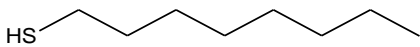
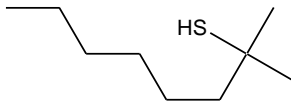
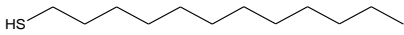
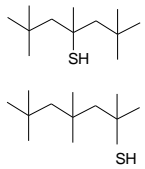
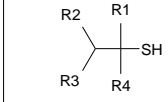


SIDS INITIAL ASSESSMENT PROFILE

Category Name	C8-C12 Aliphatic Thiols Category	
CAS No.	111-88-6 25360-10-5 112-55-0 25103-58-6	
Chemical Names	1-Octanethiol 1,1-Dimethyl-heptanethiol 1-Dodecanethiol Tertiary-Dodecanethiol	
Structural Formulae	 <p>1-Octanethiol (<i>n</i>-Octyl Mercaptan)</p>	 <p>1,1-Dimethyl-heptanethiol (<i>t</i>-Nonyl Mercaptan)</p>
	 <p>1-Dodecanethiol (<i>n</i>-Dodecyl Mercaptan)</p>	  <p>Tertiary-Dodecanethiol (<i>t</i>-Dodecyl Mercaptan) Various Isomers</p> <p>$R1 + R2 + R3 + R4 = C10$</p>
SUMMARY CONCLUSIONS OF THE SIAR		
<p>The members of the C8-C12 Aliphatic Thiols category are straight or branched aliphatic carbon chains containing a sulfhydryl functional group. The members of this category are all high molecular weight aliphatic thiols with a carbon number of C8 through C12. The representative structures (see above) represent the predominant isomer (> 95%) associated with each category member. With respect to <i>t</i>-dodecyl mercaptans, the predominant species is C₁₂H₂₅SH; however, there are also C10-C13 isomers (<2%) present because the commercial production process does not result in a single isomer. It is a complex mixture of 100+ structural isomers. The prevalent isomer will be highly branched and vary depending on product type but remains predominantly C12 rich. Similarly, <i>t</i>-nonyl mercaptan represents many different branched, C9 mercaptan isomers.</p> <p>The category is based on the presumed common metabolism of alkyl thiols. It is generally recognized that thiols are metabolized via several different pathways in vertebrates that include: S-methylation, resulting in a methyl thioether that undergo S-oxidation; reaction with glutathione to form mixed disulfides (the likely form in circulation); oxidation forming sulfenic acids that undergo further metabolism yielding sulfinic and sulfonic acids, and finally oxidative desulfuration. Each of these cellular pathways would provide supporting evidence of the likely metabolism for the members of this category. Trends in physicochemical properties (e.g. increasing log K_{ow} with increasing carbon chain) and similar stability in water support the grouping of these chemicals. Available data for human health suggest that a range of acute local effects are observed, and for repeated exposures, both local and systemic effects may be seen. Therefore, read-across from one category member to another may only be appropriate for systemic toxicity (see below). A trend for acute ecotoxicity is expected. However the low water solubility and the high degree of branching of some of the category members may cause deviation from the trends. For <i>n</i>-octyl mercaptan, the predicted value for acute toxicity to fish is close to the measured value.</p>		

Data availability used for human health endpoints for the C8-C12 Aliphatic Thiols Category

Substance	CAS No.	Repeated-Dose Toxicity	Effects on Fertility	Developmental Toxicity	Gene Mutations	Chromosomal Aberrations
<i>n</i> -Octyl Mercaptan	111-88-6	X	X	X	X	X
<i>t</i> -Nonyl Mercaptan	25360-10-5	O	O	O	X	O
<i>n</i> -Dodecyl Mercaptan	112-55-0	X	O	X	X	O
<i>t</i> -Dodecyl Mercaptan	25103-58-6	X	O	X	X	X

X = data available; O = experimental data not available

Data availability used for ecotoxicity endpoints for the C8-C12 Aliphatic Thiols Category

