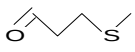
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	3268-49-3
Chemical Name	3-(Methylthio) propionaldehyde
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

3-(Methylthio) propionaldehyde can readily be recognized by its characteristic odor. The odor threshold of 0.00036 mg/m^3 is very low compared to its toxicity.
No data on toxicokinetics are available.
The mode of action is in particular characterized by the local irritation potential of 3-(methylthio) propionaldehyde to skin and mucous membranes. With regard to respiratory irritation it is unclear from the existing studies whether the observed local effects in inhalation studies are attributable to 3-(methylthio) propionaldehyde or acrolein that can be enriched in the vapor phase under the test conditions. However, at up to 50 ml/m^3 no respiratory irritation was detected in a study with repeated exposure with acrolein-free 3-(methylthio) propionaldehyde. No consistent mode of action with regard to a possible systemic toxicity can be deduced from the toxicity studies conducted.
The 4-h LC50 for rats derived from studies following OECD TG 403 and GLP ranged from 4500 to 4800 mg/m^3 (1036 to 1105 ppm) for male rats and was > 4800 mg/m^3 (1105 ppm) for female rats. The dermal LD50 for rats derived from a study conducted similar to OECD TG 402 was 2631 mg/kg bw. In rabbits dermal toxicity determined in non-GLP studies either similar to OECD TG 402 or according to US EPA OPP 8-12 ranged from 748 to 1700 mg/kg bw. The oral LD50 obtained in a GLP study similar to OECD TG 401 was 490 mg/kg bw for male and 1050 mg/kg bw for female rats. The major effects are related to local irritation at the site of contact.
3-(Methylthio) propionaldehyde was a skin irritant in rabbits in a number of studies that did not fully comply with OECD TG 404 and induced irreversible damage to rabbit eyes in studies conducted similar to OECD TG 405.
3-(Methylthio) propionaldehyde revealed a skin sensitizing potential in guinea pig maximization tests following or similar to OECD TG 406.

Limited repeated dose studies by inhalative, dermal, and oral exposure are available.
Repeated exposure of Sprague-Dawley rats to 3-(methylthio) propionaldehyde vapor for 9 days in a GLP study following OECD TG 412 did not reveal any treatment-related toxicity up to the highest tested concentration of 216 mg/m^3 (50 ppm).
Dermal exposure of Sprague-Dawley rats for 9 days (6 h occluded exposure per day) resulted in a slight decrease in body weight gain at a dose of 527 mg/kg bw/d. The systemic NOAEL in this study was 211 mg/kg bw/d.
After 28 days oral administration of 3-(methylthio) propionaldehyde by gavage to Wistar rats in a study similar to OECD TG 407 3-(methylthio) propionaldehyde revealed a slight hemolytic effect with reduced red blood cell counts and hemoglobin levels, increases in blood bilirubin levels and indications of increased hematopoesis in the spleen at 521 mg/kg bw/d. The NOAEL was 104 mg/kg bw/d.
3-(Methylthio) propionaldehyde did not induce gene mutations in bacterial cells in a GLP test following OECD TG 471 and the mouse lymphoma TK+/- assay similar to OECD TG 476. However the mouse lymphoma TK+/- assay revealed an increase in mutations for sigma colonies indicative of a clastogenic effect in vitro in particular without S9 mix. With S9 mix significant increases in mutation rates were only observed at highly cytotoxic concentrations.
An inhalation mouse micronucleus study that suffered from a number of deficiencies and inconsistencies revealed an

equivocally positive result. In a valid i.p. mouse micronucleus study according to OECD TG 474 and GLP, 3-(methylthio) propionaldehyde showed a negative result, indicating that the possible clastogenesis observed in an *in vitro* study does not occur *in vivo*.

Data on fertility are not available. Limited information is available on effects on the gonads from studies with repeated exposure. Testes were examined in two studies, while ovaries were only examined in the 9-day inhalation study. In the 28-day oral study testes weights were determined and histological examination of the testes performed. In the 9-day inhalation study testes and ovaries were weighed and examined histologically. No effects on the sex organs of rats have been observed in these studies. Because of the almost exclusive use of the product as closed system intermediate with a very low exposure potential no further study for reproductive toxicity was conducted. Due to the use as isolated intermediate with controlled transport reduced SIDS testing for the endpoint fertility is considered appropriate for this chemical.
3-(Methylthio) propionaldehyde did not reveal any developmental toxicity in a study with Sprague-Dawley rats according to OECD guideline 414 and GLP by the inhalation route at exposure concentrations that were clearly maternally toxic. Signs of maternal toxicity included reduced body weight gain and food consumption in all dose groups. High dose group dams had additional red brown stains around the snout and the nose and showed lacrimation, labored breathing and closed eyes. Some high dose dams also had a mucoid nasal discharge, salivation and chromodacryorrhea. The NOAEL was 553 mg/m^3 (128 ppm), the highest concentration tested. Slight maternal toxicity was already observed at the lowest applied concentration of 43.2 mg/m^3 (10 ppm).

