FOREWORD INTRODUCTION

3-(Methylthio) propionaldehyde

CAS N°:3268-49-3

SIDS Initial Assessment Report

For

SIAM 17

Arona, Italy, 11 -14 November 2003

1.	**Chemical Name:**	3-(Methylthio) propionaldehyde
2.	**CAS Number:**	3268-49-3
3.	**Sponsor Country:**	Germany Contact Point: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit) Contact person: Prof. Dr. Ulrich Schlottmann Postfach 12 06 29 D-53048 Bonn-Bad Godesberg
4.	**Shared Partnership with:**	Degussa AG, Germany; Degussa Antwerpen N.V., Belgium; Dow Chemical Co., USA; Adisseo, France
5.	**Roles/Responsibilities of the Partners:**	
•	Name of industry sponsor /consortium	Degussa AG Germany Contact: Dr. Sylvia Jacobi FC-TME-CSM, Postcode 266-001 Rodenbacher Chaussee 4 63457 Hanau-Wolfgang
•	Process used	see comments below
6.	**Sponsorship History**	
•	How was the chemical or category brought into the OECD HPV Chemicals Programme ?	By ICCA HPV initiative
7.	**Review Process Prior to the SIAM:**	last literature search (update): 30 April 2003 (Ecotoxicology): databases CA, biosis; search-profile CAS-No. and special search terms 1 August 2003 (Toxicology): databases medline, toxline; search-profile CAS-No. and special search terms
8.	**Quality check process:**	As basis for the SIDS-Dossier the IUCLID was used. All data have been checked and validated by BUA.
9.	**Date of Submission:**	August 15, 2003

10. Date of last Update:

11. Comments:

OECD/ICCA – The BUA * Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

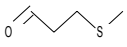
- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
- Review of data and assessment of the quality of data
- Review of data evaluation
- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
- Review of key study description according to robust summary requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability 4, i.e. reliability not assignable)
- Review of validity of structure-activity relationships
- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)

In case of gaps, review of testing plan or rationale for not testing

A final review process was performed by the Federal Institute for risk assessment in Berlin regarding the human health part.

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

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.

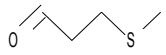
Environment:
The chemical possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate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

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 3268-49-3
IUPAC Name: 3-Methylthiopropanal
Molecular Formula: C_4H_8OS
Structural Formula:



Molecular Weight: 104.17
Synonyms: 3-(Methylthio) propanal, 3-(Methylthio) propionaldehyde, Thiapentanal, Methylmercaptopropionaldehyde, MTPA, MMP

1.2 Purity/Impurities/Additives

3-(Methylthio) propionaldehyde is a colorless to light yellow organic liquid with a purity of > 97 % (w/w). Impurities are water (≤ 2.5 %), acetaldehyde (0.1 to 0.8 %), methanol (0.1 – 0.3 %), methanethiol (≤ 0.6 %), acrylaldehyde (≤ 0.3 %) (Qualities used and tested in the past may have had higher amounts of impurities in particular acrylaldehyde and acetaldehyde).

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Reference
Physical state	liquid	Aventis (2000), Degussa (2002c)
Melting point	-58 °C	Degussa (1971)
Boiling point (1013 hPa)	170.3 °C	Degussa (1996b)
Relative density	1.036 - 1.039 g/cm^3	Aventis Animal Nutrition (2000), Pierson, Giella and Tishler (1948)
Vapor density	4.403 kg/m^3 at 15.6 °C and 1013 hPa	Degussa (1976)
Vapor pressure (20 °C)	0.53 hPa	Degussa (1987, 1996b)
Water solubility	77.9 g/l at 37.8 °C[1] ≤ 75 g/l at 20 °C[2]	Degussa (1976) Degussa (2002c)
Partition coefficient n-octanol/water (log value) (20 °C)	0.34	Rhone-Poulenc Industrialisation (1992a)
Henry's law constant	< 2.3 Pa m^3 mol^{-1} (measured) 7.36 x 10^{-2} Pa m^3 mol^{-1} (calculated)	Rhone-Poulenc Industrialisation (1992b) Degussa (1997a)
Flashpoint	61.4 – 63 °C (closed cup)	Degussa (1995a), (1996a)
Auto Flammability, Ignition temperature	280 °C	Degussa (2002c), (1995b)

[1]measured, [2]extrapolated from value at 37.8 °C

The substance has a strong and very unpleasant odor (Aventis Animal Nutrition, 2000). The odor threshold was reported to be at 0.00036 mg/m^3 (Dmitriev, 1981).

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The production of 3-(methylthio) propionaldehyde by reaction of acrolein with methylmercaptan is conducted in a closed reaction vessel followed by a destillative purification. The separated light and high boiler products are fed into a thermal oxidizer (Degussa, 2003a).

There are 3 known companies that produce 3-(methylthio) propionaldehyde. They are located in the EU and USA. Worldwide production volume was estimated by the producers to be approximately 485,000 metric t in 2000.

More than 60 % of the worldwide production volume of the substance is used as on-site intermediate. Approximately 35 % may be transported in specially designed railroad cars or trucks and to a lesser extend (ca. 5 %) ships to a limited number of industrial sites. The substance is transported in specifically designed strictly sealed ISO-containers approved according to international regulations on transport of dangerous goods. The German producer only transports the material to his own subsidiaries or to one of the other producers (Degussa, 2003a)

The vast majority of 3-(methylthio) propionaldehyde is used as intermediate in chemical industry for the production of the amino acid methionine and methionine-hydroxyl analogue (Degussa, 2003a).

A minor use of 3-(methylthio) propionaldehyde as a food flavoring agent has been identified. It is for example listed in the FDA list of synthetic flavoring substances and adjuvants, Code of Federal Regulations Title 21 § 172.515. 5 (FDA, 2002). WHO (2000) has included 3-(methylthio) propionaldehyde in the evaluation of simple aliphatic and aromatic sulfides and thiols used as flavoring agents. An annual volume of 230 kg in Europe and 130 kg in the US was reported for the use in food. Unspecified but probably low amounts of 3-(methylthio) propionaldehyde are also used as tobacco ingredient. Brown and Williamson (2001) list 3-(methylthio) propionaldehyde as an ingredient in their tobacco products at a level of 0.0001 %.

The substance is not present in marketed products registered in the product registers of Switzerland, Sweden, Denmark, Finland and Norway (Swedish Product Register, 2003, Swiss Product Register, 2003 SPIN, 2003).

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Exposure

Releases into the environment may occur during production and processing of 3-(methylthio) propionaldehyde as well as from its use as food flavoring agent.

At all the production and processing plants known to the sponsor consortium all exhausts are treated with an air scrubber and wastewater is incinerated . (Degussa, 2003a). While direct measurements of actual releases to the environment have not been made, the treatments applied are expected to result in negligible releases of the chemical.

During transport normally no exposure occurs.

From the amount reported to be used as food flavoring agent (360 kg/a in Europe and USA) a significant environmental exposure is not expected.

Natural occurrence

3-(Methylthio) propionaldehyde is also occurring naturally. Bacteria and yeasts have been reported to have the ability to synthesize 3-(methylthio) propionaldehyde (Amárita et al., 2001, Schreier et al., 1976).

3-(Methylthio) propionaldehyde has been identified as component in a variety of plants, natural and processed foods. WHO (2000) gave an annual volume of 3-(methylthio) propionaldehyde in naturally occurring foods of 637 kg.

Examples for quantities of 3-(methylthio) propionaldehyde in different plants and foods are summarized in table 2. A number of other publications have mentioned the presence of 3-(methylthio) propionaldehyde but the amount was not quantified.

Table 2 Natural occurrence of 3-(methylthio) propionaldehyde

Source	Amount detected	Remark	Reference
Scorconera hispanica, black salsify (roots)	40 µ/kg	Extracts of cooked roots GC-MS Analysis	MacLeod and Ames (1991)
Paederia foetida plant (stem)	32 µg/kg stem	steam distillation, GC-FID of extracts	Wong and Tan (1994)
Averrhoa bilimbi fruit	4 µg/kg fruit	steam distillation, GC-FID of extracts	Wong and Wong (1995)
Muntiniga calabura fruit	4.2 µg/kg fruit	steam distillation, extract, GC or GC-MS analysis	Wong, Chee and Er (1996)
Boiled carp filet	7 - 26.4 µg/kg fish	Extracts, GC, GC-olfactometry	Schlüter et al. (1999)
Brew of cooked clams	10 µg/kg clams	Extract of water used to cook clams, GC-FID and GC-MS	Sekiwa, Kubota and Kobayashi (1997)
Crab meats	µg/kg crab body 166.6 µg/kg in carapace	Meat extracts, GC-MS	Chung (1999)
Fish pastes	399 ppb	Extracts, GC-MS detected in 1 of 4 products	Cha and Cadwallader (1995)
Cheddar cheese from raw milk	1 – 2.7 µg/kg cheese	Steam distillation, extract, GC-MS	Rehman et al. (2000)
Cheddar cheese from pasteurized milk	0.4 – 1.4 µg/kg cheese	Steam distillation, extract, GC-MS	Rehman et al. (2000)
Rice cakes	5 to 10 ppb	Stripping from mixture of cakes with water, Tenax trap, GC-FID	Buttery et al. (1999)
Popcorn	12 - 14 µg/kg	Trapping from dry heated popcorn or from heated popcorn-water mixture	Buttery et al. (1997)

3-(Methylthio) propionaldehyde was also detected at a concentration of 98 ppb in waste water of oyster canning companies after hydrolysis and extraction with dichloromethane. The analytical method used was GC-MS and aroma-extract dilution analysis (Kim et al., 2000).

2.2.2 Photodegradation

In air a photochemical half-life of 7.3 hours for the reaction with OH-radicals was calculated using the AOPWIN program (Degussa, 1997b). In water a photochemical half-life of 16.3 days can be derived from the average life time of 23.5 days calculated using the method of Buxton et al. (1988) and the concentration of free OH-radicals in fresh water as published by Mill (1999). Under real environmental conditions the photodegradation rate can be reduced with increasing depth due to the presence of suspended matter or accelerated by the presence of humic acids.

2.2.3 Stability in Water

Abiotic hydrolytic degradation was determined at pH 4, 7 and 9. At pH 4 less than 10 % of the test substance had hydrolyzed after 5 days at 50 °C. At pH 7 and 25 °C the half-life was approximately

75 days and at pH 9 and 25°C it amounted to 6.5 days. Thus it can be concluded that abiotic degradation occurs preferably at alkaline pH-values (Degussa, 2001). Photodegradation in water, however will be more rapid independent of pH with a half-life of 16.3 days (see 2.2.2).

2.2.4 Transport between Environmental Compartments

3-(Methylthio) propionaldehyde has a water solubility of ≤ 75 g/l at 20 °C. It has a vapor pressure of about 0.53 hPa at 20 °C, indicating that volatilization from water is not expected to a high degree. The Henry's law constant was calculated to be 7.36 10^{-2} Pa m^3/mol indicating a low volatility from water (Degussa, 1997a).

The equilibrium partition characteristics in the environment were estimated using the Mackay level I model calculation.

Table 3 Mackay level I model calculation (Degussa, 1997a)

Compartment	Theoretical Distribution [%]
Air	2.48
Water	97.49
Soil	0.02
Sediment	0.02

Based on this calculation the most likely target compartment of theoretical environmental emissions of 3-(methylthio) propionaldehyde is the hydrosphere.

The generic Mackay level III calculation (estimated entry 3000 kg/h to air, water or soil) yielded the following distribution patterns (Degussa, 2002a).

Table 4 Mackay level III model calculation (Degussa, 2002a)

Compartment	Release 100% into air Distribution [%]	Release 100% into water Distribution [%]	Release 100% into soil Distribution [%]
Air	4.98	1.2 x 10^{-03}	0.0243
Water	51.6	99.9	52.8
Soil	43.5	0.0106	47.2
Sediment	0.0211	0.0409	0.0216

A release into air or soil will result according to that model in a distribution of the substance to water and soil, while the substance will stay in the water phase when it is released into water.

2.2.5 Biodegradation

3-(Methylthio) propionaldehyde was readily biodegradable in a DOC-die away test. Degradation was 92 % after 28 days and 68 - 74 % after 8 days (Rhone Poulenc, 2000).

2.2.6 Bioaccumulation

The low octanol-water partition coefficient (log Kow = 0.34 at 20 °C, measured) (Rhone Poulenc Industrialisation, 1992a) indicates a low potential for bio- or geoaccumulation.

2.2.7 Other Information on Environmental Fate

No data available.

2.3 Human Exposure

Human exposure from production and the main use as intermediate in chemical industry is limited to workers in the production and processing plants. Possible routes of exposure are the inhalation of vapors and dermal contact (Degussa, 2003a).

2.3.1 Occupational Exposure

As 3-(methylthio) propionaldehyde is produced and further reacted in closed systems only limited potential exposure may occur at the workplace. Procedures with the possibility of exposure are sampling and filling/loading operations as well as maintenance. During production samples are taken using special vented sampling equipment. When containment is breached, for example for maintenance operations the equipment is flushed until it is free of odor. The wash solution is fed into a thermal oxidizer. On average operation personnel does not spent more than 1 hour per shift in the production area. The product is loaded and unloaded from storage into dedicated containers or railcars by tight loading arms and balanced gas phase systems thus exposure is minimized in loading and filling operations by technical means. The cars are loaded through a closed system, under continuous monitoring. The monitoring system will automatically shut off loading valves when the set point is reached. When transported dedicated 3-(methylthio) propionaldehyde containers and railcars built according to or above DOT classification 105J300W are inspected before leaving the plants and visual check is implemented after each transport change. All safety equipment and valves are protected by a sealed cap. Containers and rail cars are checked periodically by regulatory tests by authorized workshops after being washed free of odor. They are also inspected prior to loading. Loading connections are tested and inspected prior to and after loading. Loading connections are decontaminated by flushing several times; flush material is routed to unit disposal systems for treatment (incineration). Unloading conditions are similar to loading. The German producer only transports the material to his own subsidiaries or to one of the other producers. 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 (Degussa, 2003a).

Ingestion

Ingestion of the product during production and industrial use is very unlikely. As the chemical reaction to the follow up products is complete, an exposure to residual 3-(methylthio) propionaldehyde in the amino acid is very unlikely (Degussa, 2003a).

Skin and eye exposure

Only accidental skin and eye contact is possible through spills during sampling, laboratory operations or filling operations when the containment is breached. Operators normally wear appropriate personal protective equipment to protect skin and eyes. An appropriate glove material is nitrile rubber. Eyes are protected by face shields and goggles (Degussa, 2003a).

Inhalation

Inhalation exposure is limited by technical means. Exposure measurements during production and use were all below 100 µg/m^3 (8 h TWA), or below detection limit. Short time (15 min) values (stationary worst case) of up to 285 µg/m^3 were determined during loading operations. Measurements were conducted with stationary sampling in 3 different plants in Germany, USA and

Belgium 15 measurements in the production plant including sampling operations (Degussa, 2003b). Another company reported 8 h workplace concentrations between 0.00017 and 0.00036 ppm (Dow, 2003).

On average operation personnel does not spent more than 1 hour per shift in the production area (Degussa, 2003a).

Internal occupational exposure limits were set to 0.5 mg/m^3 (8 h TWA) with a short-term (15 min) limit of 1 mg/m^3 (Degussa, 2002c).

2.3.2 Consumer Exposure through Food

As 3-(methylthio) propionaldehyde can be present in foods either from natural origin or from use as a flavoring agent the main source of oral exposure will be from ingestion of food. The typical 3-(methylthio) propionaldehyde content in different foodstuffs (see table 2) was between 1 and 40 µg/kg food, with the exception of fish paste (399 µg/kg). Assuming that fish and vegetables can contain up to 40 µg/kg, fruits and cheese up to 5 µg/kg of 3-(methylthio) propionaldehyde an estimate of the daily intake through food of about 0.6 µg/kg bw/d can be made using the data of the US-EPA exposure factors handbook (US-EPA, 1997) as outlined in table 5.

Table 5 Estimate of consumer exposure through food intake (US-EPA, 1997)

Food	**Estimated daily intake (95%ile general population) [g/kg bw/day]**	**Estimated content of 3-(methylthio) propion-aldehyde [µg/kg food]**	**Daily intake of 3-(methylthio) propion-aldehyde [µg/kg bw/day]**
Fruit	12	5	0.06
Vegetables	10	40	0.4
Fish	0.6	40	0.024
Dairy products	29.7	5	0.15
Total			0.63

2.3.3 Consumer Exposure through Food Additives

From the annual amount used as food additive a daily intake of 45 µg for Europe and 25 µg for the US was estimated resulting in a daily body burden of 0.75 and 0.4 µg/kg bw respectively. It is also mentioned that the use in food is self-limiting because of the low odor threshold 1 mg/m^3 of thio-compounds were reported to be intolerable (WHO, 2000). The combined exposure through natural content in food and food additives would be around 1.5 µg/kg bw/d.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

The mode of action is in particular characterized by the local irritation potential of 3-(methylthio) propionaldehyde to skin and mucous membranes. No consistent mode of action with regard to a possible systemic toxicity can be deduced from the toxicity studies conducted.

3.1.1 Toxicokinetics, Metabolism and Distribution

No data on toxicokinetics of the product are available. Due to the low molecular weight, the water solubility and the low octanol-water partition coefficient it can be assumed that the substance can be absorbed, via the oral and inhalation route and to a limited extend also through the skin. The physical chemical properties suggest that once absorbed the substance will be distributed throughout the body water, will not accumulate in fat tissue and is likely to be excreted via the urine. Metabolism and reaction with physiological molecules cannot be excluded.