Substance	CAS No.	Acute Toxicity to Fish	Acute Toxicity to Aquatic Invertebrates	Toxicity to Aquatic Plants
<i>n</i> -Octyl Mercaptan	111-88-6	X	X	X
<i>t</i> -Nonyl Mercaptan	25360-10-5	O	O	O
<i>n</i> -Dodecyl Mercaptan	112-55-0	O	X	X
<i>t</i> -Dodecyl Mercaptan	25103-58-6	O	X	O

X = data available; O = experimental data not available

Physico-chemical Properties

The C8-C12 mercaptans (*n*-octyl, *t*-nonyl, *n*-dodecyl, and *t*-dodecyl) are liquids at room temperature. The respective measured (and EPISuite v 4.1 calculated) melting points are -49.2 (-28.3), -43.2 (-21.4), -8.0 (15.7), and $\leq -20^\circ\text{C}$ (11.9); the measured (and calculated) boiling points are 199.1 (195.1), 188 (195.1), 274 (268.4), and 156°C (251.4); the measured (and calculated) vapour pressures are 0.57 (0.46), 0.71 (0.87), 0.01 (0.01), 0.2 (4.0) hPa (all at 25°C); the measured water solubility values are 4 at 25°C (22.6 at 25°C calculated), 9.6 at 25°C (calculated), < 1 at 22°C (0.3 at 25°C calculated), 0.25 at 20°C (0.3 at 25°C calculated) mg/L; the octanol log K_{ow} values are 4.21 (calculated), 4.59 (calculated), > 6.2 (measured), > 6.2 (measured), respectively. The calculated Henry's law constants are 0.019, 0.025, 0.059, and 0.059 $\text{atm}\cdot\text{m}^3/\text{mol}$.

Human Health

No toxicokinetic, metabolism or distribution studies were identified for any of the C8-C12 Aliphatic Thiols. A description of the likely metabolism of the C8-C12 Aliphatic Thiols is summarized above in the category rationale.

Acute toxicity data are available for the inhalation, dermal and oral routes of exposure. In rats, the inhalation 4-hour LC_{50} values range from > 40 ppm (0.24 mg/L) [*n*-octyl mercaptan] to > 1074 ppm (7.04 mg/L) [*t*-nonyl mercaptan]. Clinical signs included signs of irritation during exposure and ataxia, lethargy, salivation, lacrimation and piloerection following exposure. The dermal LD_{50} value following 24-hour exposure is greater than 1700 mg/kg bw in rabbits [*n*-octyl mercaptan] and greater than 2000 mg/kg bw in rats [*n*-octyl, *t*-nonyl and *n*-dodecyl mercaptans]. Erythema and induration were observed in one study with *n*-octyl mercaptan. In rats, the oral LD_{50} values are 1293 mg/kg bw [*n*-octyl mercaptan], 5550 mg/kg bw [*t*-nonyl mercaptan] and greater than 5000 mg/kg bw [*n*-dodecyl mercaptan]. Clinical signs included abnormal posture, decreased activity, ataxic gait, tremors and lacrimation [*n*-octyl mercaptan].

n-Octyl mercaptan and *t*-nonyl mercaptan are, at most, slightly irritating to rabbit skin. *t*-Dodecyl mercaptan and *n*-dodecyl mercaptan are irritating and corrosive to rabbit skin, respectively. *n*-Octyl and *t*-nonyl

mercaptans are slightly irritating to the eyes of rabbits. Based on the available data, the C8-12 Aliphatic Thiols category members are irritating to rabbit skin and eyes. Respiratory irritation was observed after repeated inhalation exposure of rats to ***n*-dodecyl mercaptan**. In addition, the C8-C12 Aliphatic Thiols category members are considered to be weak to moderate skin sensitizers in guinea pigs and humans. Repeated-dose toxicity studies are available via the inhalation route for ***n*-dodecyl mercaptan** and ***t*-dodecyl mercaptan** and via the oral route for ***n*-octyl mercaptan**.

