proportion (one-tailed). Because of multiplicity of comparisons, a Dunnett adjustment was made.
Remarks field for test conditions	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.
<u>Results</u>	
Remarks	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 mironucleated PCEs in femoral bone marrow for

	<p>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.</p>
<u>Conclusions</u>	<p>Methyl propene derivative administered IP at 3.5 g/kg body weight did not induce the formation of micronuclei in PCEs in male or female mice at any time interval and is not considered clastogenic in this test system.</p>
<u>Data Quality</u>	<p>Reliable without restrictions. Guideline study.</p>
<u>References</u>	<p>This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).</p>

Robust Summary 1-GenTox-7

<u>Test Substance</u>	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	modified OPPTS 870.5395
Test Type	Mammalian bone marrow erythrocyte micronucleus test; adjunct to 13 week dermal subchronic toxicity study
GLP (Y/N)	Y
Year (Study Performed)	1987
Species	Rat
Strain	Sprague Dawley (Tac:N[SD]fBR)
Sex	Male and female
Route of administration	dermal to shaved skin of backs
Doses/concentrations	500 and 2000 mg/kg/day undiluted test material; 500 mg/kg/day diluted 50%w/v in 100" mineral oil base stock 10 (5M,5F/group): 3 treatment groups,1 untreated controls vehicle = mineral oil (100" solvent refined naphthenic base stock) density 0.88 g/ml
Exposure Period	5 days/week for 13 weeks
Statistical methods	SAS ANOVA and ANOVA F test; Tukey's Studentized Range test and Scheffe's test; SAS General Linear Model, a studentized linear regression analysis to determine dose responsiveness. Statistical analyses compared test values to negative control data; a significant increase in micronuclei is an indicator of clastogenic activity by the test material
Remarks field for test conditions	Age at initiation: 7 weeks old following 2 weeks acclimation 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.
<u>Results</u>	
Remarks	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.
<u>Conclusions</u>	Methyl propene derivative does not cause chromosome damage in rats following regular and prolonged dermal exposure in this test system. NOEL= 2000 mg/kg/day
<u>Data Quality</u>	Reliable with restrictions. Study does not include a positive control. Samples were collected only once approximately 24 hours after the final dose. Information on test material composition, purity and stability are not part of this report but are referred to the 13 week subchronic study report.
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).

Robust Summary 1-GenTox-8

<u>Test Substance</u>	
CAS #	CAS# 68515-88-8
Chemical Name	Pentene, 2,4,4-trimethyl-, sulfurized
Remarks	97% purity This chemical is also referred to as trimethyl pentene derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.
<u>Method</u>	
Method/Guideline followed	OECD 474
Test Type	Mammalian erythrocyte micronucleus test
GLP (Y/N)	Y
Year (Study Performed)	1988
Species	Mouse
Strain	B6C3F1
Sex	Male and female
Route of administration	Oral gavage
Doses/concentrations	5 gm/kg (limit dose)
Exposure Period	One dose, dose groups sacrificed after 18, 24 and 48 hours
Statistical methods	Group mean body weights, total polychromatic erythrocytes (PCEs), normochromatic erythrocytes (NMEs), PCEs with micronuclei, and NMEs with micronuclei were compared. For each animal, a minimum of 1000 PCEs were counted for the presence of micronucleated PCEs. The frequency of micronucleated cells per animals was expressed as the number of micronucleated PCEs per 1000 PCEs counted. The ratio of PCEs/NMEs was also recorded. The data were analyzed for statistical significance on a binomial distribution, at a level of significance of 0.05, and using the table of Kastenbaum and Bowman (Mutation Res. 9:527-549, 1970).
Remarks field for test conditions	# 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.
<u>Results</u>	
Remarks	The frequency of 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

	<p>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/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.</p>
<u>Conclusions</u>	<p>The subject material was tested for its genotoxicity using mouse in vivo micronucleus screening assay in bone marrow. There was no significant increase in micronucleated PCEs in animals exposed to the test substance. Thus, the test material was negative in this assay.</p>
<u>Data Quality</u>	<p>Reliable without restrictions (Klimisch code)</p>
<u>References</u>	<p>This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).</p>

Robust Summary 1-GenTox-9

<u>Test Substance</u>	
CAS #	CAS # 91770-97-4
Chemical Name	Alkyl (C12-C16) sulfide.
Remarks	<p>This chemical is an analog to the C15-C18 alkene derivative (CAS # 67762-55-4; Alkenes, C15-18 alpha, sulfurized) in the HERTG's Test Plan for Alkyl Sulfide Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Alkyl Sulfide Category.</p>
<u>Method</u>	
Method/Guideline followed	Method consistent with OECD 474 and EPA OPPTS 870.5395
Test Type	Mouse micronucleus test
GLP (Y/N)	Y
Year (Study Performed)	1996
Species	Mice
Strain	B6C3F1
Sex	Male
Route of administration	Intraperitoneal
Doses/concentrations	0, 500, 1000, and 2000 mg/kg/day, plus negative control (vehicle = corn oil) and positive control (= cyclophosphamide)
Exposure Period	Three consecutive days
Statistical methods	Statistical analysis was not performed on the frequency of micronucleated PCEs since test article animals had lower average numbers of micronucleated PCEs compared to controls.
Remarks field for test conditions	<p>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.</p> <p>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.</p> <p>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.</p>
<u>Results</u>	
Remarks	<p>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</p>

	confirmed the reliability that the test system was capable of detecting compounds that induce micronuclei.
<u>Conclusions</u>	The test article did not cause an increase in micronuclei in developing erythrocytes in bone marrow from male B6F3C1 mice at the doses tested. There was a slight cytotoxic effect on developing erythrocytes at 2000 mg/kg/day, the maximum dose typically used in the mouse micronucleus phase.
<u>Data Quality</u>	Reliable without restrictions.
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).