The substance belongs to the group of acyclic sulfides with oxidized side-chains. The presence of other functional groups, in this case an aldehyde, provides centers of greater polarity and additional sites for the biotransformation of thioethers. The presence of these polar groups would also result in increased renal excretion. The biotransformation of such oxygenated, carbon-containing, functional groups is well characterized and has been described for groups of flavoring agents previously evaluated by the JECFA (WHO 2000). Concurrent metabolism of various substrates at both sulfur and oxygenated functional groups has been reported, and sulfoxide formation usually predominates as the major metabolic pathway of detoxification. Experiments in vitro suggest that hydrolysis of carboxyl esters occurs in the presence of thioether (sulfide) groups. In consequence, thioethers with oxidized side-chains would be expected to be eliminated more rapidly than simple sulfides.

3.1.2 Acute Toxicity

Studies in Animals

Several acute toxicity studies in rats and rabbits are available indicating a moderate toxicity via the oral, inhalation and dermal route. Male animals seemed to be more sensitive than females.

Inhalation

The acute inhalation toxicity was relatively low, the 4-h LC_{50}, inhalation rat, ranging between 4500 and 4800 mg/m^3 (1036 - 1105 ppm) for males and > 4800 mg/m^3 (1105 ppm) for females in GLP studies following OECD TG 403. Deaths occurred up to several days after exposure (Degussa, 1988, Monsanto, 1986d).

It is unclear whether the observed local symptoms in the inhalation studies are attributable to 3-(methylthio) propionaldehyde or to acrolein which is contained in a concentration of up to 0.3 % in the materials tested. The irritation threshold for acrolein in rat nasal epithelium was approximately 0.25 ppm (0.6 mg/m^3) (Cassee *et al.*, 1996). As the developmental toxicity study (chapter 3.1.8) has shown, the actual concentration of acrolein in the inhalation chamber can be much higher i.e. about 2 % of the concentration of 3-(methylthio) propionaldehyde and it is possible that acrolein can be enriched in the vapor phase under the test conditions. However, at concentrations up to 217 mg/m3 (50 ppm) no respiratory irritation was detected in a study with repeated exposure to acrolein-free 3-(methylthio) propionaldehyde.

Dermal

The dermal LD_{50} in studies similar to OECD TG 402 was reported to be 2631 mg/kg bw in rats (Degussa, 1981). An earlier study reported a dermal LD_{50} in rats of 676 mg/kg bw (Rhone Poulenc, 1975). In the latter study the substance was applied undiluted (24 h occlusive) and led to severe skin irritation that may have contributed to the higher toxicity. Dermal LD_{50} values in rabbits ranged between 748 and 1700 mg/kg bw (Ballantyne, Cawley and Blaszcak, 2000, Union Carbide, 1986, Monsanto, 1986a). These studies were conducted similar to OECD TG 402 or according to US EPA OPP 8-12. The predominant clinical symptom was local irritation. Other clinical signs included symptoms as hypoactivity and ataxia. In one dermal study aggressiveness, increased motor activity

and convulsions prior to death were also reported. No systemic macroscopic organ findings were observed.

Oral

An LD_{50} oral of 490 mg/kg bw for male rats and 1050 mg/kg bw for female rats was the lowest acute oral toxicity value obtained in a GLP study similar to OECD TG 401 (Monsanto, 1986b). Clinical signs included ocular and nasal discharge, hypopnea, dyspnea, wet rales, urinary staining, ataxia, hypoactivity and prostration after dosing. Decreased food consumption was observed from day 2. Surviving animals recovered from symptoms by day 3. No substance related macroscopic changes were observed at necropsy.

Conclusion

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). 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.

3.1.3 Irritation

Skin Irritation

None of the studies fully complies to OECD TG 404: 3-(methylthio) propionaldehyde was irritating when applied undiluted to rabbit skin for 4 h under semi-occluded (purity not stated, Monsanto, 1986e) conditions. In two other studies with 4 h occlusive application to rabbits symptoms from slight irritation (Union Carbide, 1996) to necroses (Ballantyne, Cawley and Blaszcak, 2000, Union Carbide, 1986) were observed. As occlusion might have aggravated the effects, the overall evaluation is that 3-(methylthio) propionaldehyde is irritating to the skin.

Eye Irritation

When undiluted 3-(methylthio) propionaldehyde was administered to rabbit eyes (0.1 ml) without rinsing, eye irritation including conjunctival redness chemosis and corneal opacity were observed that were not completely reversible at the end of the observation period (Degussa, 1979a, Monsanto 1986c, Rhone Poulenc, 1975). The studies were conducted similar to OECD TG 405 but in two of them only one animal was used because of the irritant properties of the substance (Degussa, 1979a, Monsanto, 1986c).

Conclusion

3-(Methylthio) propionaldehyde was a skin irritant in rabbits in a number of studies that did not fully comply with OECD TG 404 and caused irreversible damage to rabbit eyes in studies conducted similar to OECD TG 405.

3.1.4 Sensitisation

3-(Methylthio) propionaldehyde revealed a skin sensitizing potential in the guinea pig maximization test following OECD TG 406 and GLP (Ballantyne, Cawley and Blaszcak, 2000, Union Carbide, 1999a) or similar to OECD TG 406 (Degussa, 1979 b).

Conclusion

3-(Methylthio) propionaldehyde revealed a mild skin sensitizing potential in guinea pig maximization tests following or similar to OECD TG 406.

3.1.5 Repeated Dose Toxicity

Limited repeated dose studies by inhalative, dermal, and oral exposure are available.

Studies in Animals

Inhalation

A 9-day inhalation study following OECD TG 412 and GLP (5 consecutive days, 2 days rest, 4 days exposure) was conducted using groups of 5 male and 5 female Sprague Dawley rats per group exposed to target concentrations of 0.5, 5, and 50 ppm (corresponding to 2.16, 21.6 or 216 mg/m^3) of 3-(methylthio) propionaldehyde. Acrolein levels were below detection limit in this study. Complete physical examinations and body weight determinations were performed during the exposure period (days 1, 2, 5, 8, and 9) and weekly after cessation of exposure. Prior to necropsy standard hematological and clinical chemistry parameters were determined and ophthalmological examinations were performed on all animals. At necropsy the liver, lungs, spleen, brain, adrenals and kidneys from all rats and the testes of the males were weighed. The following organs were examined histopathologically: Adrenal glands, brain, heart, kidneys, larynx, liver, lungs, nasopharyngeal tissues, ovaries, spleen, trachea, testes, and urinary bladder. No exposure related effects were observed in this study at all exposure concentrations compared to air exposed controls. The NOAEL was consequently 216 mg/m^3 (50 ppm), the highest concentration tested in this study (Ballantyne and Cawley, 2000, Union Carbide, 1998).

Dermal

Groups of 10 male and 10 female Sprague-Dawley rats in the low and mid dose group and 15 animals per sex in the high dose group were exposed to dermal doses of 52.7, 210.8 and 527 mg/kg bw/d (6 h occluded contact) for 9 days (5 consecutive days, 2 days rest, 4 days exposure). The study was not conducted according to OECD guidelines, but under GLP. Controls (15 animals) received water in the same manner. Five animals per sex of the high dose and control were kept for a 28-day recovery period. Animals were examined for signs of toxicity and local skin alterations daily during the dosing period, and weekly during the recovery period. A neurobehavioral test was performed before dosing, after the fifth dosing and before necropsy. Recovery animals were additionally evaluated the day following cessation of treatment. Body weights were recorded every 2 days during dosing and at 6 day intervals during the recovery period. Standard hematological and clinical chemistry analysis was performed at the end of the study. The following organs were examined macroscopically and organ weights determined: adrenal glands, brain, liver, kidneys, ovaries and testes. Brain, kidneys, skin, nerves and spinal cord of high dose and control animals were examined microscopically. Slight reductions in body weight gain were seen in the high dose group in both sexes compared to controls while food and water consumption were not different from controls. No mortality and no clinical signs attributable to treatment were observed. Responses in the neurobehavioral screen were not significantly different between control and treated animals. Very slight to slight or moderate (few high dose animals) erythema and desquamation was observed at the site of administration in most mid and high dose animals. Erythema and desquamation were reversible by day 18 and 25 respectively in the recovery groups. No treatment related hematology, clinical chemistry, macroscopic or microscopic organ changes were observed apart from the site of contact findings. The NOAEL for systemic toxicity is based on the body weight effects and was reported to be 210.8 mg/kg day (Ballantyne, Cawley and Blaszak, 2000, Union Carbide, 1999b).

Oral

In a non-GLP study similar to OECD TG 407 groups of 10 male and female Wistar rats received doses of 21, 104, and 521 mg/kg bw/d of 3-(methylthio) propionaldehyde by gavage for 6 days per week over a 28-day period. No recovery group was included and macroscopic and microscopic pathological examination at study termination was restricted to kidneys, liver spleen, lung, heart and testes. No substance related clinical signs were observed during the study. Body weight gain was slightly decreased in the high dose animals compared to controls, while food consumption did not differ from controls. Red blood cell counts and hemoglobin levels were lower compared to controls in the high dose group animals, but the difference only reached significance for hemoglobin in high dose females. White blood cell counts were increased in males of the 521 mg/kg bw group only. Changes in clinical chemistry values included an increased bilirubin level in high dose group animals of both sexes. Creatinine levels were slightly increased (68.3 µmol/l in the mid dose group and 69.1 µmol/l in the high dose group) compared to controls (63.3 µmol/l) in males of the mid and high dose group, but this finding was not considered treatment related as it was a small effect that only occurred in males. Organ weights and gross pathology did not reveal any treatment-related changes. In the histopathological examination a deposition of pigment and blood in the red pulp of the spleen was observed in animals of the 521 mg/kg bw dose group indicating an increased extramedullary hematopoesis. The NOAEL in this study was therefore 104 mg/kg bw/d (Degussa, 1979c).

Conclusion

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 non-GLP 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.

3.1.6 Mutagenicity

In vitro Studies

3-(Methylthio) propionaldehyde (97.1 %) was not mutagenic in a standard Ames assay in *S. typhimurium* strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 at concentrations up to the cytotoxic concentration of 0.316 µl/plate according to OECD TG 471 and GLP with and without metabolic activation. The material had a purity of 97.1 % and contained 0.05 % acrolein, 0.1 % hydroquinone, 0.15 % acetaldehyde, 0.3 % methyl mercaptane, 0.25 % acetic acid, 0.6 % acetone and 0.3 % pyridine (Union Carbide, 1994b, NTIS, 1994).

In an in vitro mouse lymphoma assay similar to OECD TG 476 with L5178Y/tk+/- mouse lymphoma cells at a concentration range of 0.0001 to 0.1 µl/ml a concentration dependent increase of the mutation frequency was observed with and without metabolic activation. The cytotoxic concentration ranged between 0.02 and 0.15 µl/ml. With S9 however, significant increases in

mutation rates were only seen at concentrations with a cell survival less than or equal to 10 %. The increase in mutation frequency was almost exclusively attributable to an increase in sigma-colonies indicating that the test substance primarily induced chromosomal aberrations in this test system. Lambda colonies were only increased at the highest concentrations tested (survival rate below 3 %). The material had a purity of 97.1% and contained 0.05 % acrolein, 0.1 % hydroquinone, 0.15 % acetaldehyde, 0.3 % methyl mercaptane, 0.25 % acetic acid, 0.6 % acetone and 0.3 % pyridine (Union Carbide, 1994a, NTIS, 1994).

In vivo Studies

99.8 % 3-(Methylthio) propionaldehyde was tested in a mouse micronucleus test according to OECD TG 474 and GLP with i.p. administration in CD-1 mice. The maximum tolerated dose had been determined in a pre-test. Groups of 6 male and 6 female CD-1 mice received 2 doses of 50, 100 or 200 mg/kg bw/d in corn oil by i.p. injection on 2 consecutive days. Bone marrow smears were prepared after 24 h and a minimum of 1000 cells per animal and 2000 PCEs were counted. 6 of 6 male and 2 of 6 female animals of the high dose group died before the bone marrow was prepared. Clinical signs of toxicity were observed in animals of the high and mid dose groups. PCE/NCE ratios of the treated animals were similar to those of controls. 3-(Methylthio) propionaldehyde did not induce an increase in the number of micronucleated polychromatic erythrocytes compared to controls in male and female mice treated with up to 200 mg/kg bw/d on 2 consecutive days. At this dose level clear signs of toxicity and mortality were observed (Degussa-Hüls and Rhodia Services, 2000).

Another less reliable mouse micronucleus study was conducted following TSCA test guideline, Fed. Reg. 50 § 188 part 798 and GLP using a test substance of lower purity (97.1 %, see above) and exposing groups of 5 male and 5 female C57BL mice by inhalation to concentrations of 37.4, 88.5 and 155.6 ppm of 3-(methylthio) propionaldehyde for 1 h nose only on 2 consecutive days. Negative controls were exposed to air. 24 h after the last exposure blood was collected from the animals and the peripheral erythrocytes were examined for micronuclei. The amount of cells counted per animal was not given in the report. No clinical effects were observed in the exposed animals. A dose related decrease in the PCE/NCE ratio was reported for female animals, but the ratio was higher than in controls. A significant increase of the number of micronucleated polychromatic erythrocytes was reported in the high and low dose males, but not in the females. An additional evaluation of 1000 PCEs in the mid dose males resulted also in a significantly increased rate of micronucleated PCEs. The study suffers from a number of deficiencies and inconsistencies. The number of erythrocytes counted per animal is not given; there are big differences between the number of micronuclei/1000 PCEs between animals of the same dose groups. With regard to males of all dose groups, 1 to 3 animals did not have an increased amount of micronucleated PCEs, while the ratio varied between 2.5 and 15 in the other animals. Therefore the results of this study are regarded as equivocal, and the hint of a positive effect may have resulted from one or more of the contaminants (Union Carbide, 1994c, NTIS, 1994).

Conclusion

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 clastogenesis that was demonstrated in an *in vitro* study does not occur *in* vivo.

3.1.7 Carcinogenicity

No data are available.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

Data on fertility are not available. In the 28-day oral gavage study absolute and relative testes weights were determined in all dose groups. Testes of the high dose and control animals were also examined macroscopically and microscopically. Female sex organs were not evaluated. No effects on absolute or relative testes weights, macroscopic or microscopic changes were observed. In the 9-day inhalation study absolute and relative testes and ovary-weights were determined. Testes and ovaries were also examined histopathologically. No effects on absolute or relative testes and ovary-weights and no histopathological changes in testes or ovaries were observed. Because of the almost exclusive use of the product as closed system intermediate with a very low exposure potential no further study for this endpoint was conducted.

Developmental Toxicity

In a developmental toxicity study conducted according to OECD guideline 414 and GLP in groups of 24 female Sprague-Dawley rats exposed to 0, 10, 58 and 128 ppm (43.2, 250.6, 553 mg/m^3) of 3-(methylthio) propionaldehyde 6 h/day at gestation day 6 to 15 no effects on the pregnancy rates, implantation and the developing embryo or fetus were observed. The atmospheres also contained acrolein in concentrations of 0, below detection limit, 1.19 and 2.34 ppm. 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 for developmental toxicity was 553 mg/m3 (128 ppm), the highest dose tested, while slight maternal toxicity was observed at the lowest exposure concentration of 43.2 mg/m^3 (10 ppm) already (Degussa-Hüls, Rhone Poulenc and Union Carbide, 1999).

Conclusion

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.

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).

3.2 Initial Assessment for 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. 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 ranged from 4500 to 4800 mg/m^3 (1036 to 1105 ppm). 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 mild skin sensitizing potential in guinea pig maximization tests following or similar to OECD TG 406.

Limited repeated dose studies by inhalative, dermal, and oral uptake 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 a possible in vitro clastogenic effect is not expressed 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.

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).

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute Toxicity Test Results

Effects on Fish

In a study with *Brachidanio rerio*, following the ISO 7346/1 under static conditions, the 24 hour LC_{50} was reported to be 14 mg/l. (Rhone Poulenc, 1988). No analytical monitoring was performed and the effect value is based on nominal concentrations. The study was of shorter duration than required in the most recent guidelines and by SIDS. In analogy to the results with daphnia it can be expected that the 96 h LC_{50} value will be lower. It is however, not expected that the LC_{50} will be below 1 mg/l after 96 h. Regarding this and considering animal welfare, a 96h-fish test is not requested for 3-(methylthio) propionaldehyde. This is also supported by QSAR estimations. Using ECOSAR a 96 h-LC_{50} for fish of 29 mg/l can be estimated, while with another QSAR model a value of 9 mg/l was calculated (Danish EPA, 2003).

Effects on invertebrates

The 48 hour EC_{50} in *Daphnia magna* was 4.5 mg/l (Degussa, 2002b). The 24 h EC_{50} was > 12.4 mg/l. The test substance concentration was monitored analytically and was found to be stable. Therefore, the effect values are related to nominal concentrations.

Effects in aquatic plants / algae

The 72 h EC_{50} for *Scenedesmus subspicatus* was 5.7 mg/l based on growth rate (based on biomass an EC_{50} of 2.1 mg/l was determined). The E_rC_{10} was 1.3 mg/l (E_bC_{10} = 0.6 mg/l), the NOEC (growth rate) was 1.0 mg/l (biomass: 0.5 mg/l) and the LOEC (growth rate) was 2.5 mg/l (biomass: 1 mg/l). Growth rates decreased over time, but the validity criteria of 16 fold increase over 72 h was fulfilled in the critical tests. Thus these results can be used to derive ECx and NOEC values. No analytical monitoring was performed and the effect values are based on nominal concentrations. (Degussa, 1992a). As the pH in the test rose up to 9.6 after 72 h it cannot be excluded that some hydrolysis of the test substance has occurred during the test ($t_{1/2}$ at pH 9: 6.5 d). However, as there is no information on the course of the pH during the whole exposure period, a quantification is not possible.

Toxicity to Microorganisms

For *Pseudomonas putida* an EC_{50} of ca. 46 mg/l (18 hours) was reported and the EC_{10} amounted to 35 mg/l. (Degussa, 1992b)

PNEC derivation

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.

4.2 Terrestrial Effects

No data are available.

4.3 Other Environmental Effects

No data are available.