Systemic Toxicity: In a 4-week inhalation toxicity study (comparable to OECD TG 407), rats were exposed (whole body) to nominal concentrations of 0, 0.5 (0.004 mg/L), 2.0 (0.016 mg/L), or 7.0 ppm (0.058 mg/L) (measured 0, 0.44, 1.7, or 7.7 ppm, respectively) ***n*-dodecyl mercaptan** for six hours/day, five days/week. Signs of respiratory and dermal irritation were observed at the high concentration more frequently as the exposure period progressed. Body weight reduction in males (7.0 ppm; 0.058 mg/L) and reduced food consumption in both sexes (2.0 and 7.0 ppm; 0.016 and 0.058 mg/L, respectively) were observed. At 7.0 ppm (0.058 mg/L), both sexes showed increased AST and ALT levels; males also had increased urea nitrogen levels. However, there were no microscopic changes in the liver or kidneys. Macroscopic changes in the 7.0 ppm (0.058 mg/L) group consisted of skin irritation and enlargement of superficial lymph nodes. At 7.0 ppm (0.058 mg/L), the most marked microscopic findings were as follows: acanthosis (10/10 males and females), hyperkeratosis (10/10 males and females), and chronic active inflammation in the skin (8/10 males and 9/10 females) and secondary changes in regional lymph nodes in a few animals (3/10 males and 1/10 females). The NOAEC for systemic toxicity was 2.0 ppm (0.016 mg/L).

Local Effects: There was no evidence of respiratory damage; however, ***n*-dodecyl mercaptan** did appear to be a skin irritant at 7.0 ppm (0.058 mg/L). Similar exposure to dogs resulted in skin irritation but no other evidence of toxicity; the NOAEC was 2.0 ppm (0.016 mg/L). Similar exposure to mice resulted in death of all mice at 7.0 ppm (0.058 mg/L) by week 3. No exposure-related effects were observed at 0.5 (0.004 mg/L) or 2.0 ppm (0.016 mg/L); the NOAEC was 2.0 ppm (0.016 mg/L).

Systemic Toxicity: In another 4-week inhalation study (comparable to OECD TG 407), rats were exposed to nominal concentrations of 0, 26 (0.22 mg/L) or 98 ppm (0.81 mg/L) (the high concentration was a saturated vapour) ***t*-dodecyl mercaptan** for six hours/day, five days/week. Body weight reduction in males (98 ppm; 0.81 mg/L) with a corresponding reduction in food consumption was observed. High-dose males showed an increase in creatinine, and liver weights showed an exposure-related increase. Male rats at both concentrations exhibited mild renal tubular degeneration and granular cysts which were consistent with species-specific hydrocarbon nephropathy. High-dose female rats exhibited hydronephrosis. The LOAEC was 26 ppm (0.22 mg/L). Similar exposure to dogs (25 and 109 ppm; 0.22 and 0.90 mg/L, respectively) resulted in increases in alanine aminotransferase and reductions in blood urea nitrogen in females. Both sexes showed increases in alkaline phosphatase and exposure-related increases in liver weights with microscopic hepatocellular hypertrophy observed at the high dose for both sexes. The LOAEC was 25 ppm (0.21 mg/L). Similar exposure to mice (25 and 109 ppm; 0.21 and 0.90 mg/L, respectively) resulted in death of one male and one female at the high concentration. At the high concentration, reductions in erythrocyte counts and hematocrit, and increases in MCH and MCHC levels were observed at termination and females exhibited dermal inflammation, acanthosis, and hyperkeratosis, and showed increases in alanine aminotransferase and blood urea nitrogen, and decreased alkaline phosphatase values. These females also had decreased ovary weights, and histopathological evaluation revealed either an absence of, or few, corpora lutea. Low-concentration females showed statistically significant increases in blood glucose. Liver weights revealed exposure-related increases; both sexes showed liver enlargement, discoloration and hepatocellular hypertrophy at both concentrations. The LOAEC for systemic toxicity was 25 ppm (0.21 mg/L); the NOAEC was not established.