Environment

3-(Methylthio) propionaldehyde is a colorless to light yellow organic liquid with a water solubility of about 75 g/l at 20 °C, a melting point of -58°C, a boiling point of 170 °C at 1013 hPa, a vapor pressure of 0.53 hPa at 20 °C, a density of about 1.04 g/cm^3, and a measured log Kow of 0.34. The low octanol-water partition coefficient indicates a low potential for bio- or geoaccumulation. 3-(Methylthio) propionaldehyde is readily biodegradable (92 % after 28 days in a DOC-die away test) and undergoes hydrolytic degradation at pH 7 and 9 (half-lives of 75 and 6.5 days respectively). A photochemical degradation via oxidation by OH-radicals with estimated half-lives of about 7.3 hours in air and about 16 days in water takes place. The generic fugacity model level I indicates that 3-(methylthio) propionaldehyde is preferably distributed to the water phase (97.5 %) with a low amount distributing potentially into air (2.5 %).

Acute data for 3 trophic levels are available indicating similar sensitivity of the tested species. The 24 h LC50 for fish (*Brachydanio rerio*) was 14 mg/l, the 48 h EC50 for *Daphnia magna* 4.5 mg/l and the 72 h EC50 for algae (*Scenedesmus subspicatus*) was 5.7 mg/l with a NOEC of 1 mg/l (EbC50 = 2.1 mg/l, NOEC = 0.5 mg/l). This is also supported by QSAR estimations for the 96h LC50 for fish of 9 resp. 29 mg/l.
Based on the lowest EC_{50} for daphnia of 4.5 mg/l a PNEC of 4.5 µg/l can be derived using an assessment factor of 1000 according to the EU Technical Guidance Document.

Exposure

Worldwide production was estimated by the producers to be approximately 485,000 t in 2000.
The substance is almost exclusively used as an on-site and off-site intermediate with controlled transport by rail car or ship. A minor use of 3-(methylthio) propionaldehyde as a food flavoring agent has been identified.
The substance is not present in marketed preparations registered in the product registers of Switzerland, Sweden, Denmark, Finland and Norway
3-(Methylthio) propionaldehyde was quantified in a number of plant and aqueous animal species as well as in processed foods (4 - 40 µg/kg in plants, 1.1 – 167 µg/kg in crab meats, and 0.4 – 399 µg/kg in different foods). The use as a flavoring agent with amounts of 230 kg/a (Europe) and 130 kg/a (USA) as well as natural occurrence in plants, aquatic animal species and processed foods (estimated amount 637 kg/a) results in an estimated combined exposure of 1.5 µg/kg bw/d. Another minor use in probably low amounts as flavoring agent in tobacco products has been allocated.
Due to the almost exclusive use as industrial intermediate and the incineration or stripping of wastewater and

exhausts there is very little possibility for 3-(methylthio) propionaldehyde to enter the environment from production and use.
3-(Methylthio) propionaldehyde is produced and further reacted in closed systems. Only limited potential exposure may occur at the workplace. When used in chemical synthesis, the only process relevant for use, the substance is completely converted by reaction with hydrogen cyanide to produce intermediate products of the methionine process. Workplace exposure to humans is anticipated to be low, because exposure in occupational settings is well-controlled and because indirect exposure is low. Exposure measurements during production and use were all below 100 µg/m^3 (8 h TWA), or below detection limit.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:
The chemical possesses properties indicating a hazard for human health (skin sensitization, irritant effects on skin and respiratory system, irreversible damage to the eye). In the sponsor country the substance is only used as an isolated intermediate with controlled transport, exposure in occupational settings is well-controlled and indirect exposure is anticipated to be low. The use of the substance as food additive is regulated by food agencies of national governments. This use has been evaluated by JECFA and it was concluded, that based on a category approach using toxicological data of the analogue methylsulfide and intake figures from 2000 the use as a flavoring agent is of no safety concern for human health. Countries may wish to investigate any exposure scenarios that were not presented by the sponsor.

Environment:
The chemical possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.