4.4 Initial Assessment for the 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 vapor pressure of 0.53 hPa at 20 °C and a measured log Kow of 0.34. 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 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 %). The measured octanol-water partition coefficient (log Kow = 0.34) indicates a low potential for bio- or geoaccumulation.

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 ErC50 for algae (*Scenedesmus subspicatus*) was 5.7 mg/l with a NOEC of 1 mg/l. This is also supported by QSAR estimations for the 96h-LC_{50} 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.

5 RECOMMENDATIONS

Human Health

The chemical is currently of low priority for further work. 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 is currently of low priority for further work. 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.

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I U C L I D

Data Set

Existing Chemical	:	ID: 3268-49-3
CAS No.	:	3268-49-3
EINECS Name	:	3-(methylthio)propionaldehyde
EC No.	:	221-882-5
TSCA Name	:	Propanal, 3-(methylthio)-
Molecular Formula	:	C4H8OS

Producer related part

Company	:	Degussa AG
Creation date	:	04.06.2000

Substance related part

Company	:	Degussa AG
Creation date	:	04.06.2000
Status	:	
Memo	:	Überarbeitungsversion
Printing date	:	04.05.2004
Revision date	:	19.11.2003
Date of last update	:	04.05.2004
Number of pages	:	1
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : other: contact point
Name : Degussa AG - ZN Wolfgang
Contact person : Dr. W. Mayr
Date :
Street : Rodenbacher Chaussee 4
Town : 63457 Hanau
Country : Germany
Phone : +49 6181 59 4139
Telefax : +49 6181 59 2083
Telex :
Cedex :
Email : wilfried.mayr@degussa.com
Homepage :

Type : cooperating company
Name : Degussa Antwerpen N.V.
Contact person : Mr. Peter Van Stappen
Date :
Street : Tijsmanstunnel West
Town : 2040 Antwerpen 4
Country : Belgium
Phone : +32 3 5603 305
Telefax : +32 3 5603 877
Telex : 32918
Cedex :
Email : peter.van_stappen@degussa.com
Homepage :

Type : cooperating company
Name : Dow Chemical Co.
Contact person : P. T. Robbertz
Date :
Street :
Town : Danbury CT
Country :
Phone : +1 203 794 5003
Telefax : +1 203 794 3133
Telex :
Cedex :
Email :
Homepage :

Type : cooperating company
Name : other: Adisseo
Contact person : Hélène LIONET
Date :
Street : 25, Quai Paul Doumer
Town : 92408 Courbevoie Cedex
Country : France
Phone :
Telefax :
Telex :
Cedex :
Email :

Homepage :

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	3-(methylthio)propionaldehyde
Smiles Code	:	O=CCCSC
Molecular formula	:	C4H8OS
Molecular weight	:	104.17
Petrol class	:	

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	liquid
Purity	:	>= 97 % w/w
Colour	:	
Odour	:	

Remark : Intermediate in the synthesis of methionine and methionine hydroxy analogue.

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

3-(Methylthio)propanal

3-(Methylthio)propionaldehyde

4-Thiapentanal

beta-(methylthio)propionaldehyde

Methional

Methylmercaptopropionaldehyd

Methylmercaptopropionaldehyde

MMP

MTPA

Propanal, 3-(methylthio)-

Propionaldehyde, 3-(methylthio)-(8CI)

Thioaldehyd

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No : 7732-18-5
EC-No : 231-791-2
EINECS-Name : water
Molecular formula : H2O
Value : <= 2.5 % w/w

Flag : Critical study for SIDS endpoint

Purity : typical for marketed substance
CAS-No : 74-93-1
EC-No : 200-822-1
EINECS-Name : methanethiol
Molecular formula : CH4S
Value : <= .6 % w/w

Flag : Critical study for SIDS endpoint

Purity : typical for marketed substance
CAS-No : 107-02-8
EC-No : 203-453-4
EINECS-Name : acrylaldehyde
Molecular formula : C3H4O
Value : <= .3 % w/w

Remark : Synonym (Acrolein)
Flag : Critical study for SIDS endpoint

Purity : typical for marketed substance
CAS-No : 75-07-0
EC-No : 200-836-8
EINECS-Name : acetaldehyde
Molecular formula : C2H4O
Value : ca. .1 - .8 % w/w

Flag	:	Critical study for SIDS endpoint
Purity	:	typical for marketed substance
CAS-No	:	67-56-1
EC-No	:	200-659-6
EINECS-Name	:	methanol
Molecular formula	:	CH4O
Value	:	ca. .1 - .3 % w/w
Flag	:	Critical study for SIDS endpoint

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity	:	ca. 485000 - tonnes produced in 2000
Remark	:	Estimate of the MTPA consortium, worldwide production.
Flag	:	non confidential, Critical study for SIDS endpoint

1.6.1 LABELLING

Labelling	:	provisionally by manufacturer/importer
Specific limits	:	
Symbols	:	Xn, , ,
Nota	:	, ,
R-Phrases	:	(20/21/22) Harmful by inhalation, in contact with skin and if swallowed (37/38) Irritating to respiratory system and skin (41) Risk of serious damage to eyes (43) May cause sensitization by skin contact
S-Phrases	:	(9) Keep container in a well-ventilated place (23) Do not breathe vapour (26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (36/37/39) Wear suitable protective clothing, gloves and eye/face protection

1.6.2 CLASSIFICATION

Classified	:	provisionally by manufacturer/importer
Class of danger	:	harmful
R-Phrases	:	(20/21/22) Harmful by inhalation, in contact with skin and if swallowed
Specific limits	:	

Classified	:	provisionally by manufacturer/importer
Class of danger	:	irritating
R-Phrases	:	(37/38) Irritating to respiratory system and skin
Specific limits	:	

Classified : provisionally by manufacturer/importer
Class of danger : irritating
R-Phrases : (41) Risk of serious damage to eyes
Specific limits :

Classified : provisionally by manufacturer/importer
Class of danger : sensitizing
R-Phrases : (43) May cause sensitization by skin contact
Specific limits :

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Use in closed system

28.01.2004

Type of use : industrial
Category : Chemical industry: used in synthesis

Type of use : use
Category : Food/foodstuff additives

Remark : Very minor use
28.01.2004

Type of use : use
Category : Intermediates

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : other: internal limit value
Limit value : .5 mg/m3
Short term exposure limit value
Limit value : 1 mg/m3
Time schedule : 15 minute(s)
Frequency : times

Result : 0.5 mg/m3 = 0.11 ppm (20 °C and 1013 hPa).
1 mg/m3 = 0.23 ppm (20 °C and 1013 hPa).

03.02.2004 (53)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 1 (weakly water polluting)

(65)

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

Type : degradation product
CAS-No : 74-93-1
EC-No : 200-822-1
EINECS-Name : methanethiol
IUCLID Chapter :

Flag : Critical study for SIDS endpoint

Type : degradation product
CAS-No : 107-02-8
EC-No : 203-453-4
EINECS-Name : acrylaldehyde
IUCLID Chapter :

Remark : 2-Propenal
Flag : Critical study for SIDS endpoint

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Source of exposure : Human: exposure by production
Exposure to the : Substance

Result : As 3-(methylthio) propionaldehyde is produced and further

reacted in closed systems only limited potential exposure may occur at the workplace. Procedures with the possibility of exposure are sampling and filling/loading operations as well as maintenance. During production samples are taken using special vented sampling equipment. When containment is breached, for example for maintenance operations the equipment is flushed until it is free of odor. The wash solution is fed into a thermal oxidizer. On average operation personnel does not spent more than 1 hour per shift in the production area. The product is loaded and unloaded from storage into dedicated containers or railcars by tight loading arms and balanced gas phase systems thus exposure is minimized in loading and filling operations by technical means. The cars are loaded through a closed system, under continuous monitoring. The monitoring system will automatically shut off loading valves when the set point is reached. When transported dedicated 3-(methylthio) propionaldehyde containers and railcars built according to or above DOT classification 105J300W are inspected before leaving the plants and visual check is implemented after each transport change. All safety equipment and valves are protected by a sealed cap. Containers and rail cars are checked periodically by regulatory tests by authorized workshops after being washed free of odor. They are also inspected prior to loading. Loading connections are tested and inspected prior to and after loading. Loading connections are decontaminated by flushing several times; flush material is routed to unit disposal systems for treatment (incineration). Unloading conditions are similar to loading. The German producer only transports the material to his own subsidiaries or to one of the other producers. 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.

Only accidental skin and eye contact is possible through spills during sampling, laboratory operations or filling operations when the containment is breached. Operators normally wear appropriate personal protective equipment to protect skin and eyes. An appropriate glove material is nitrile rubber. Eyes are protected by face shields and goggles.

Inhalation exposure is limited by technical means. Exposure measurements during production and use were all below 100 µg/m3 (8 h TWA), or below detection limit. Short time (15 min) values (stationary worst case) of up to 285 µg/m3 were determined during loading operations. Measurements were conducted with stationary sampling in 3 different plants in Germany, USA and Belgium 15 measurements in the production plant including sampling operations. Another company reported 8 h workplace concentrations between 0.00017 and 0.00036 ppm.
On average operation personnel does not spent more than 1 hour per shift in the production area.

Flag **:** Critical study for SIDS endpoint

(17) (18) (59)

1.11 ADDITIONAL REMARKS

Memo : Formation of acrolein from methylthio propionaldehyde

Remark : Methional (3-(methylthio)propionaldehyde) in buffered aqueous solution at 100°C decomposes to acrolein. After a reaction time of 30 min, the yield is 95% with methional heated alone and 98% with methional heated together with ascorbic acid or hydrogen peroxide.

(1)

Memo : Bacterial transformation of methionine to methylthio propionaldehyde

Remark : The lacticacid bacterial strain Lactococcus lactis IFPL730 produces methylthio propionaldehyde from methionine in high rates (60 µg/mg protein · h) via 4-methylthio-2-ketobutyrate by the action of enzymes (aminotransferase and ketoacid de-carboxylase).

Flag : Critical study for SIDS endpoint

(2)

Memo : Formation of methylthio propionaldehyde by baker's yeast

Remark : Anaerobic incubation of methionine with baker's yeast (Saccaromyces cerevisiae) results in the formation of methylthio propionaldehyde: after 6 - 8 days at 13 - 16°C, up to 61% of me-thionine (10 - 100 mg/l) was transformed into methylthio propionaldehyde.

Flag : Critical study for SIDS endpoint

(96)

Memo : Methylthio propionaldehyde as constituent of the plant Paederia foetida occurring in South and East Asia

Remark : Intact leaves, chopped stems and intact flowers were separately steam distilled.
The dichloromethane extraction yielded extracts of 8 mg/kg leaves, 10 mg/kg stem and 30 mg/kg flowers. GC-FID analyses revealed methylthio propionaldehyde in the stems (0.4% of the extract, i. e. 32 µg/kg stem). In the leaves only traces were found. In the flowers, methylthio propionaldehyde was not found.

Flag : Critical study for SIDS endpoint
28.01.2004

(109)

Memo : Methylthio propionaldehyde in four tropical plant species

Remark : Four plant species from Costa Rica (Central America) were analysed for volatile compounds at different times of day by trapping on Tenax and GC-MS of the trapped volatiles. Methylthio propionaldehyde was found in volatiles from flowers of Theobroma mammosum (0.4% of all volatiles, concentration related to peak areas).

(61)

Memo : Methylthio propionaldehyde in Scorzonera hispanica (black salsify)

Remark : Extracts from Scorzonera hispanica (extraction with 2-methylbutane from 2 cm cubes in water) were analysed by GC and GC-MS. Methylthio propionaldehyde was found at a

relative abundance of 0.02% in the volatiles analysed. With a content of 200 micro-l/kg of volatiles extracted, 0.02% in the extract is equivalent to 0.04 mg methylthiopropionaldehyde/kg plant.

Flag : Critical study for SIDS endpoint

(69)

Memo : Methylthio propionaldehyde in nuts of the tree Corylus avellana in North America

Remark : Volatiles of the nuts (filberts) were collected from steam distillation (headspace analysis), from roasting (trapping of the volatiles), by extracting the distillate from steam distillation and by molecular distillation from the oil expressed from roasted filberts. Methylthio propionaldehyde was detected in the volatiles from the oil expressed from roasted filberts (no concentrations given).

(67)

Memo : Methylthio propionaldehyde in peaches

Remark : Diethyl ether extracts of homogenized fresh peaches and cooked peaches were analysed by GC-MS and aroma extract dilution analysis (AEDA). Methylthio propionaldehyde was found in the juice of fresh peaches (no quantitative data reported).

(56)

Memo : Methylthio propionaldehyde in raw and cooked potatoes

Remark : Potatoes (variety Bintje) (raw and boiled or 20 min at 100°C) were extracted with diethyl ether / pentane. The extracts were analyzed by GC-MS and GC-olfactometry. The concentration reported for cooked potatoes was 0.01 relative to the internal standard 4-methyl-1-pentanol (2 ml of a 50 µl/l solution added to 150 g potatoes in 300 g tap water). Methylthio propionaldehyde was not found in raw potatoes.

(81)

Memo : Methylthio propionaldehyde in the Averrhoa bilimbi fruit (in South and South-East Asia)

Remark : Blends of the fruits with water were steam distilled. The dichloromethane extract was analyzed by GC-FID. The total yield of volatiles was 3.9 mg/kg fruit. Methylthio propionaldehyde was found at a concentration of 0.1% in the volatiles, corresponding to about 4 µg/kg fruit.

Flag : Critical study for SIDS endpoint

(110)

Memo : Methylthio propionaldehyde in the bean Ceratonia siliqua

Remark : Extracts from mature beanpods (no details on extraction reported) were analysed by GC and GC-MS. Methylthio propionaldehyde was found; the reported concentration is 0.05% of the sum of all compounds analysed.

(70)

Memo : Methylthio propionaldehyde in the fruits of Muntingia calabura (South Asia and tropical America)

Remark : Ripe fruits were blended with water and vacuum-distilled (1) or steam-distilled at atmospheric pressure (2). The dichloromethane extracts of the distillates yielded 1.8 mg/kg (1) and 4.2 mg/kg (2). Analyses by GC and GC-MS revealed methylthio propionaldehyde at 0.1% only in the steam-distillate (2) corresponding to a methylthio propionaldehyde concentration of 4.2 µg/kg fruit. In the vacuum distillate, methylthio propionaldehyde was not found.

(108)

Memo : Methylthio propionaldehyde in tomatoes

Remark : Samples of ripe tomatoes were analysed by headspace sampling of volatiles and GC-FID / olfactometric analysis and GC-MS. Methylthio propionaldehyde was detected olfactometrically as "weak" in 2 of 3 analysed tomato mutants (no concentrations reported).

(71)

Memo : Methylthio propionaldehyde in volatiles of flowers of the autumn olive in North America

Remark : Flowers were treated by steam distillation / extraction with pentane. The pentane extract was concentrated and analyzed by GC-MS. Methylthio propionaldehyde was present with 0.09% of the total ion current (MS analysis).

28.01.2004 (83)

Memo : Occurrence of methional in orange juice

Remark : Analyses were performed with juice samples directly after preparation (fresh), after heating to 100°C (pasteurized) and after heatung to 100°C and following storage for 21 days at 35°C in sealed bottles (stored). The results (in ng methylthio propionaldehyde/l orange juice) were: fresh: 530, pasteurized: 830, stored: 11550.

(7)

Memo : Methylthio propionaldehyde in boiled carp fillet

Remark : Carp fillet was boiled, frozen, ground and extracted with diethyl ether. After distillation, the extracted components were analysed by GC and GC-olfactometry. Methylthio propionaldehyde was found at concentrations of 7.0 / 15.9 ± 3.3 / 26.35 ± 5.25 µg/kg.

Flag : Critical study for SIDS endpoint

(95)

Memo : Methylthio propionaldehyde in cooked mussels (Mytilus edulis)

Remark : Oysters were cooked in a vapor cooker. A sample of cooked mussel was heated with water and dichloromethane. GC-MS and GC-FID analyses of the extracts revealed the presence of methylthio propionaldehyde.

(68)

Memo : Methylthio propionaldehyde in crab meats in Hong Kong.

Remark : Live crabs (Charybdis feriatus) were steamed. Manually picked meat from these crabs was extracted. Extracts were analysed by GC-MS and quantified by comparison of

GC-MS-peaks with an internal standard. Methylthio propionaldehyde was found in the crab body (1.1 µg/kg) and the carapace (166.6 µg/kg).

Flag : Critical study for SIDS endpoint

(16)

Memo : Methylthio propionaldehyde in oyster cooker effluent

Remark : Waste water from oyster canning companies was hydrolysed and extracted with dichloromethane. The extract was analysed by GC-MS and aroma extract dilution analysis (AEDA).Methylthio propionaldehyde was found at a concentration of 98 ppb.

Flag : Critical study for SIDS endpoint

(66)

Memo : Methylthio propionaldehyde in processed fish and shrimps in Korea

Remark : Extracts of four fish pastes were analysed by GC-MS and quantified by calibration curves of amount ratios (compound/internal standard) vs. Peak area ratios (compound/internal standard). Methylthio propionaldehyde was found in one of four products at a concentration of 399 ppb (± 51%).

Flag : Critical study for SIDS endpoint

(14)

Memo : Methylthio propionaldehyde in the brew of cooked clams

Remark : Live clams (Meretrix lusoria) were cooked in water after different times of storage at 4°C. The liquid was processed in order to isolate the volatiles. The extract containing among others methional was analyzed by GC-FID and GC-MS. Methylthio propionaldehyde was quantified as 0.28% of the volatiles analysed. With a yield of 3.7 mg/kg clams, this correspondends to about 10 µg methylthio propionaldehyde/kg clams set free by cooking.

Flag : Critical study for SIDS endpoint

(97)

Memo : Methylthio propionaldehyde in Cheddar cheese

Remark : Dichloromethane extracts of steam distillates from cheese were analysed by GC-MS. Methylthio propionaldehyde was found in Cheddar cheese from raw milk (1.0 and 2.7 µg/kg) and from pasteurised milk (0.4 and 1.4 µg/kg).