Systemic Toxicity: In the combined repeated-dose/reproductive/developmental toxicity screening test (OECD TG 422), rats were administered ***n*-octyl mercaptan** in olive oil by gavage at 0, 10, 50 or 250 mg/kg bw/day for 35 days (males) or from 14 days prior to mating until 4 days post-parturition (females). Treatment-related clinical signs observed at 250 mg/kg bw/day included salivation and a decrease in locomotor activity (both sexes), and abnormal gait (females). Effects at 250 mg/kg bw/day included: decreased body weight and body weight gain (both sexes); decreased food consumption (females); decreased red blood cells (both sexes), hemoglobin concentration (males) and MCHC (both sexes); increased MCV and reticulocyte ratio (both sexes); increased MCH (females). Effects at 250 mg/kg bw/day on organ weights included: for males, increased spleen weight and increased relative (to bw) heart, liver (also for 50 mg/kg bw/day), spleen, and kidney weights; for females included increased liver, spleen and adrenal weights and increased relative (to bw) liver, spleen, kidneys and adrenal weights. Histopathological findings for both sexes at 250 mg/kg bw/day included several findings consistent with stomach irritation/corrosion, congestion, extramedullary hematopoiesis and hemosiderin deposition in the spleen, and increased erythropoiesis in the bone marrow. In addition, atrophy of the thymus was noted in females. The NOAEL for systemic toxicity was 50 mg/kg bw/day.

The C8-12 Aliphatic Thiol category members were negative in bacterial mutagenicity assays [OECD TG 471] *in vitro*. ***n*-Octyl mercaptan** was negative in a chromosomal aberration assay [OECD TG 473] *in vitro*; the results for ***t*-dodecyl mercaptan** were equivocal. ***n*-Octyl, *n*-dodecyl and *t*-dodecyl mercaptans** were negative in the sister chromatid exchange [OECD TG 479] and mouse lymphoma assays [OECD TG 476] *in vitro*. ***n*-Dodecyl mercaptan** was negative in the *in vivo* mouse micronucleus test [OECD TG 474]. The C8-12 Aliphatic Thiol category members are not considered to be genotoxic *in vitro* or *in vivo*.

No carcinogenicity studies were identified for the C8-C12 Aliphatic Thiols.

Data are available for reproductive/developmental toxicity for ***n*-octyl mercaptan** via the oral route and developmental toxicity for ***n*-dodecyl mercaptan** and ***t*-dodecyl mercaptan** via the inhalation route. In a combined repeated-dose/reproductive/developmental toxicity test in rats via the oral route, ***n*-octyl mercaptan** showed no effects on fertility but showed potential for developmental toxicity (post implantation loss) at 250 mg/kg bw/day (highest dose tested). The NOAEL for reproductive toxicity was 250 mg/kg bw/day (highest dose tested). The NOAEL for developmental toxicity was 50 mg/kg bw/day. In prenatal developmental toxicity studies via the inhalation route in rats and mice, ***n*-dodecyl mercaptan** showed maternal toxicity in rats at 7.4 ppm (0.06 mg/L) or greater; development was unaffected. The NOAEC for maternal toxicity was not established (< 7.4 ppm; 0.06 mg/L). The NOAEC for developmental toxicity was 7.4 ppm (0.06 mg/L) (highest concentration tested). In rats and mice exposed via inhalation to ***t*-dodecyl mercaptan**, no treatment-related maternal or developmental toxicity was observed at concentrations up to 88.6 ppm (0.73 mg/L). Based on available data, the C8-C12 Aliphatic Thiols show maternal toxicity at low exposure concentrations (<0.1 mg/L); however, they do not elicit developmental effects at the concentrations tested in reliable studies via the inhalation route. However a reproductive study showed the potential for developmental toxicity via the oral route (i.e. post implantation loss at the highest dose tested).