Flag : Critical study for SIDS endpoint
28.01.2004

(85)

Memo : Methylthio propionaldehyde in blue cheese

Remark : Blue cheese from Wisconsin / USA was analysed by dynamic headspace - GC/MS - olfactometry. Analyses were performed on cheese samples starting at 10.28 g with reducing their mass by half from one test to the next one in a series of 10 test runs. Methylthio propionaldehyde was olfactometrically detected down to a sample size of 0.02 g (no concentration reported).
28.01.2004

(84)

Memo : Methylthio propionaldehyde in Swiss mountain cheese volatiles

Remark : Nine samples of cheese from Gruyere (French speaking part of Switzerland) were extracted by Freon 11. The extracts were analyzed by GC-FID. Methylthio propionaldehyde is listed in the cumulative list of volatile components found in the cheese samples investigated (concentrations not reported).

04.05.2004 (60)

Memo : Methylthio propionaldehyde in linden honey

Remark : The dichloromethane extract of linden honey was concentrated, distilled and separated by column chromatography. Gas chromatographic-mass spectrometric and gas chromatographic-olfactometric analyses resulted in the detection of methylthio propionaldehyde (no quantitative results reported).

28.01.2004 (8)

Memo : Methylthio propionaldehyde in Frankfurter sausages.

Remark : Volatiles isolated from chopped and heated sausages were analysed by GC-MS. Methylthio propionaldehyde was found in traces.

(15)

Memo : Methylthio propionaldehyde in beers

Remark : The dichloromethane extracts of several beer samples were analysed by GC-olfactometry and aroma extract dilution analysis (AEDA). Methylthio propionaldehyde was found in alcohol-free beer (no concentration reported).

(80)

Memo : Methylthio propionaldehyde in popcorn

Remark : Volatile compounds were analysed in popcorn samples after heating in a microwave oven. In the first instance, volatiles escaping from the popcorn were adsorbed on Tenax and analysed by GC-MS using internal standards. In the second instance, the heated popcorn was mixed with water. The slurry was heated, and the volatiles were adsorbed and analysed as desribed in the first instance. The results (µg methylthio propionaldehyde/kg popcorn) were 14 (dry method) and 12 (wet method).

Flag : Critical study for SIDS endpoint

(9)

Memo : Methylthio propionaldehyde in popcorn

Remark : Dichloromethane extracts from freshly prepared popcorn were separated by column chromatography and analysed by GC-MS. Methylthio propionaldehyde was found, but not quantified in terms of absolute concentrations, only in terms of olfactometry (FD factor 8).

(94)

Memo : Methylthio propionaldehydein rice cakes in the USA

Remark : Methylthio propionaldehyde was analysed by GC-FID of volatiles isolated from rice cakes by stripping the organic volatiles from a mixture of the cakes with water and a large excess of so-dium sulfate on a Tenax trap. In 2 samples, 5

and 10 ppb methional were found.

Flag : Critical study for SIDS endpoint

(10)

Memo : Methylthio propionaldehyde in sweet corn products in the USA

Remark : Methylthio propinaldehyde was analysed in can cream, can kernel, frozen kernel and fresh kernel by dynamic headspace-GC-MS. It was positively identified but could not be quantified because of a very low recovery.

(11)

Memo : Conversion factors

Result : Conversion factors at a temperature of 20°C and an atmospheric pressure of 1013 hPa:

3-(Methylthio) propionaldehyde:
1 ppm = 4.3 mg/m3
1 mg/m3 = 0.23 ppm

Acrylaldehyde:
1 ppm = 2.33 mg/m3
1 mg/m3 = 0.43 ppm

03.02.2004

Memo : Odour threshold

Remark : Odour limit (human): 0.00036 mg/m3 (0.00008 ppm)

Odour not noticeable (human): 0.00018 mg/m3 (0.0000414 ppm)

03.02.2004 (57)

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered : 3, 4, 5
Date of search : 05.11.2002

Remark : chapters covered: 2, 3, 4, 5
Flag : Critical study for SIDS endpoint

Type of search : External
Chapters covered : 3, 4
Date of search : 29.04.2003

Remark : Chapters covered: 2, 3, 4
Flag : Critical study for SIDS endpoint

1.13 REVIEWS

2.1 MELTING POINT

Value : = -58 °C
Sublimation :
Method : other: no data
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (4) not assignable
Brief description
Flag : Critical study for SIDS endpoint
28.01.2004 (19)

Value : = -75 °C
Sublimation :
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

2.2 BOILING POINT

Value : ca. 170.3 °C at 1013 hPa
Decomposition :
Method : other: extrapolated from measured data with dynamic method (vapour pressure)
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Recalculated from data of vapour pressure determination (Degussa AG Report-No.: 88/00147 from 07.10.1987)
Result : ca. 170 °C at 1009 hPa
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
(41)

Value : = 164 °C at 1013 hPa
Decomposition :
Method : other: no data
Year :
GLP : no data
Test substance :

Reliability : (4) not assignable
Secondary reference
(3)

Value : = 166 °C at 1000 hPa
Decomposition : no
Method : other: no data

Year :
GLP : no
Test substance :

Reliability : (2) valid with restrictions
Original study, no details reported
(13)

Value : = 165 °C at
Decomposition :
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

Value : = 170 °C at 1000 hPa
Decomposition :
Method : other: no data
Year :
GLP :
Test substance :

Reliability : (4) not assignable
Secondary reference
(51)

2.3 DENSITY

Type : density
Value : = 1.039 g/cm³ at 20 °C
Method : other: no data
Year :
GLP : no data
Test substance :

Remark : Density at 20 degree C relative to water at 4 degree C
Reliability : (4) not assignable
Acceptable literature reference
Flag : Critical study for SIDS endpoint
02.02.2004 (3)

Type : density
Value : = 1.036 g/cm³ at 20 °C
Method : other: no data
Year :
GLP : no
Test substance :

Reliability : (2) valid with restrictions
Acceptable literature reference
Flag : Critical study for SIDS endpoint
(82)

Type :

Value : 4.403 kg/m3 at 15 °C
Method : other: not reported
Year :
GLP :
Test substance :

Remark : vapour density
Result : 4.403 kp/m3 at 15.6 degree C / 1 atm
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

(23)

Type : relative density
Value : = 1.03 at °C
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.

02.02.2004 (63)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : ca. .53 hPa at 20 °C
Decomposition :
Method : other (measured): extrapolated from measured data to 20 °C with dynamic method
Year : 1996
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Test condition : The vapour pressure was determined at 6 different temperatures between 27 and 170 °C.
The curve followed the equation:
ln P(kPa) = 12.8 - 2561.5/(T(Kelvin)-130.41)
Using this equation the value of 0.58 hPa at 20 °C (293.15 Kelvin) was obtained.
Test substance : Purity: 99.96 %
Impurities: 0.0039 % water
Reliability : (2) valid with restrictions
Good documented experimental study with valid extrapolation method.
Flag : Critical study for SIDS endpoint
02.02.2004 (32) (41)

Value : = 5 hPa at 20 °C
Decomposition :
Method : other (measured): extrapolated from measured data with Isoteniskope to 20 °C
Year :
GLP : no
Test substance :

Test substance : Distilled quality, no further data
Reliability : (3) invalid
The uncertainty in the extrapolation to lower temperatures (20 °C) is relatively high. The test substance was not adequately defined.
02.02.2004 (19)

Value : = 1.3 hPa at 30 °C
Decomposition :
Method : other (measured): no data
Year :
GLP : no data
Test substance :

Reliability : (4) not assignable
Secondary reference
(3)

Value : = 133 hPa at 105 °C
Decomposition :
Method : other (measured): no data
Year :
GLP : no data
Test substance :

Reliability : (4) not assignable
Secondary reference
(3)

Value : = 1 hPa at 20 °C
Decomposition :
Method :
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = .34 at 20 °C
pH value :
Method : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year : 1992
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Standard deviation = 0.07 (log)
Reliability : (1) valid without restriction
Standard test method
Flag : Critical study for SIDS endpoint
(90)

Partition coefficient : octanol-water

Log pow : ca. .41 at °C
pH value :
Method : other (calculated): KOWWIN (LOGKOW (c)) Program, Version 1.51, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U. S. A.
Year : 1996
GLP : no
Test substance :

Reliability : (2) valid with restrictions
Calculated data, internationally accepted method
(42)

Partition coefficient : octanol-water
Log pow : = -.04 at °C
pH value :
Method : other (calculated): Hansch C.; Leo, A. J.: Substituent constants for correlation analysis in chemistry and biology. John Wiley, NY
Year : 1979
GLP : no
Test substance :

Reliability : (2) valid with restrictions
Calculated data, internationally accepted method
(36)

Partition coefficient : octanol-water
Log pow : = -.16 at °C
pH value :
Method :
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : = 77.9 g/l at 37.8 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Solubility related to pure substance
Result : 80 - 150 g/l (20 °C) dependent on puritiy

77.9 g/l at 37.8 °C (pure substance)

The pH was not given, but as the substance does not contain any groups capable of protonation or deprotonation the determination of the pH is not necessary.

Reliability : (2) valid with restrictions
Limited documentation.
Flag : Critical study for SIDS endpoint
(23)

Solubility in : Water
Value : ca. 100 g/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: no data
Year :
GLP : no data
Test substance :

Result : approx. 10 g per 100 g of water at 25 degree C
Reliability : (4) not assignable
Secondary reference
(3)

Solubility in : Water
Value : <= 75 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Solubility related to pure substance, calculated from the solubility at 37.8 °C.
Reliability : (4) not assignable
Secondary reference
Flag : Critical study for SIDS endpoint
(51)

Solubility in : Water
Value : = 175 g/l at 37.8 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

2.6.2 SURFACE TENSION

Test type	:	Ring method
Value	:	= 40.2 mN/m at 20 °C
Concentration	:	
Method	:	
Year	:	1975
GLP	:	no
Test substance	:	other TS: no data
Method	:	Ring method according to Lecomte du Nouy (comparable to test
Result	:	40 dyn/cm at 20 °C.
Reliability	:	(3) invalid Pure substance was tested instead of an aqueous solution of

(22)

2.7 FLASH POINT

Value	:	= 61.4 °C
Type	:	closed cup
Method	:	other: ASTM D-56
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(1) valid without restriction Standard test method, no details reported
Flag	:	Critical study for SIDS endpoint

(39)

Value	:	= 63 °C
Type	:	closed cup
Method	:	other: DIN 51755 (according to Abel-Pensky)
Year	:	1996
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(1) valid without restriction Standard test method
Flag	:	Critical study for SIDS endpoint

(40)

Value	:	= 68 °C
Type	:	closed cup
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	
Reliability	:	(4) not assignable Secondary reference

(3)

Value	:	°C
Type	:	other: no data
Method	:	other: no data
Year	:	2001

GLP : no data
Test substance : other TS: no data

Result : 58-63 °C
Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

2.8 AUTO FLAMMABILITY

Value : = 255 °C at
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: no data

Reliability : (4) not assignable
Secondary reference, no details reported, primary reference not reported.
02.02.2004 (63)

Value : = 280 °C at
Method : other: DIN 51794
Year :
GLP :
Test substance :

Reliability : (1) valid without restriction
Test procedure in accordance with national standard methods.
Flag : Critical study for SIDS endpoint
(38)

Value : = 290 °C at
Method : other: DIN 51794
Year :
GLP :
Test substance :

Reliability : (1) valid without restriction
Test procedure in accordance with national standard methods.
02.02.2004 (20)

2.9 FLAMMABILITY

Result : non flammable
Method : other: estimation from experience in production and handling
Year :
GLP : no
Test substance :

Remark : From the experience in production and handling of 3-(methyl-thio)propionaldehyde (C4H8OS) it can be excluded that the substance is liable to spontaneous combustion or emission of flammable gases in contact with water.
Flag : Critical study for SIDS endpoint
02.02.2004

Method : other: DIN 51794
Year :
GLP :
Test substance :

Remark : No details on test method reported
Result : ignition temperature: 280 degree C
Reliability : (1) valid without restriction
Standard test method, no details reported

(51)

2.10 EXPLOSIVE PROPERTIES

Result : other: see Freetext
Method :
Year :
GLP : no
Test substance :

Result : Explosion limits in air: lower 1.3 vol% upper 26.1 vol%
Reliability : (4) not assignable
Flag : Critical study for SIDS endpoint

(3) (23) (63)

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties
Method : other: estimation from molecule structure
Year :
GLP : no
Test substance :

Remark : The test for oxidising properties is not appicable to liquids or gases. As 3-(methylthio)propionalde-hyde is a liquid under ambient conditions the test is not appilcable. Furthermore from the molecular structure of 3-(methylthio)propionalde-hyde (C4H8OS) it is not expected that the substance has oxidizing properties, because the molecule contains only one oxygen atom which is bound to carbon and no elements are present at high oxidation levels (e.g N > 0, Cl > -1 or O > -2).
Flag : Critical study for SIDS endpoint

(3) (62)

2.12 DISSOCIATION CONSTANT

Acid-base constant : Not relevant, substance does not contain dissociable groups or groups capable of protonation or deprotonation.

02.02.2004

2.13 VISCOSITY

Test type : other: dynamic viscosity
Test procedure :

Value : = 1551 - mPa s (dynamic) at 20 °C
Result :
Method : other: not reported
Year :
GLP :
Test substance :

Reliability : (4) not assignable
Secondary reference

(51)

2.14 ADDITIONAL REMARKS

Memo : Harzardous reactions

Remark : Polycondensation may occur. Violent reactions may occur in contact with alkalines, amines and oxidants.

(51)

Memo : Odour

Remark : Extremely bad odour.

(51)

Memo : Degradation of methylthio propionaldehyde by fungi producing hydrogen peroxide

Remark : To a culture of the fungus Phanerochaete chrysosporium that produces hydrogen peroxide and from this OH radicals, methylthio propionaldehyde is added. This assay starts producing ethylene within 1 hour of incubation.

(6)

Memo : Stability

Remark : Stable under normal conditions of use.

(3)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm³
Rate constant	:	= .0000000000528 cm³/(molecule*sec)
Degradation	:	= 50 % after 7.3 hour(s)
Deg. product	:	
Method	:	other (calculated): AOPWIN (AOP (c)) Program, Version 1.75, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U. S. A.
Year	:	1995
GLP	:	no
Test substance	:	
Reliability	:	(2) valid with restrictions Calculated data, internationally accepted method
Flag	:	Critical study for SIDS endpoint

(43)

Type	:	water
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	36000 molecule/cm³
Rate constant	:	= .0000000000136 cm³/(molecule*sec)
Degradation	:	= 63 % after 23.5 day(s)
Remark	:	Calculated from the reaction rate constant of MTPA with hydroxyl radicals in fresh water as published by Buxton et al. (1988) and the concentration of OH radicals in fresh water as published by Mill (1999).
Test condition	:	Reaction rate constant: 8.2 x 10 E(+9) l/ (mol x s)
Reliability	:	(2) valid with restrictions Calculated data, generally accepted method
Flag	:	Critical study for SIDS endpoint

16.04.2004 (12) (72)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	> 1 year at 25 °C
t1/2 pH7	:	= 75.4 day(s) at 25 °C
t1/2 pH9	:	= 6.5 day(s) at 25 °C
Degradation	:	35 % after 101 hour(s) at pH 7 and 50 °C
Deg. product	:	not measured
Method	:	Directive 92/69/EEC, C.7
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The main test was performed for pH7 and 9.

Test condition : TEST TYPE: Full test at pH 7 and 9, Pretest for pH 4
- Test medium: buffer solutions pH4, 7 and 9 according to EC guideline

- Initial concentration of test substance:
Pretest:
pH4: 759.5 mg/l
pH7: 606.5 mg/l
pH9: 562.3 mg/l
Method of analysis: HPLC
Incubation at 50 °C, duration 5 d
Initial concentration in main test:
pH 7: 782.08 mg/l
pH 9: 757.19 mg/l
Temperatures: pH 7 50, 55, 65°C, pH 9:50, 39°C

DURATION: pH 7: 101 h (50°C), pH 9: 50.9 h

Analytical Method: HPLC analysis

Reliability : (1) valid without restriction
Guideline study

Flag : Material Safety Dataset, Critical study for SIDS endpoint

(47)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Henry's Law Constant determinated experimentally
Year : 1992

Result : Henry's law constant < 2.30 Pa * m3/mol
Volatility from water is expected to be low.

Reliability : (1) valid without restriction
Good documented experimental study

Flag : Critical study for SIDS endpoint

(89)

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)

Soil : % (Fugacity Model Level II/III)
Method : other: HENRYWIN (c) Program, Version 2.51, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U. S. A.
Year : 1995

Method : METHOD FOLLOWED: Bond estimation method and group estimation method
GLP: no
METHOD OF CALCULATION: HENRIWIN c, Syracuse Research corporation, Merrill Lane, Syracuse, N.Y., 13210, USA, 1995.
Result : Based upon QSAR (quantitative structure activity relationship) estimations from the molecular structure of 3-(methylthio)propionaldehyde the Henry's Law Constant was estimated with the
bond estimation method as: 9.7 x 10 E(-2) Pa x m³/mol
and with the
group estimation method as: 4 x 10 E(-2) Pa x m³/mol
This indicates that 3-(methylthio)propionaldehyde is not volatile from aqueous solutions.
Reliability : (2) valid with restrictions
Calculated data, internationally accepted method

(44)

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Henry's Law Constant (calculated)
Year :

Result : Based upon the water solubility at 20 °C (<= 75 g/l) and the vapour pressure at 20 °C (53 Pa) the Henry's Law Constant of 3-(methylthio)propionaldehyde was estimated as
7.36 x 10 E(-2) Pa x m³/mol. This indicates that 3-(methylthio)propionaldehyde is not volatile from aqueous solutions.
Reliability : (2) valid with restrictions
Calculated data, internationally accepted method
Flag : Critical study for SIDS endpoint

(46)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year : 1999

Method : Mackay level I model, Version 2.11 (1999) based on Mackay et al.: Chemosphere, 24, 695-717 (1992) and earlier publications.
Result : The equilibrium partitioning characteristics in the environment of 3-(methylthio)propionaldehyde was estimated:

Compartment	Theoretical Distribution [%]
Air	2.48
Water	97.49
Soil	0.02

		Sediment 0.02 Suspended Sediment 0 Biota (as fish) 0 That means that the most likely target compartment of theoretical environmental emissions of 3-(methylthio)propionaldehyde is the hydrosphere.
Test condition	:	Input parameters Molecular Mass: 104.2 g/mol Temperature: 25 °C log Kow: 0.34 Water solubility: 75000 g/m3 Vapour pressure: 53 Pa Melting point -58 °C Henry's law constant: 0.0736 Pa m3/mol Volumes: (m3) Air: 6 x 10E9 Water: 7 x 10E6 Soil: 4.5 x 10E4 Sediment: 2.1 x 10E4 Suspended sediment: 3.5 x 10E1 Aquatic biota (fish): 7 Aerosol: 0.12 Densitiy (kg/m3) Air: 1.19 Water: 1000 Soil: 1500 Sediment: 1500 Suspended sediment: 1500 Aquatic biota (fish): 1000 Aerosol: 1500 Organic carbon (g/g) Soil: 0.02 Sediment: 0.05 Suspended sediment: 0.167 Lipid content (g/g) Aquatic biota (fish): 0.05
Reliability	:	(2) valid with restrictions Origin of the calculation program (BASIC programme) is not documented. Little differences of some standard values of the program (density of soil and sediment) to newer pulications of Mackay et al. (see Method).
Flag	:	Critical study for SIDS endpoint
04.05.2004		(46)
Media	:	air - biota - sediment(s) - soil - water
Method	:	Calculation according Mackay, Level III
Year	:	2002
Method	:	Estimation of the Equilibrium Partitioning Characteristics in the Environment. Calculation Mackay Level III, V2.20 Model (1999) Environmental Modelling Centre, Trent Universitiy, Peterborough, Ont. Canada.
Result	:	Compartment % Amount Concentrations Volume (m3) Air 0.2 2.8x10E-3 ng/m3 5.96 x 10 E14

	Water	92	3.14 ng/l	2.54 x 10 E11
	Soil	7.9	1.6x10E-3 ng/g	2.85 x 10 E10
	Sediment	0.04	2x10 E-3 ng/g	1.27 x 10 E8

Conclusion: The majority of the substance distributes to water and a minor amount to soil. Relatively low amounts distribute into air and sediment.

Test condition : Input parameters
Molecular Mass: 104.17 g/mol
Temperature: 20 °C
log Kow: 0.34
Water solubility: 75000 g/m3
Vapour pressure: 53 Pa
Melting point -58 °C
Henry's law constant: 0.0736 Pa m3/mol

Emission rates (estimated, not based on measured data):
To Air: 1 kg/h
To water 1 kg/h
to soil 0.1 kg/h
to sediment: 0 kg/h

Reliability : (4) not assignable
Emission values not supported by data.

04.05.2004 (48)

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year : 2002

Method : Estimation of the Equilibrium Partitioning Characterisitcs in the Environment.
Calculation
Mackay Level III, V2.70 Model (2002) Environmental Modelling Centre, Trent Universitiy, Peterborough, Ont. Canada.

Result :

Compartment	Release 100% in air	Release 100% into water	Release 100% onto soil
Air	4.98%	1.21 10E-03%	0.0243%
Water	51.6%	99.9%	52.8%
Soil	43.5%	0.0106%	47.2%
Sediment	0.0211%	0.0409%	0.0216%

Conclusion:
Under equilibrium steady state flow conditions the substance distributes to water and soil when released into the air or soil compartment, while the majoritiy of the substance will stay in the water compartment when released into water.

Test condition : Input parameters
Molecular Mass: 104.17 g/mol
Temperature: 25 °C
log Kow: 0.34 (20 °C)
Water solubility: 75000 g/m3
Vapour pressure: 53 Pa (20 °C)
Melting point -58 °C
Henry's law constant: 0.0736 Pa m3/mol
Half-life in air: 7.3 hours

Half-life in water: 1810 hours (pH 7.0)

Emission rates default 3000 kg/h to either air, water or soil.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

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Media : water - soil
Method : other (calculation): PCKOCWIN (PC-KOC (c)) Program, Version 1.57, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U. S. A.
Year : 1995

Result : The soil or sediment adsorption coefficient (Koc) of 3-(methylthio)propionaldehyde was calculated as Koc = 9.4. This indicates high mobility of 3-(methylthio)propionaldehyde in soil (adsorption to soil is not expected).
Reliability : (2) valid with restrictions
Calculated data, internationally accepted method

(45)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : domestic sewage
Concentration : 21.4 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time : 28 day(s)
Degradation : 92 (±1) % after 28 day(s)
Result : readily biodegradable
Kinetic of testsubst. : 2 day(s) = 5 - 8 %
6 day(s) = 33 - 67 %
8 day(s) = 68 - 74 %
14 day(s) = 74 - 76 %
28 day(s) = 91 - 93 %
Control substance : Acetic acid, sodium salt
Kinetic : 2 day(s) = 56 %
8 day(s) = 86 %
Deg. product : no
Method : Directive 92/69/EEC, C.4-A
Year : 2000
GLP : yes
Test substance : other TS: purity: 99.49%

Method : Off. J. of the European communities, method C4-A of 29.12.1992
Result : · Kinetic of biodegradation :

day	FE1 (%)	FE2 (%)	FC (%)	FI (%)	FA (%)
0	0	0	0	0	0
2	8	5	56	37	0
6	67	33	85	75	4
8	68	74	86	87	2
14	74	76	92	81	0

19	85	86	98	89	1
21	95	90	97	93	0
28	93	91	96	94	0

FE1 and FE2 : flasks with the test substance
FC : flask with the reference substance (sodium acetate)
FI : flask for checking possible inhibitory effect of the test substance (test substance and sodium acetate)
FA : flask for checking a possible abiotic degradation (test substance and NaN3)

· Breakdown product : no
· Remarks : the difference of biodegradation between the two flasks containing the substance at the end of the test is less than 20%
More than 70% of biodegradation was reached within 14 days in the control flask containing sodium acetate (92% of biodegradation after 14 days). The inoculum activity is correct.
More than 35% of biodegradation was obtained within 14 days in the inhibitory flask (81% of biodegradation after 14 days). No inhibitory effect was observed.
No abiotic degradation was observed in the flask containing the test medium, the substance and the biocide NaN3.

CONCLUSIONS

The test is considered as valid and the 3-[methylthio]propionaldehyde is considered as readily biodegradable (conclusion from the study director).

Test condition : Inoculum : influent of a municipal wastewater treatment plant dealing with municipal sewage. Final concentration in the test medium is 77 000 bact/ml.
· Test conditions :
- the concentration of the chemical in the test medium is 21,4 mg/l expressed as organic carbon. No vehicle was used. The inoculum was not pre-exposed to the chemical
- the temperature of incubation was 20,7°C - 22,8°C
- the sampling frequency was : 0, 2, 6, 8, 14, 19, 21 and 28 days
- the following flasks were prepared : 2 blank flasks without the tested substance, 2 flasks with the tested substance, 1 flask with the reference substance (sodium acetate), 1 flask for checking inhibitory effect (test substance and sodium acetate) and 1 flask for checking abiotic elimination (test substance and NaN3)
- Analysis of dissolved organic carbon was used to measure the biodegradation
- Statistical method : the mean between the two values of biodegradation was chosen

Test substance : AMTP from Aventis NA - Batch No. 996610/02 - Purity 99,49%

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : WGK (DE), Material Safety Dataset, Critical study for SIDS endpoint (92)

Type : aerobic

Inoculum : domestic sewage, non-adapted

Concentration : 40 mg/l related to DOC (Dissolved Organic Carbon) related to

Contact time :
Degradation : = 100 (±) % after 18 day(s)
Result : readily biodegradable
Kinetic of testsubst. : 4 day(s) = 5.5 - 6.5 %
18 day(s) = 99.8 - 100 %
%
%
%
Control substance : Acetic acid, sodium salt
Kinetic : 18 day(s) = 93.5 %
%
Deg. product : no
Method : other: ISO 9439 with DOC measurements during the assay; method similar to OECD 301 B
Year : 1993
GLP : yes
Test substance : other TS: Rhone-Poulenc Chimie

Method : · Method : method ISO 9439 from 1st December 1990 (method by analysis of the carbon dioxide released). Measurements of the dissolved organic carbon (DOC) were performed in addition to the CO2 measurements.
Remark : CO2 evolution reached 50 % in 28 days. As COD was shown to be 100 % eliminated in 18 days in inoculated test vessels, and 10 % in sterile vessels, this DOC removal was concluded to be biotic. It has been shown in the literature (de Morsier et al.) that organic carbon could be integrated into the biomass at more than 50 %. The remaining carbon is evolved as CO2, and therefore a 50 % CO2 evolution can be the result of a total biodegradation. So the substance was concluded to be readily biodegradable.
Result : · 50 % biodegradation after 28 days with the CO2 measurements and 100% biodegradation after 18 days
· Kinetic of biodegradation :
Table with the kinetic of biodegradation based on the CO2 measurements:

days	FE1 (%)	FE2 (%)	FC (%)	FI (%)	FA (%)
0	0	0	0	0	0
1	0	0	16	0	0
4	3	3	43	29	0
5	3	3	49	43	0
8	2	2	52	51	0
11	29	24	55	57	0
12	35	41	55	60	0
15	37	48	58	61	0
22	39	51	62	63	0
28	41	52	72	67	1

FE1 and FE2 : flasks with the test substance
FC : flask with the reference substance (sodium acetate)
FI : flask for checking possible inhibitory effect of the test substance (test substance and sodium acetate)
FA : flask for checking a possible abiotic degradation (test substance and NaN3)

Table with the kinetic of biodegradation based on the DOC measurements:

days	FE1 (%)	FE2(%)	FC (%)	FI (%)	FA (%)

0	0	0	0	0	0
4	6.5	5.5	-	54.1	5.2
18	99.8	100	93.5	95.7	10.2

FE1 and FE2 : flasks with the test substance
FC : flask with the reference substance (sodium acetate)
FI : flask for checking possible inhibitory effect of the test substance (test substance and sodium acetate)
FA : flask for checking a possible abiotic degradation (test substance and NaN3)

· Breakdown product : no
· Remarks on the results obtained with the CO2 measurements:
The difference of biodegradation between the two flasks containing the substance at the end of the test is more than 20% (41% and 52% after 28 days). The approximate value of 50% biodegradation at the end of the test was proposed by the study director.
Less than 60% of biodegradation was reached within 14 days in the control flask containing sodium acetate (58% of biodegradation after 15 days). Nevertheless the level of 72% of biodegradation was reached at the end of the test.
More than 25% of biodegradation was obtained within 14 days in the inhibitory flask (61% of biodegradation after 15 days). No inhibitory effect was observed.
No abiotic degradation was observed in the flask containing the test medium, the substance and the biocide NaN3.

· Remarks on the results obtained with the DOC measurements :
The difference of biodegradation between the two flasks containing the substance at the end of the test is less than 20% (99,8% and 100% after 18 days). The value of 100% biodegradation after 18 days was proposed by the study director.
More than 70% of biodegradation was reached within 18 days in the control flask containing sodium acetate (93,5% of biodegradation after 18 days).
95,7% of biodegradation was obtained within 18 days days in the inhibitory flask. No inhibitory effect was observed.
No significant abiotic degradation was observed in the flask containing the test medium, the substance and the biocide NaN3 (10,2% of degradation after 18 days).

CONCLUSIONS

The test is considered as valid by the study director even if the difference of biodegradation between the two flasks containing the substance at the end of the test is more than 20% with the CO2 measurements. The CO2 measurements indicate that 50% of the carbon added in the medium is mineralised to CO2. Additional measurements of DOC showed that the substance is degraded to 100% within 18 days. There is no significant degradation in the abiotic control and the DOC measurements performed at the beginning of the test (day 4) indicate that there is no adsorption on the inoculum. So the DOC eliminated from the test medium which is not released as CO2, is probably incorporated into the bacterial biomass.

The value of 100% of biodegradation within 18 days is proposed by the study director and the 3-[methylthio] propionaldehyde is considered as readily biodegradable.

Test condition : - The concentration of the chemical in the test medium is 40 mg/l expressed as organic carbon. No vehicle was used. The inoculum was not pre-exposed to the chemical
- the temperature of incubation was 22°C +/- 2°C
- the sampling frequency was : 0, 1, 4, 5, 8, 11, 12, 15, 22 and 28 days for the CO2 measurements and 0, 4 and 18 days for the DOC measurements
- the following flasks were prepared : 2 blank flasks without the tested substance, 2 flasks with the tested substance, 1 flask with the reference substance (sodium acetate), 1 flask for checking inhibitory effect (test substance and sodium acetate) and 1 flask for checking abiotic elimination (test substance and NaN3)
- The analysis of the CO2 released and the analysis of the dissolved organic carbon was used to assess the biodegradation. The CO2 released was trapped as barium carbonate and the DOC was measured with the Dorhmann DC 190 analyser of carbon with oxidation at 900°C
- Statistical method : the highest and round value of biodegradation was chosen.

Reliability : (2) valid with restrictions
Guideline study slightly modified test procedure. (DOC measurements were performed in addition to CO2 measurements and the precise kinetic of the DOC measurements was not provided).

(91)

3.6 BOD5, COD OR BOD5/COD RATIO

COD
Method :
Year :
COD : mg/g substance
GLP : no

Remark : Biochemical oxygen demand (BOD):
Method: DEV DIN 38409 H51 (dilution method)
Concentration: a) 1000 mg/l related to test substance
b) 2000 mg/l related to test substance
Results:
a) BOD5 = 615 mg/l
b) BOD5 = 1170 mg/l
mean value: BOD5 ca. 600 mg/g
GLP: no
Chemical oxygen demand (COD):
Method: DEV DIN 38409 H41
Concentration: a) 1000 mg/l related to test substance
b) 2000 mg/l related to test substance
Results:
a) COD = 1500 mg/l
b) COD = 2950 mg/l
mean value: COD ca. 1500 mg/g
GLP: no
Ratio BOD5 / COD = 0.4 (not readily biodegradable)

Test substance : purity: 97.3 % (impurities: methyl mercaptan, acrolein, methanol, acetaldehyde)

Reliability : (2) valid with restrictions

Test procedure in accordance with national standard methods with acceptable restrictions

(35)

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	24 hour(s)
Unit	:	mg/l
LC0	:	= 9.1
LC50	:	= 14
LC100	:	= 18.1
Limit test	:	no
Analytical monitoring	:	no
Method	:	other: ISO 7346/1-3, year: no data
Year	:	1988
GLP	:	yes
Test substance	:	other TS: Rhone Poulenc Chimie

Method :

· Species/Strain/Supplier: Brachydanio rerio (Hamilton Buchanan) from the "Centre de Recherche de la Station de Lagunage de Mèze". The sensitivity of the fish was checked in an additional study (CL50/24h = 210 mg/l with the potassium dichromate).
· Statistical methods : log-probit analysis

· Nominal concentrations: 5.5 - 9.1 - 12.5 - 18.1 - 27.7 - 40.3 - 57.7 mg/l.
· Measured concentrations: not determined.
· Unit : result expressed as mg/l
· LC50/24h = 14 mg/l, LC0/24h = 9.1 mg/l and the LC100/24h = 18.1 mg/l based on nominal concentration
· Remark :
- The concentration in the test solutions was not measured during the assay but the water solubility of the substance is high and it is not suspected to volatilise from the water. Therefore due to its physico-chemical properties, the substance is considered as stable in the test medium.

Remark : The study is of shorter duration than demanded in the most recent test guidelines (24 h instead of 96 h). In analogy to the results in the Daphnia study it can be expected that the LC50 will be lower after 96 hours. However, it is not expected that the LC50 will be below 1 mg/l after 96 h and the fish study can be used for the hazard evaluation.

Result : - Table with the cumulative mortality :

Concentration (mg/l)	Mortality (number of fish)	Mortality (%)
0	0	0
5.5	0	0
9.1	0	0
12.5	1	10
18.1	10	100
27.7	10	100
40.3	10	100
57.7	10	100

CONCLUSIONS

The LC50/24h on Brachydanio rerio of the (methylthio)propionaldehyde (batch from 7/09/88) is equal to

14 mg/l (study director).

Test condition : - Test fish: the fish were maintained during 2 weeks in the dilution water at 23°C +/- 1°C. They were fed normally, except 24 hours before the test. No disease was observed. The medium weight of the fish used in the definitive test was 0.44 +/- 0.21 g and the medium size was 3.5 +/-0.3, cm which is a little more than the size required by the ISO standard.
- Test conditions: A reconstituted dilution water was used (pH 7.9 at 23°C, conductivity 590 µS.cm-1, oxygen concentration 98%). The test solutions were prepared by direct dissolution of the product into the dilution water using an ultra-turrax T 45/6 during 3 min. A preliminary and a definitive test were performed.
The temperature during the definitive test was between 21.9 and 22.8°C. The temperature was lower of 1/10°C compared to the 23 +/- 1°C required by the ISO standard.
Seven nominal concentrations were tested. Ten fish were added in the 10L of each test solution and in the 10L of the dilution water for the control. The actual concentrations were not measured during the test. The pH was between 7.84 and 7.44 and the oxygen concentration was higher than 82% at the end of the test.

Test substance : ALDEHYDE METHYL THIOPROPIONIQUE, 7/09/1988 from the "Roches de Condrieu" plant. The purity is not indicated.

Reliability : (2) valid with restrictions
Test procedure in accordance with standard methods. No analytical measurements were performed. The test duration was only 24 hours.