These chemicals possess properties indicating a hazard for human health (skin sensitisation, repeated-exposure toxicity and potential for developmental toxicity via the oral route). The local effects (skin, eye and respiratory irritation, are chemical specific; *n*-dodecyl mercaptan is corrosive to rabbit skin while the other members of the category are considered irritants to skin and eyes. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

The C8-C12 Aliphatic Thiols do not react with water; the only functionality other than carbon-hydrogen bonds is the sulfhydryl group. Predicted Atmospheric Oxidation half lives for these chemicals are 2.6 hours (***n*-octyl mercaptan**), 3.2 hours (***t*-nonyl mercaptan**), 2.3 hours (***n*-dodecyl mercaptan**), and 3.0 hours (***t*-dodecyl mercaptan**). There are no photoreactive groups in these molecules and, therefore, direct photolysis is not expected.

The level III fugacity model calculation with equal and continuous release to air, water, and soil show similar results for the category members with main distributions to water and soil and less significant distributions to air and sediment. All of the C8-C12 Aliphatic Thiols have been evaluated in biodegradation studies conducted according to OECD TG 301D or 301F. The 28-day degradation for ***t*-nonyl, *n*-octyl, *n*-dodecyl and *t*-dodecyl mercaptan** is 0%, 10%, 39.2% and 10.4%, respectively; therefore, C8-C12 Aliphatic Thiols are not readily biodegradable.

Volatilization of these chemicals from the water phase is expected to be high based on the Henry's law constant presented in the following table. For bioaccumulation, no reliable studies for the C8-C12 Aliphatic Thiols were identified. Based on BCF values estimated using the BCFBAF model (v. 3.01) presented below, bioaccumulation potentials are expected to be low except for highly branched ***t*-dodecyl mercaptan**.

Substance	<u><i>n</i>-Octyl Mercaptan</u>	<u><i>t</i>-Nonyl Mercaptan</u>	<u><i>n</i>-Dodecyl Mercaptan</u>	<u><i>t</i>-Dodecyl Mercaptan</u>
CAS No.	111-88-6	25360-10-5	112-55-0	25103-58-6
Henry's law constant (atm m ³ /mol)	0.019 (Calculated – Bond Estimate)	0.025 (Calculated – Bond Estimate)	0.059 (Calculated – Bond Estimate)	0.059 (Calculated – Bond Estimate)
Half-life (12 hr day;	2.6 hours	3.2 hours	2.3 hours	3.0 hours

1.5E06 OH/cm ³)				
Overall OH Rate Constant (cm ³ /molecule- sec)	5.0 x 10 ⁻¹¹	4.0 x 10 ⁻¹¹	5.5 x 10 ⁻¹¹	4.4 x 10 ⁻¹¹
BCF ^a	11.8	499	234	198 ^b 3338 ^c

^aBCF estimates based on the EPA BCFBAF model (v 3.01)

^bEstimate for structure that is not highly branched

^c Estimate for highly branched structure

The following acute toxicity test results have been determined for the members of this category:

Fish [*Oryzias latipes*]

96 h LC₅₀ = 0.326 mg/L (measured) for **n-octyl mercaptan**.

96 h LC₅₀ = 0.160 mg/L (estimated; ECOSAR v.1.00a) for **n-octyl mercaptan**

96 h LC₅₀ = 0.096 mg/L (estimated; ECOSAR v.1.00a) for **t-nonyl mercaptan**

96 h LC₅₀ = 0.01 mg/L (estimated; ECOSAR v.1.00a) for **n-dodecyl mercaptan**

96 h LC₅₀ = 0.01 mg/L (estimated; ECOSAR v.1.00a) for **t-dodecyl mercaptan**

Invertebrate [*Daphnia magna*] 48 h LC₅₀ = 0.024, 1-10 and 0.16 mg/L (measured) to 0.42 mg/L (measured) for **n-octyl**, **n-dodecyl** and **t-dodecyl mercaptans**, respectively. Some values provided are above the water solubility limit for **n-** and **t-dodecyl mercaptans**.