Flag : WGK (DE), Material Safety Dataset, Critical study for SIDS endpoint

04.05.2004 (88)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : = 25
Analytical monitoring : no
Method : other: AFNOR T90301; year: 1983
Year : 1985
GLP : no
Test substance : other TS: Purity: 99.2%

Method : · Species/Strain/Supplier: Daphnia magna, Straus, 1820.
· Statistical methods: not indicated
· Nominal concentrations: not indicated
· Measured concentrations: not determined.
· Unit: result expressed as mg/l
· Remark: the product is indicated as miscible to water at the tested concentrations.

Test condition : Test medium with a pH = 8.0 +/- 0.2, a conductivity equal to 250 mg/l +/- 25 mg/l and a ratio Ca/Mg ~ 4/1

Test substance : ALDEHYDE METHYL THIOPROPIONIQUE, 28/11/1985 from the "Roches de Condrieu" plant. The purity is 99.2 %

Reliability : (4) not assignable
Abstract; complete report not yet available

Flag : non confidential, WGK (DE)

04.05.2004 (93)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 4.5
EC100 : > 12.4
EC10 : = 1.72
EC90 : = 11.64
Limit Test : no
Analytical monitoring : yes
Method : other: Directive 92/69/EEC, C.2 1992 and OECD 202 (I) 1984
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical method: Probit analysis according to Cavalli-Sforza (1972).

Result : RESULTS: EXPOSED
- Nominal/measured concentrations (mg/l):

Nominal	measured
0.15	< 1*
0.3	< 1*
0.6	< 1*
1.2	< 1*
2.5	2.8
5.0	6.2
10	12.4

Stock solution:

Nominal	measured (mg/l)
100	112

* = below limit of quantification

- Effect data (Immobilisation) (48 h): EC50 4.5 mg/l 95% confidence limits: 2.4-8.3 mg/l

Concentration / response curve:

Concentration (mg/l)	number	number mobile	number immobile	%
control	20	20	0	0
0.15	20	20	0	0
0.3	20	20	0	0
0.6	20	20	0	0
1.2	20	20	0	0
2.8	20	15	5	25
6.2	20	6	14	70
12.4	20	2	18	90

- Effect data (immobilisation) (24 h): EC50: > 12.4 mg/l

Concentration / response curve:

(mg/l)	number	number mobile	number immobile	%
control	20	20	0	0
0.15	20	20	0	0
0.3	20	20	0	0
0.6	20	20	0	0
1.2	20	20	0	0
2.8	20	20	0	0

6.2	20	15	5	25
12.4	20	12	8	40
0.15				

Test condition : TEST ORGANISMS
- Strain: Daphnia magna Straus, clone 5
- Source/supplier: Infracor, Marl
- Breeding method: M4 medium, 1 l beakers, water exchange every 2 to 3 days
- Age: < 1 day
- Feeding: Desmodesmus subspicatus
- Feeding during test: none
- Control group: yes

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Solvent: water
- Concentration: 102 mg/l

STABILITY OF THE TEST CHEMICAL SOLUTIONS: Stability under the test conditions was demonstrated in the hydrolysis as function of pH study. Stability of stock solution and a serious test dilutions was demonstrated: recovery > 80% DOC.

DILUTION WATER
- Source: Synthetic fresh water
- Hardness: 250 mg CaCO3/l
- Ca/Mg ratio: 4:1
- Na/K ratio: 10:1
- pH: 8.0-8.2
- Oxygen content: 8.0 - 8.5 mg/l

TEST SYSTEM
- Test type: static
- Concentrations: 0.15, 0.3, 0.6, 1.2, 2.5, 5, 10, 100 mg/l
- Number of replicates, individuals per replicate: 4, 5
- Test temperature: 20 +- 1 °C
- Dissolved oxygen: 7.4-8.5 mg/l
- pH: 7.6-8.2
- Adjustment of pH: no
- Intensity of irradiation: dark

DURATION OF THE TEST: 48 hours
TEST PARAMETER: Immobilisation
SAMPLING: 0, 48 hours
MONITORING OF TEST SUBSTANCE CONCENTRATION: TOC analysis

Reliability : (1) valid without restriction
Flag : Material Safety Dataset, Critical study for SIDS endpoint

(49)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= 1
LOEC	:	= 2.5
EC10	:	= 1.3
EC50	:	5.7
Limit test	:	no
Analytical monitoring	:	no
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	1993
GLP	:	no

Test substance : as prescribed by 1.1 - 1.4

Method : METHOD FOLLOWED: OECD guideline No. 201, 1984
DEVIATIONS FROM GUIDELINE:
GLP: no
METHOD OF CALCULATION: graphical evaluation, aerea under the curve
ANALYTICAL METHODS: no substance analysis performed, based on nominal concentrations.
· Species/Strain/Source: Scenedesmus subspicatus SAG 86.81 - Pflanzenphysiologisches Institut der Universität Göttingen.

Remark : Growth rates decreased over time, but the validity criterion of 16 fold increase over 72 h was fulfilled in the critical tests. Thus these results can be used to derive ECx and NOEC values.

Result : - Nominal concentrations only.
- Growth curves:
Experiment 1:

Cell densitiy:

Conc. (mg/l)	Cell count/ml 24 h x10E5	Cell count/ml 48 h x 10E6	Cell count/ml 72 h x 10E6
control 1	4.2	1.2	2.0
0.1	4.1	1.3	2.1
0.25	4.2	1.1	1.9
0.5	3.9	1.0	1.8

Experiment 2
Cell density:

Conc. (mg/l)	Cell count/ml 24 h x 10E5	Cell count/ml 48 h x 10E6	Cell count/ml 72 h x 10E6
control 2	4.9	1.1	1.7
1	4.3	86	1.6
2.5	3.3	55	85
5	2.5	37	56

Experiment 3
Cell density:

Conc. (mg/l)	Cell count/ml 24 h x 10E5	Cell count/ml 48 h x 10E5	Cell count/ml 72 h x 10E5
control 3	5.1	0.13	0.23
10	3.0	2.9	2.6
25	2.3	2.0	1.7
50	2.3	2.0	1.7

Cell count at t=0: 1.1 10E5 to 2 10E5
control values are means of 3 experiments

Growth rates

Experiment 1:

Concentration (mg/l)	0-24 h	0-48 h	0-72 h
Control 1	1.261	1.154	0.929
0.1	1.229	1.191	0.954
0.25	1.253	1.108	0.921
0.5	1.179	1.060	0.903

Experiment 2

Concentration (mg/l)	0-24 h	0-48 h	0-72 h
Control 2	1.556	1.161	0.945
1	1.363	1.028	0.892
2.5	1.099	0.805	0.682
5	0.821	0.607	0.542

Experiment 3

Concentration (mg/l)	0-24 h	0-48 h	0-72 h
control 3	0.936	0.924	0.782
10	0.140	0.000	-0.054
25	0.140	0.000	-0.054
50	0.405	0.186	0.087

Percent inhibition compared to controls

Experiment 1

Concentration (mg/l)	0-24 h	0-48 h	0-72 h
0.1	2.5	-3,2	-2.7
0.25	0.6	4.0	0.9
0.5	6.5	8.1	2.9

Experiment 2

Concentration (mg/l)	0-24 h	0-48 h	0-72 h
1	12.4	11.4	5.6
2.5	29.4	30.7	27.9
5	47.3	47.8	42.6

Experiment 3

Concentration (mg/l)	0-24 h	0-48 h	0-72 h
10	85.1	100	106.9
25	85.1	100	106.9
50	56.7	79.9	88.8

control values are means of 3 experiments

The cell count in the controls in experiments 1 and 2 was > than a factor of 16 higher at the end of the study than at t=0. In Experiment 3 the factor was only 10.45 and the validity criterion was not fulfilled in the third experiment.

Results for biomass:

RESULTS: EXPOSED
- Effect data:
3 experiments with 3 concentration ranges were performed:

Experiment 1

Conc. (mg/l)	initial cell count x10E5	cell count 24 h x10E5	cell count 48 h x10E5	cell count 72 h x10E5	% inh.
0.1	1.2	4.1	13	21	0
0.25	1.2	4.2	11	19	0.1
0.5	1.2	3.9	10	18	14.3

RESULTS CONTROL (mean of 3 controls):

initial cell count cell count cell count
cell count 24 h x10E5 48 h x10E5 72 h x10E5
1.2 4.2 12 20

Experiment 2:
Conc.
(mg/l) initial %
cell count cell count cell count cell count inh.
x10E5 24 h 48 h 72 h
x10E5 x10E5 x10E5

1.0	1.1	4.3	8.6	16	15.4
2.5	1.1	3.3	5.5	8.5	51.9
5.0	1.1	2.5	3.7	5.6	71.2

RESULTS CONTROL:
initial cell count cell count cell count
count x10E5 24 h x10E5 48 h x10E5 72 h x10E5
1.1 4.9 11 17

Experiment 3:
Conc.
(mg/l) initial %
cell count cell count cell count cell count inh.
x10E5 24 h 48 h 72 h
x10E5 x10E5 x10E5

10.0	2.0	3.0	2.9	2.6	91.1
25.0	2.0	2.3	2.0	1.7	100
50.0	2.0	2.3	2.0	1.7	100

(values are means of 3 single measurements)

RESULTS CONTROL:
initial cell count cell count cell count
cell count 24 h x10E5 48 h x10E5 72 h x10E5
x 10E5
2.0 5.1 13 23

(values are means of 3 single measurements)

Based on the data of all 3 experiments the original study derived the following values:
EbC50 = 2.45 mg/l (0-72 h)
ErC50 = 7.4 mg/l (24-72 h)

NOEC= 0.25 mg/l

If only the experiments fulfilling the validity criteria are used (experiments 1 and 2) the following values were derived:
For Biomass:
EbC50 = 2.1 mg/l
EbC10 = 0.6 mg/l
NOEC = 0.5 mg/l
LOEC = 1.0 mg/l

For growth rate:
ErC50 = 5.7 mg/l
ErC10 = 1.3 mg/l
NOEC = 1.0 mg/l

LOEC = 2.5 mg/l

The pH varied between 8.0 and 8.1 at the start of the study and between 8.1 and 9.6 after 72 hours. No information is given on the course of the pH during the whole exposure period. It can therefore not be excluded that some hydrolysis of the test substance has occurred during the test (t½ at pH 9: 6.5 d), but a quantification is not possible.

Test substance : purity: presumably 97.3 % (impurities: methyl mercaptan, acrolein, methanol, acetaldehyde)

Reliability : (2) valid with restrictions
guideline study, no analytical measurements were performed.

Flag : WGK (DE), Material Safety Dataset, Critical study for SIDS endpoint

04.05.2004 (37)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
EC0 : ca. 30
EC10 : = 35
EC50 : = 46
EC100 : = 70
Analytical monitoring : no
Method : other: according to Umweltbundesamt-guidelines (1979) and slightly modified to DEV DIN 38412 part 8 (1991)
Year : 1979
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : METHOD FOLLOWED: Method is in accordance with DEV (prior developed).
GLP: no
METHOD OF CALCULATION: graphical
ANALYTICAL METHODS: turbimetric determination of cell density.

Test substance : purity: presumably 97.3 % (impurities: methyl mercaptan, acrolein, methanol, acetaldehyde)

Reliability : (2) valid with restrictions
Test procedure in accordance with national standard methods with acceptable restrictions

Flag : WGK (DE), Material Safety Dataset, Critical study for SIDS endpoint

(34)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

Remark : Cumulation: In animal experiments no cumulative properties are seen.

(57)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	4400 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	1984
GLP	:	no data
Test substance	:	other TS
Reliability	:	(4) not assignable No details reported

(57) (58)

Type	:	LD50
Value	:	5966 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male
Number of animals	:	10
Vehicle	:	other: undiluted
Doses	:	
Method	:	other: comparable to OECD Guide-line 401
Year	:	1974
GLP	:	no
Test substance	:	other TS
Remark	:	male
Result	:	Lowest dose with signs of toxicity: ca. 4172 mg/kg bw. Symptoms: Sedation, Ataxia, Mydriasis, reduced feed intake. At 5257 mg/kg bw. Additional Hypopnoe and Coma. Deaths occured in some animals after 12 h to 4 days. survivors recovered within 2 days. No substance related macroscopic findings apart from small hematoma in animals that died intercurrently.
Reliability	:	(2) valid with restrictions No information on purity of the test substance, only 7 days observation period.

(21)

Type	:	LD50
Value	:	6623 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	female
Number of animals	:	10
Vehicle	:	other: undiluted
Doses	:	
Method	:	other: similar to OECD Guide-line 401
Year	:	1974

GLP : no
Test substance : other TS

Result : Lowest dose with signs of toxicity: ca. 4172 mg/kg bw. Symptoms: Sedation, Ataxia, Mydriasis, reduced feed intake. At 5257 mg/kg bw. Additional Hypopnoe and Coma. Deaths occured in some animals after 12 h to 4 days. survivors recovered within 2 days. No substance related macroscopic findings.
Reliability : (2) valid with restrictions
No information on purity of the test substance.

(21)

Type : LD50
Value : 755 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle : other: Suspension in gummi arabicum 10%
Doses : 100, 500, 1000, 2500, 5000 mg/kg bw
Method : other: similar to OECD Guide-line 401
Year : 1981
GLP : no
Test substance : other TS: no data

Method : For doses of 100 and 500 mg/kg bw a 5% suspension of the test substance in gummi arabicoum (10%) in water was administered (2 and 10 ml/kg bw respectively).

For doses between 1000 and 5000 mg/kg bw the undiluted test substance was administered.

Observation period: 14 days
Result : Clinical symptoms:
400, 500 and 700 mg/kg bw: reduced spontaneous activity, apathy, slight piloerection between 1 h and 6 h p.a..
Full recovery of survivors within 1 day.
At 800 and 1000 mg/kg bw additionally tremor was observed.

Macroscopic findings:
In animals that died during the study: haemorrhage of the lungs and in single animals of the gastrointestinal tract.

In animals that were killed at the end of the observation period the only finding observed was a dark discoloration of the spleen in the 1000 mg/kg bw dose group.
Reliability : (2) valid with restrictions
No information on purity of the test substance.

(87)

Type : LD50
Value : 490 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 5
Vehicle : other: undiluted
Doses :
Method : other
Year : 1986

GLP : yes
Test substance : other TS: identified by lot No., no details given

Method : METHOD FOLLOWED: FIFRA Pesticide assessment Guidelines F, US EPA, office of pesticides and toxic substances, Section 81-1, Nov. 1982, TSCA Health effects test guidelines, US ePA, August 1982, Acute toxicity, oral exposure.
GLP: Yes
STATISTICAL METHODS: Logarithmic-Probit analysis
Remark : male
Result :

Dose mg/kg bw	mortality	time of death
250	0/5	-
350	0/5	-
500	4/5	1 hr to day 2
600	2/5	2 hrs
700	5/5	2-4 hrs

CLINICAL SIGNS: After dosing: ocular and nasal discharge, hypopnea, dyspnea, wet rales, unrinary staining, ataxia, hypoactivity or prostration. Decreased food consumption beginning on day 2. Surviving animals recovered from symptoms by day 3.
NECROPSY FINDINGS: No substance related macroscopic findings.
SEX-SPECIFIC DIFFERENCES: males were more sensitive than females (see below). Therefore data of male and female animals of the same study are reported in 2 entries into IUCLID.

95% confidence limits of LD50: 402-578
Reliability : (2) valid with restrictions
No information on purity of the test material.
Flag : Critical study for SIDS endpoint

(75)

Type : LD50
Value : 1050 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : female
Number of animals : 5
Vehicle : other: undiluted
Doses :
Method : other
Year : 1986
GLP : yes
Test substance : other TS: identified by lot No., no details given

Method : METHOD FOLLOWED: FIFRA Pesticide assessment Guidelines F, US EPA, office of pesticides and toxic substances, Section 81-1, Nov. 1982, TSCA Health effects test guidelines, US ePA, August 1982, Acute toxicity, oral exposure.
GLP: Yes
STATISTICAL METHODS: Logarithmic-Probit analysis
Remark : female
Result :

Dose mg/kg bw	mortality	time of death
700	1/5	2 hrs
850	1/5	2 hrs
1000	2/5	2 hr

1200	5/5	1-4 hrs
1700	4/5	1 hr-day 1

CLINICAL SIGNS: After dosing: ocular and nasal discharge, hypopnea, dyspnea, wet rales, unrinary staining, ataxia, hypoactivity or prostration. Decreased food consumption beginning on day 2. Surviving animals recovered from symptoms by day 3.
NECROPSY FINDINGS: No substance related macroscopic findings.
SEX-SPECIFIC DIFFERENCES: males were more sensitive than females (see above). Therefore data of male and female animals of the same study are reported in 2 entries into IUCLID.

95% confidence limits of LD50: 854-1246

Reliability : (2) valid with restrictions
No information on purity of the test material.
Flag : Critical study for SIDS endpoint
02.02.2004 (75)

Type : LD50
Value : 2300 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 5
Vehicle : other: corn oil
Doses :
Method : other: no data
Year : 1956
GLP : no
Test substance : other TS: no data

Result : Survival time 8 to 36 hours.
Symptoms: lethargy, salivation and weakness.
Macroscopic pathology: pulmonary hyperaemia, inflammation of the gastric mucosa.
Test substance : diluted in corn oil (50%)
Reliability : (2) valid with restrictions
No information on purity of the test material, brief description.

(77)

Type : LD50
Value : ca. 1342 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals :
Vehicle : other: undiluted
Doses :
Method : other: no data
Year : 1984
GLP : no
Test substance : other TS

Method : 2 to 4 animals per group.

Dose level	Number of animals
5.23 ml/kg	4
3.5 ml/kg	3

2.6 ml/kg 3
1.29 ml/kg 2
0.65 ml/kg 2

Remark : No guideline test, research study
Result : Symptoms: Sedation, Ataxia. Praemortal: laboured breathing.
Reliability : (3) invalid
Number of animals too low.

(52)

Type : LD50
Value : ca. 1054 mg/kg bw
Species : rat
Strain :
Sex : male
Number of animals :
Vehicle : other: corn oil
Doses : 0.5, 1.0, 2.0 ml/kg
Method : other: no data
Year : 1986
GLP : no data
Test substance : other TS:

Result : The LD50 was given as 1.00 ml/kg bw. With a density of 1.054 g/ml this corresponds to a dose of 1054 mg/kg bw.
Observations: Sluggishness, lacrimation, unsteady gait, labored breathing, salivation, dark red discharg on perinasal fur, mottled red lungs in animals that died. Time to death 4 h after administration of the test substance.
Test condition : The test substance was diluted in corn oil (25%).
Test substance : Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).
Reliability : (2) valid with restrictions
Brief description

(98)

Type : LD50
Value : ca. 1770 mg/kg bw
Species : rat
Strain :
Sex : female
Number of animals :
Vehicle : other: corn oil
Doses : 0.25, 0.5, 1.0, 2.0, 4.0 ml/kg bw
Method : other: no data
Year : 1986
GLP : no data
Test substance : other TS:

Result : The LD50 was given as 1.68 ml/kg bw. With a density of 1.054 g/ml this corresponds to a dose of 1770 mg/kg bw.

Observations: Sluggishness, unsteady gait, salivation, mottled lungs in animals that died.
Time to death 1.5 h to 1 day after application.
Test condition : 3 to 5 animals per group.
The test substance was diluted in corn oil (25%).
Test substance : Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).

Reliability : (2) valid with restrictions
Brief description

(98)

Type : LD50
Value : 1620 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1984
GLP : no data
Test substance : other TS

Reliability : (4) not assignable
No details reported

(57) (58)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC0
Value :
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other
Year : 1956
GLP : no
Test substance : other TS

Result : 4 males were exposed, no death occurred.
The vapors of 3-(Methylthio)propionaldehyde were quite irritating.
Test substance : probably saturated vapor (78.5° F)
Reliability : (4) not assignable

(77)

Type : LC0
Value : = 289 ppm
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle :
Doses : 277 +- 2, 289 +- 3 ppm, (1191 +-8.6, 1243 +- 12.9 mg/m3), acrolein not detected
Exposure time : 4 hour(s)
Method : other: dynamic exposure, whole body
Year : 1994
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Rats were exposed whole body in a 900 l stainless steel

glass and steel chamber to MTPA vapours.
Observation period: 14 days.

Result : Symptoms:
lacrimation, salivation, blepharospasm, salivation.
No mortality occurred. Body weight gains were reduced in the first week and regained during the second week. No gross pathologcial changes were observed at necropsy and no histopathological changes were seen in the lungs.

Reliability : (2) valid with restrictions
Well documented scientific publication, 2 dose levels that are very close together only

03.02.2004 (4)

Type : LC50
Value : > 4.33 mg/l
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 10
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other: similar to OECD Guide-line 403
Year : 1979
GLP : no
Test substance : other TS

Method : Airflow: 1.5 m3/h
The concentration used was the maximum attainable aerosol concentration. Whole body exposure. Analysis of test atmosphere every 45 minutes with an impinger. Receptor fluid: ethanol. GC Analysis of solution. Droplet size analysis with a cascade impactor, 95% of particles < 6.7 µm.
Concentration: > 4.33 mg/l, > 4330 mg/m3, > 996 ppm

Remark : Generally it is unclear whether the observed local symptoms are attributable to 3-methylthio propionaldehyde or to acrolein. In the developmental toxicity study it has been demonstrated that acrolein can be enriched in the vapour phase and the concentration of acrolein in the inhalation chamber can be much higher than that in the tested product.

Result : Nasal discharge, mouth breathing; reversible body weight loss; after the exposure some rats had blood around their noses. Two males died on the 3rd and 12th day.

Test substance : Purity: 97,8%
Impurities: Acrolein: 0.1%, Methanethiol, 0.2%, Water 1.9%

Reliability : (2) valid with restrictions
Test procedure in accordance with standard methods

03.02.2004 (24)

Type : LC50
Value : = 5.82 mg/l
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other: no data
Year : 1984
GLP : no

Test substance : other TS

Method : Concentration: 5.82 mg/l, 5820 mg/m3, 1339 ppm
Reliability : (4) not assignable
No details reported
03.02.2004 (57) (58)

Type : LC50
Value : > 4.84 mg/l
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 10
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : OECD Guide-line 403 "Acute Inhalation Toxicity"
Year : 1981
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Exposure conditions:
Aerosol exposure, nose only. Mass medium aerodynamic dyameter of aerosol particles: <= 3 µm.
Determination of concentration, particle size distribution oxygen content and relative humidity was performed at the position of the animals snout. The particle size distribution was however, not documented in the report.
Limit test with a measured dose of 4.84 mg/l

STATISTICAL METHODS:
Logit model could not be applied to the data, estimation without statisitcal analysis.

ANALYTICAL METHODS:
Sampling of the test atmosphere directly from the test atmosphere feed tube that delivers the air to the animals nose. The atmospheric samples were passed through 3 bottles with ethylacetate. The ethylacetate solutions were analysed by GC for test substance content.
The oxygen concentration was measured once during exposure. Relative humidity and temperature were determined once during exposure.

Concentration:
> 4.84 mg/l, > 4840 mg/m3, > 1113 ppm
Remark : Given the high irritating potential of acrolein to the respiratory tract it is likely that the effects observed are related to acrolein exposure (LC50, inhalation, rat for acrolein vapour was 18-21 mg/m3 (equals microg/l).
Result : MORTALITY:
2/5 males died 8 and 11 days after exposure. No mortality of female animals.
CLINICAL SIGNS:
Somnolence; hunched posture, rales, piloerection, epitaxis, recovery within 3 days. Rales reapeared on test day 10 and 11.
NECROPSY FINDINGS: The 2 males that died had reddening of the lungs. No abnormal findings were observed in the surviving animals.
Test condition : The acrolein content of the test atmosphere was determined

to be up to 22.9 micro-g/l although some decomposition may have occurred during sample storage and preparation.

Test substance : 97.54% puritiy, identified through batch No.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
03.02.2004 (33)

Type : LC50
Value :
Species : rat
Strain : other: no indicated
Sex : no data
Number of animals :
Vehicle :
Doses : 1.2, 6.0, 12, 24 ml/m3 (ppm) (5.16, 25.8, 51.6, 103.2 mg/m3)
Exposure time : 4 hour(s)
Method :
Year : 1975
GLP : no
Test substance : other TS: purity not indicated

Method : Rats were exposed in a 500 litre chamber with a flow of 1 m3/h for 4 hours. In the 1.2 and 6.0 ppm groups 10 anmials were used, in the 12 and 24 ppm groups 8 anmials were used. Observation period: 14 days.
Remark : Generally it is unclear whether the observed local symptoms are attributable to 3-methylthio propionaldehyde or to acrolein. In the developmental toxicity study it has been demonstrated that acrolein can be enriched in the vapour phase and the concentration of acrolein in the inhalation chamber can be much higher than that in the tested product.
Result : In the 1.2 to 12 ppm exposure groups no animal died during the study. At 24 ppm all animals died within 4 days post exposure. The LC0 was > 6300 mg/m3.
At the beginning of the exposure period the animals had eye irritation.
At necropsy no substance related macroscopic were observed.
Reliability : (4) not assignable
LC50 not comprehesible, no purity given.
03.02.2004 (86)

Type : LC50
Value : ca. 4.5 - 4.8 mg/l
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other: similar to OECD Guide-line 403
Year : 1986
GLP : yes
Test substance : other TS

Method : Exposure conditions:
Vapour exposure, introduced via nebulizer, no particles according to pre-test, whole body.
Exposure levels: 4.8 and 4.5 mg/l. (4800 and 4500 mg/m3 or 1104 and 1035 ppm).

STATISTICAL METHODS: Could not be applied to the data, estimation without statisitcal analysis.

ANALYTICAL METHODS:
Sampling of the test atmosphere 4 times at 1 h intervals by a gas analyser. Samples were drawn directly through an infrared analyser and the concentrations determined by infrared analysis (absorbance at 5.8 µm).
The oxygen concentration was measured once during exposure. Relative humidity and temperature were determined once during exposure.

Remark : Generally it is unclear whether the observed local symptoms are attributable to 3-methylthio propionaldehyde or to acrolein. In the developmental toxicity study it has been demonstrated that acrolein can be enriched in the vapour phase and the concentration of acrolein in the inhalation chamber can be much higher than that in the tested product. LC50 for male animals only

Result : MORTALITY:
At 4.8 mg/l 4/5 males and 0/5 females died. Deaths occurred between day 1 and day 9 after exposure. At 4.5 mg/l 1/5 males died on day 10 after exposure.
CLINICAL SIGNS: Respiratory irritation (nasal discharge, gasping, labored breathing, salivation)and decreased body weights.
NECROPSY FINDINGS: Congested red lungs, focal corneal opacity, abnormal colour of liver, congested red turbinates. None of the findings could be conclusively attributed to the test substance exposure.

The LC50 was > 4.8 mg/l for females and males and females combined and 4.5-4.8 mg/l for males.

Test substance : Puritiy: 96%, no data on impurities.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
03.02.2004 (73)

Type : other: LC0, mixed exposure with acrolein
Value : = 320 ppm
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle :
Doses : 320 ppm, 4.4 ppm Acrolein (1376 mg/m3, 10.3 mg/m3 Acrolein)
Exposure time : 1 hour(s)
Method : other: dynamic exposure, nose only, vapour
Year : 1994
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : MTPA was administered as a vapor, via nose-only inhalation, to 5 male and female Sprague Dawley rats. The rats were exposed to a 1 hour dynamic exposure with MTPA at 320 ppm. Acrolein level was 4.4 ppm. All rats were subjected to a gross necropsy following the 14 day observation period.

Result : All rats exposed survived the 14 day post-exposure period. Upon removal from the nose only tubes, after exposure the majority of the rats exhibited salivation which returned to normal 1-hour post-exposure. Gross pathology noted two males with lung foci, all others were within normal limits.

It is probable that the clinical signs observed are attributable to the acrolein content of the atmosphere rather than to MTPA alone.

Reliability : (3) invalid
No information on purity of the test material, mixed exposure with acrolein,

03.02.2004 (4) (101)

Type	:	other: LCLo, mixed exposure with acrolein
Value	:	= 306 ppm
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	306+- 80 ppm, 6.8 +- 0.4 ppm Acrolein (1316 +-344 mg/m3, 15.8 +-0.93 mg/m3 Acrolein)
Exposure time	:	4 hour(s)
Method	:	other: dynamic exposure, nose only, vapour
Year	:	1994
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : MTPA was administered as a vapor, via nose-only inhalation, to 5 male and 5 female Sprague Dawley rats. The rats were exposed to a 4 hour
dynamic exposure with MTPA at 306+-80 ppm. Acrolein levels ranged from 6.6 - 7.4 ppm. All rats were subjected to a gross
necropsy following the 14 day observation period.

Result : One male animal died on the 4th day postexposure. Animals had slight lacrimation and blepharospasm during exposure. Upon removal from the nopse only tubes, after exposure, the majoritiy of the rats exhibited salivation, and dyspnea was noted. All rats returned to normal by day 4. No gross pathologcical changes were seen at necropsy, histologic lesions were present in the lungs and consisted of hemorrhage, neutrophil infiltration/inflammation, congestion and oedema.

The clinical signs and the death of one animal may be related to the acrolein content of the test atmosphere rather than to MTPA.

Reliability : (3) invalid
No information on purity of the test material, mixed exposure with acrolein.

03.02.2004 (4)

Type	:	other: LT100
Value	:	
Species	:	rat
Strain	:	
Sex	:	male
Number of animals	:	5
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	other: static
Year	:	1986
GLP	:	no data

Test substance	:	other TS
Result	:	40 min exposure and longer killed 5/5 animals. Symptoms: lacrimation, gasping, perioral wetness, periocular encrustation, audible and slow breathing, perinasal encrustation, unkempt appearance, livers dark purple,lungs red, thoracic cavities filled with clear liquid.
Test condition	:	Exposure time: 40, 80, 160 min. Exposure to substentially saturated vapor at 25°C,
Test substance	:	Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C). The test substance was diluted in corn oil (25%).
Reliability	:	(3) invalid No guideline test.

(98)

Type	:	other: LT100
Value	:	
Species	:	rat
Strain	:	
Sex	:	female
Number of animals	:	5
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	other: static
Year	:	1986
GLP	:	no data
Test substance	:	other TS
Result	:	24 min exposure and longer killed 5/5 animals. Symptoms: lacrimation, gasping, perioral wetness, periocular encrustation, audible and slow breathing, perinasal encrustation, unkempt appearance, livers dark purple,lungs red, thoracic cavities filled with clear liquid.
Test condition	:	Exposure time: 24, 49, 97, 195 min. Exposure to substantially saturated vapor at 25 °C.
Test substance	:	Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).
Reliability	:	(3) invalid No guideline test.

(98)

Type	:	other: static exposure mixture with acrolein
Value	:	
Species	:	rat
Strain	:	
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	935 ppm, 16.7 ppm Acrolein (4021 mg/m3, 39 mg/m3 Acrolein)
Exposure time	:	1 hour(s)
Method	:	other: static exposure, nose only, vapour
Year	:	1994
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	MTPA was administered as a vapor, via nose-only inhalation,

to 3 male and 7 female Sprague Dawley rats. The rats were exposed to a 1 hour
static exposure with MTPA at 935 ppm. Acrolein level was from 16.7 ppm. All rats were subjected to a gross necropsy following spontaneous death. A histopathological examination of the lungs was performed.

Result : All rats exposed died during the study. No body weight gains were obtained since the rats died by day 1. Upon removal from the nose-only tubes, after exposure, all the surviving rats in the static exposures exhibited salivation. Dyspnea was noted following the 1-hour static exposure and breathing difficulties worsened in the static exposed rats into wheezing, rales and gasping. Other observations noted included clear/red nasal discharge, discoloration around the nose and mouth, rough hair coat, ptosis, shaking, and cold to touch. At necropsy, all
rats exhibited red/puffy lungs. Congestion, edema, inflammation and
hemorrhage were observed in the lungs when examined microscopically.

The deaths and signs of toxicity as well as the pathological findings were attributable to acrolein rather than to MTPA.

Reliability : (3) invalid
Unsuitable test system, static exposure resulted in high levels of acrolein which attributed to death of all animals.

16.04.2004 (4) (101)

Type : other: static exposure, mixed exposure with acrolein
Value :
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle :
Doses : 957 +- 220 ppm, 84 +- 88 ppm acrolein (4115 +-946 mg/m3, 196 +-205 mg/m3 acrolein)
Exposure time : 4 hour(s)
Method : other: static exposure, nose only, vapour
Year : 1994
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : MTPA was administered as a vapor, via nose-only inhalation, to 5 male and 5 female Sprague Dawley rats. The rats were exposed to a 4 hour
static exposure with MTPA at 957 ppm (4115 mg/m3). Acrolein levels ranged 29-185 ppm (68 to 431 mg/m3) with a mean of 84 ppm (196 mg/m3).
All rats were subjected to a gross necropsy following spontaneous death.

Result : All rats exposed died during the study. No body weight gains were obtained since the rats died during exposure. At necropsy, all rats exhibited red/puffy lungs. All rats also contained a reddish liquid in the chest cavity.

The deaths and signs of toxicity as well as the pathological findings were attributable to acrolein rather than to MTPA.

Reliability : (3) invalid
Unsuitable test system, static exposure resulted in high levels of acrolein which attributed to death of all animals.

03.02.2004 (101)

Type	:	other: static vapour exposure sparged with N2, mixed exposure with acrolein
Value	:	
Species	:	rat
Strain	:	
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	733 +- 22 ppm, 216 +- 12.7 ppm acrolein (3152 +-95 mg/m3, 503 +-30 mg/m3)
Exposure time	:	1 hour(s)
Method	:	other: static exposure, nose only, vapour
Year	:	1994
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : MTPA was administered as a vapor, via nose-only inhalation, to 5 male and 5 female Sprague Dawley rats. The rats were exposed to a 1 hour
static exposure with MTPA that was sparged with N2 at 733 ppm. Acrolein levels ranged from 216 +- 12.7 ppm. Sparging the MTPA increased the acrolein levels in the chamber atmosphere. All rats were subjected to a gross necropsy following spontaneous death. A histopathological examination of the lungs was performed.

Result : All rats exposed died during the study. No body weight gains were obtained since the rats died by day 1. Upon removal from the nose-only tubes, after exposure, all the surviving rats in the static exposures exhibited salivation. Dyspnea was noted following the 1-hour static sparged exposures. Breathing difficulties worsened in the static exposed rats into wheezing, rales and gasping. Other observations noted included, shaking, hypoactive and cold to touch. At necropsy, all
rats exhibited red/puffy lungs. They also had a reddish liquid in the cavity chest. The thymus in four of the animals had either red areas or was enlarged with red areas. One female rat had pale liver. Congestion, edema and hemorrhage
were observed in the lungs when examined microscopically. Sparging the MTPA liquid with N2 in an attempt to reduce exposure to volatile contaminants, did not significantly reduce mortality and help to clarify the situation. Acrolein content was increased rather than decreased.

The deaths and signs of toxicity as well as the pathological findings were attributable to acrolein rather than to MTPA.

Reliability : (3) invalid
Unsuitable test system, static exposure resulted in high levels of acrolein which attributed to death of all animals.