Algae [*Pseudokirchneriella subcapitata*] 72 h ErC₅₀ = 0.039 and < 0.0145 mg/L (measured) for **n-octyl** and **t-dodecyl mercaptans**, respectively

The following chronic toxicity test results have been determined (aquatic invertebrates/OECD TG 211):

[*Daphnia magna*] 21-d, NOEC = 0.0011 and 0.0108 mg/L (measured) **n-octyl** and **t-dodecyl mercaptans**, respectively.

These chemicals possess properties indicating a hazard for the environment (acute toxicity values lower than 1 mg/L for fish, aquatic invertebrates, and algae, and chronic toxicity values lower than 0.1 mg/L for aquatic invertebrates; not readily biodegradable). The chemicals have the potential to bioaccumulate: t-dodecyl mercaptan is being further investigated within the framework of the EU. These chemicals are not readily biodegradable. Adequate screening-level data are available to characterize the environmental hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

In the United States (Sponsor country) in 2006, companies produced or imported between 450-4500 metric tons of **n-octyl** and **t-nonyl mercaptan**, between 4500-22,500 metric tons of **n-dodecyl mercaptan** and between 22,500 and 45,000 metric tons of **t-dodecyl mercaptan**. The total annual global production estimates by the Mercaptans/Thiols Council, for the C8-C12 Aliphatic Thiols is approximately 100 million pounds (45,000 metric tons).

n-Octyl mercaptan is produced by the reaction of hydrogen sulfide with octene-1, followed by purification by distillation. **t-Nonyl mercaptan** is produced by the addition of H₂S to propylene trimer under acid catalysis conditions, followed by distillation to remove light and heavy components. **n-Dodecyl mercaptan** is produced by the reaction of hydrogen sulfide with dodecene-1, followed by purification by distillation. **t-Dodecyl mercaptan** is produced by the reaction of hydrogen sulfide with propylene tetramer over catalysts with elevated temperature, followed by purification by distillation.

Thiols possess a sulfhydryl group (-SH) that is instrumental in introducing a sulfur group into various biologically active molecules in the pharmaceutical and agrochemical industries. Thiols in the C8-C12 carbon range are commonly used as intermediates in the organic synthesis and as polymerization chain transfer agents. **t-Dodecyl mercaptan** may also be used directly as an end product in ore collection operations.

***n*-Octyl, *t*-nonyl and *t*-dodecyl mercaptans** are primarily used in closed systems and environmental exposure is expected to be very limited during manufacturing of the mercaptans. There are no deliberate releases to the environment during manufacture; however, certain applications of *t*-dodecyl mercaptan use aqueous processing which may result in environmental exposure. Residual mercaptans in finished products are low (e.g., the odour threshold for ***n*-dodecyl mercaptan** is 0.5 ppb and for *t*-dodecyl mercaptan is <0.5 ppm) because of the processes used and the need to remove the thiols due to odour and customer acceptability.

In the Sponsor country, workplace exposure values are in place for ***n*-octyl mercaptan** [NIOSH ceiling is 0.5 ppm (3.0 mg/m³) 15-min] and ***n*-dodecyl mercaptan** [NIOSH ceiling is 0.5 ppm (4.1 mg/m³) (15-min); ACGIH TLV 0.1 ppm TWA (8-h)], and *t*-dodecyl mercaptan (NIOSH ceiling is <0.5 ppm). Due to very low odour thresholds, even low concentrations of the aliphatic thiols can be detected and mitigated to avoid odour complaints. Although mercaptans are handled in closed systems and engineering controls limit potential exposure, proper personal protective equipment (PPE) should always be worn in accordance with the recommendations of the manufacturers.

The C8-C12 Aliphatic Thiols are substances manufactured and used for chemical processing at very low concentrations during polymerization. The resulting polymers undergo several transformations before being used for the production of final consumer products. If there are any residual thiols, they are expected to be trapped in the articles and no release is expected to occur under normal or reasonably foreseeable conditions of use. However, due to the high affinity of these substances for organic matter, the amount volatilized may not be representative of the amount remaining in the polymer.