16.04.2004 (4) (101)

Type	:	LC50
Value	:	= 5.4 mg/l
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	

Doses	:	
Exposure time	:	2 hour(s)
Method	:	other: no data
Year	:	1984
GLP	:	no data
Test substance	:	other TS

Method	:	Concentration: 5.4 mg/l, 5400 mg/m3, 1242 ppm.
Reliability	:	(4) not assignable No details reported

03.02.2004 (57) (58)

Type	:	LC50
Value	:	
Species	:	mouse
Strain	:	other: not indicated
Sex	:	no data
Number of animals	:	8
Vehicle	:	
Doses	:	1.2, 6, 12, 24 ml/m3 (ppm), (5.2, 25.8, 52, 103 mg/m3)
Exposure time	:	4 hour(s)
Method	:	other: no data
Year	:	1975
GLP	:	no
Test substance	:	other TS: purity not indicated

Method	:	Mice were exposed in a 500 litre chamber with a flow of 1 m3/h for 4 hours. Observation period: 14 days.
Result	:	No mortality in the 1.2 ppm group. 2 of 8 animals died in the 6 ppm group. 8 of 8 animals died in the 12 and 24 ppm groups. The authors conclude an LD0 of > 1260 mg/m3.
Reliability	:	(4) not assignable LC50 not comprehesible, no purity given.

03.02.2004 (86)

Type	:	LC50
Value	:	> 12 mg/m³
Species	:	mouse
Strain	:	other: no data
Sex	:	male
Number of animals	:	10
Vehicle	:	
Doses	:	
Exposure time	:	1 hour(s)
Method	:	other
Year	:	1984
GLP	:	no
Test substance	:	other TS

Method	:	Exposure concentrations: 12 mg/m3 and 1390 mg/m3 (2.8 and 320 ppm) vapour exposure. Whole body exposure, Analytical determination of test atmosphere via GC. Discontinous sampling, intervals not stated.
Result	:	All animals of the 12 mg/m3 group survived. Of the 1390 mg/m3 group 2/10 animals died. Clinical signs: restlessness, closed eyes during exposure. Ataxia and disturbance of motor coordination at the high dose after 37 min of exposure. No conclusions on possible delayed mortality in the high dose group can be drawn from this study as the animals died from accumulation of

MTPA-fluid in the exposure chamber after the expsoure period.

Reliability : (3) invalid
No guideline test, range finding research study.

16.04.2004 (52)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : = 2631 mg/kg bw
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 10
Vehicle : water
Doses :
Method : other
Year : 1981
GLP : no
Test substance : other TS

Method : METHOD FOLLOWED:
The test substance was applied to the shaved skin of 5 males and 5 females for 24 h under occluded conditions. Reeding of skin reactions: immediately after removal of the dressing and after 3 days. Clincal observations during the 24 hour dosing period and daily throughout the 14 d postexposure observation period.

METHOD OF CALCULATION of LD50
Weil, biometrics 8 (1952) 249-263

Result : MORTALITY:

Dose mg/kg bw	mortality males	mortality females	%
1800	2/5	0/5	20
2080	2/5	2/5	40
2590	4/5	1/5	50
3120	5/5	5/5	100

(dose is given in ml/kg and was calculated in mg/kg using a density of 1.040 g/ml)
- Time of death: between 1 and 2 h after application.
CLINICAL SIGNS: aggressiveness, increased motor activity, convulsions, asphyxation and coma prior to deaths.
NECROPSY FINDINGS: No treatment related findings
95% confidence intervals for LD50: 2361-2933 mg/kg bw.

Test substance : 30% aqueous solution, no information on purity etc.
Reliability : (2) valid with restrictions
Good documented experimental study
Flag : Critical study for SIDS endpoint

(29)

Type : LD50
Value : = .65 ml/kg bw
Species : rat
Strain :
Sex : male/female
Number of animals : 10

Vehicle :
Doses : 0.25, 0.5, 1, 2 ml/kg bw
Method :
Year : 1975
GLP : no
Test substance :

Remark : Occlusive application for 24 hours. 0.25 ml/kg induced 10% mortality and 2000 mg/kg induced 100% mortality.
Result : The LD50 is given as 0.65 ml/kg. With a density of 1.04 this would correspond to a dose of 676 mg/kg bw.
Severe oedema was observed after 24 h. Scab formation was observed that detached from the skin between 4 to 15 days post applicationem.
No macroscopic organ findings were observed at necropsy.
Reliability : (2) valid with restrictions
Purity of test material not indicated.
Flag : Critical study for SIDS endpoint

(86)

Type : LD50
Value : = 1700 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 10
Vehicle : other: undiluted
Doses :
Method : EPA OPP 81-2
Year : 1986
GLP : no
Test substance : other TS

Method : METHOD FOLLOWED:
The test substance was applied to the clipped skin of 5 males and 5 females for 24 h under occluded conditions.
Clincal observations: viability check: twice daily, observations: 1,2, 4 h after dosing, and daily throughout the 14 d postexposure observation period.

METHOD OF CALCULATION of LD50
Probit-Test (Miller et al., 1944)

Result : MORTALITY:

Dose mg/kg bw	mortality males	mortality females	time of death
1000	1/5	0/5	Day 3
1500	0/5	3/5	6 h-day 4
2000	4/5	4/5	4-24 h

The death in the 1000 mg/kg dose group was not attributed to the test substance, but to a non-substance related mucoid enteritis in this animal.
CLINICAL SIGNS:
Local: necrosis and eschar formation and exfoliation of the eschar tissue.
All dose groups: hypoactivity or prostration during first 24 h.
At 1500 and 2000 mg/kg bw: irregular breathing during dosing.
At 1000 mg/kg bw. Ataxia after 4 h. Symptoms were reversible within 2 to 6 days.

NECROPSY FINDINGS: Dermal tissue lesions, no treatment related findings.
95% confidence intervals for LD50: males: 1552-2048 mg/kg bw, female: 1106-1894, combined: 1467-1933
(excluding the dead male in the 1000 mg/kg group)

Test substance : Material identified by batch No., no information on purity.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(74)

Type : LD50
Value : > 2250 mg/kg bw
Species : rabbit
Strain : other: no data
Sex : male/female
Number of animals : 1
Vehicle : other: no data
Doses :
Method : other
Year : 1956
GLP : no
Test substance : other TS

Method : Doses between 1000 and 3100 mg/kg/per one animal were applied to six rabbits (3 females/3 males).
Result : Death occurred at 2500 and 3100 mg/kg (males).
Test substance : undiluted application
Reliability : (3) invalid
Number of animals too low.

(77)

Type : LD50
Value : = 748 - 833 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 4
Vehicle : other: undiluted
Doses : males: 0.25, 0.5, 1.0 ml/kg bw, females: 0.5, 1.0 ml/kg bw
Method : other: similar to OECD Guide-line 402
Year : 1986
GLP : no data
Test substance : other TS

Method : Deviations from guideline: only 4 animals per dose used.
Result :

Dose ml/kg bw	Mortality	Time to death	local effects
Male			
1.0	4/4	3 h-5days	Erythema, edema, necrosis
0.5	0/4	-	Erythema, edema, necrosis
0.25	1/4	9 days	Erythema, edema, necrosis
Female			
1.0	3/4	1 day	Erythema, edema, necrosis
0.5	0/4	-	Erythema, edema, necrosis fissures, desquamation

CLINICAL SIGNS: Salivation, sluggishness, unsteady gait.
Survivors recovered within 2 days.
NECROPSY FINDINGS: Light to dark red mottling of the lungs.
No gross pathological findings were reported in sacrificed

surv

Test substance : Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).

Reliability : (2) valid with restrictions
Good documented experimental study, only 4 animals per group.

Flag : Critical study for SIDS endpoint

(5) (98)

Type : other: NOED
Value : > 200 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 10
Vehicle : water
Doses :
Method : other
Year : 1982
GLP : no
Test substance : other TS

Method : Department of Transportation, Fed. Reg.: Subpart F, 173.343.a3: Poison B, 1981
Application of a 10% aqueous solution, 24 h occlusive application. 24 h post exposure observation period.

Result : No deaths occurred and no abnormalities with respect to condition and behaviour were observed. Slight to moderate erythema and edema of the treated skin area was observed. No pathological examination was conducted.

Reliability : (2) valid with restrictions
No information on purity of the test material.

(30)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Value : ca. 300 mg/kg bw
Species : rat
Strain :
Sex : male/female
Number of animals : 10
Vehicle : water
Doses : 420, 210, 105 mg/kg bw
Route of admin. : i.p.
Exposure time :
Method :
Year : 1975
GLP : no
Test substance :

Result : i.p. injection of 420 mg/kg induced 90% death; no death nor toxic signs were observed at 210 mg/kg or below.
Prostation was observed as the only clincal symptom.
No macorscopic organ changes were observed at necropsy.

Reliability : (4) not assignable
Short documentation, purity of test material not indicated.

(86)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	other: no vehicle
PDII	:	
Result	:	highly irritating
Classification	:	irritating
Method	:	other:
Year	:	1979
GLP	:	no
Test substance	:	other TS
Method	:	6 animals, with intact skin, 6 animals with abraded skin, 24 hours occluded exposure,3 days observation time.
Result	:	There were no significant difference between the reactions of intact skin and those of the abraded skin. Well-defined erythema and slight to moderate oedema were observed at 24 and 72 hours after removal of the patch. Means were as follows:

	intact skin		abraded skin	
	24 h	72 h	24 h	72h
Mean erythema	4	4	3.6	3.6
Mean oedema	2.3	1.6	2.5	1.6

Conclusions:
It is concluded that Methyl-mercapto-propionaldehyde is considered as severe primary irritant to the skin.

Test substance	:	Purity: 97,8% Impurities: Acrolein 0.1%, Methanethiol 0.2%, water 1.9%.
Reliability	:	(2) valid with restrictions Occlusive instead of semi-occlusive application, 24 h instead of 4 h application, pre-GLP study, short documentation, 2 reading times only.

(26)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	other: no vehicle
PDII	:	
Result	:	irritating
Classification	:	irritating
Method	:	other: Patch-Test (4h)
Year	:	1982
GLP	:	no
Test substance	:	other TS: purity not specified
Method	:	Department of Transportation, Fed. Reg.37 (244), 27635,1972 (6 animals, 0.5 ml, 4 hours occlusive, 2 days observation time)
Result	:	Well-defined erythema and slight oedema were observed at 24 and 48 hours after removal of the patch. Heamorrhages were

also observed. Means were as follows:

	24 h	48 h
Mean Erythema	3.6	3.6
Mean Oedema	2.3	2.0

CONCLUSIONS
It is concluded that Methyl-mercapto-propionaldehyde is considered as irritating to the skin.

Reliability : (2) valid with restrictions
Standard test method for transportation. Pre-GLP study, short documentation, postexposure observation period to short, occlusive instead of semiocclusive application.

(31)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : other: no vehicle
PDII :
Result : irritating
Classification : irritating
Method :
Year : 1975
GLP : no
Test substance : other TS: no data

Method : 0.5 ml was applied on normal and abraded skin, 6 animals pe r group, 24 h occlusive application, 3 days observation period.

Result : Well-defined erythema and no oedema were observed at 24 hours after removal of the patch. No erythema was observed at 72 hours but moderate oedema appeared. Means were as follows:

	Intact skin		abraded skin	
	24 h	72 h	24 h	72 h
Mean erythema	0.8	0	0.8	0
Mean oedema	0	2.1	0	3.5

CONCLUSIONS
It is concluded that Methyl-mercapto-propionaldehyde is considered as irritating to the skin.

Reliability : (2) valid with restrictions
Purity not stated. 24 h instead of 4 h application, occlusive instead of semi-occlusive application.

(86)

Species : rabbit
Concentration : undiluted
Exposure :
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : other: no vehicle
PDII :
Result : corrosive
Classification :
Method : other: FIFRA, Vol. 43 No. 143, Fed. Reg. Aug. 22, 1978 Part 163.81-5, TSCA, Vol. 44, No. 145, Fed. Reg., July 1976, 1979 Part 772.112-25

Year : 1986
GLP : no
Test substance : other TS

Method : · Species: rabbit
· Strain: New Zealand White albino
· Route of administration: dermal application 4 hours semi-occlusive and 24 hours occlusive patches on 4 areas using the same rabbit
· Doses: 0.5 ml of the test substance as such in 4 applications
· Sex: 3 males and 3 females
· Exposure period: 24 hours
· Frequency of the treatment: single
· Control group and treatment: none
· Post exposure observation period: 14 days
· Statistical method: none
· Test subjects:
· Age at the study initiation: not reported
· No of animals per dose: 6

Result : All animals showed moderate to severe erythema and edema at the sites exposed for 24 h under occlusion. Necrosis was observed at these sites from 24 h up to the termination at 14 days.
In addition the test substance was applied on 4 areas of the back of each animal. It means that exposure is 4 X 0.5 ml per rabbit.

Means were as follows:
Mean scores 24 hour exposure

	24 h	48 h	72 h	14 d
Mean erythema	3,8	4	4	3.7
Mean oedema	3.8	3	2,7	2.1

CONCLUSIONS
It is concluded that Methyl-mercapto-propionaldehyde is considered as corrosive to the skin.

Reliability : (2) valid with restrictions
Puritiy of test material not indicated, 24 h exposure time to long, in 24 h experiment additionally occlusive instead of semi-occlusive application.

(78)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : moderately irritating
Classification :
Method : Draize Test
Year : 1956
GLP : no
Test substance : other TS

Remark : 3 animals were tested (2 females/1 male).
Result : 2 h after the exposure period well defined erythema and

slight oedema in 2 animals. After 24 hours inflammation increased (average score of 4 of 8). Gradual decrease up to day 5 (end of observation period) with an average score of 0.6 of 8.

Test substance : undiluted application
Reliability : (3) invalid
Pre-GLP study, to few animals, purity not stated.

(77)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 4 hour(s)
Number of animals : 12
Vehicle :
PDII :
Result : slightly irritating
Classification :
Method : other: DOT 173.1300
Year : 1996
GLP : yes
Test substance : other TS: purity 97.1 %

Method : This study was conducted in order to evaluate the corrosive effects produced by inhibited and uninhibited MTPA after a 4 hour exposure to the skin of rabbits. The term inhibited refers to production samples without and with a catalyst to test the effect of the catalyst on the copleteness of the process reaction with respect to skin irritation (no further information available).
The hair of 12 (3/sex/test material) New Zealand White rabbits was closely clipped to expose the back. 0.5 ml of each test material (inhibited, uninhibited, and the control) was applied, as received, beneath a 6cmk2 gauze square, placed directly on the one intact site on each animal. The site was occluded during the 4 hour exposure period. At the end of the exposure period, the patch was removed and the site evaluated for skin irritation. The site was then wiped free of test material. Observations for skin irritation were made again 48 hours, 7 and 14 days after test material administration.

Result : The only irritation seen in the animals treated with inhibited MTPA was very slight (barely perceptible) erythema in four of the six animals. All animals were free of skin irritation within 7 days. Five of the six animals treated with uninhibited MTPA exhibited very slight or slight edema. This is unusual since erythema, which usually accompanies edema, was very slight and was only seen in three of the five animals. Four of the five animals were free of all skin irritation within 7 days post-dose; the remaining animal was free of skin irritation by 14 days post-dose. The sixth animal was free of skin irritation throughout the study. In conclusion, inhibited MTPA, under the conditions of the study, was slightly less irritating to the skin than uninhibited MTPA. Inhibited MTPA produced very mild, transient
skin irritation; uninhibited MTPA produced mild, transient skin irritation. Since no tissue damage was seen, both inhibited and uninhibited MTPA would not be considered a "Class 8 Dangerous Goods". according to the DOT guidelines.

Reliability : (2) valid with restrictions

Occlusive instead of semi-occlusive application.

Flag : Critical study for SIDS endpoint
16.04.2004 (104)

Species	:	Rabbit
Concentration	:	Undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	Corrosive
Classification	:	
Method	:	
Year	:	1986
GLP	:	no data
Test substance	:	other TS
Remark	:	Corrosive by department of Transportation (DOT) definition.
Result	:	AVERAGE SCORE, 24, 48, 72 h - Erythema: 2.3 - Edema: 2.9 REVERSIBILITY: In 50% of the animals within 14 days in all animals within 17 days. Necrosis was present in 5/6 animals at 1 h and persisited until day 10 in 3 animals. It was not completely reversible in only one animal at day 17. Desquamation and scab formation was seen from week 1 onwards.
Test substance	:	Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).
Reliability	:	(2) valid with restrictions Occlusive instead of semi-occlusive application.
Flag	:	Critical study for SIDS endpoint

(5) (98)

Species	:	Rabbit
Concentration	:	Undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	moderately irritating
Classification	:	irritating
Method	:	other: FIFRA, Nov. 1982, Sect. 81-5, TSCA, Aug. 1982.
Year	:	1986
GLP	:	no
Test substance	:	other TS
Method	:	· Species: rabbit · Strain: New Zealand White albino · Route of administration: dermal application 4 hours semi-occlusive and 24 hours occlusive patches on 4 areas using the same rabbit · Doses: 0.5 ml of the test substance as such in 4 applications · Sex: 3 males and 3 females · Exposure period: 4 hours · Frequency of the treatment: single · Control group and treatment: none

· Post exposure observation period: 14 days
· Statistical method: none
· Test subjects:
· Age at the study initiation: not reported
· No of animals per dose: 6

Result : The 4 hours semi-occlusive application did not induce tissue destruction and reversibility was complete or very slight (barely perceptible) erythema (score 1) was still present by day 14.

Means were as follows:
Mean scores 4 hour exposure

	24 h	48 h	72 h	14 d
Mean erythema	2.7	2.2	2	0.6
Mean oedema	2.7	2.1	1.7	0

Mean Score for 24, 48,72 h: Erythema 2.3, oedema: 2.2

CONCLUSIONS
It is concluded that Methyl-mercapto-propionaldehyde is considered as irritating to the skin.

Reliability : (2) valid with restrictions
Purity of test material not indicated.

Flag : Critical study for SIDS endpoint

(78)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 168 hour(s)
Comment : not rinsed
Number of animals : 1
Vehicle : none
Result : highly irritating
Classification : risk of serious damage to eyes
Method : Draize Test
Year : 1979
GLP : no
Test substance : other TS

Method : Only one animal was used for the experiment.
Result : Well-defined erythema and moderate oedema together with iris lesion and corneal opacity were observed from the beginning of the observation. No reversibility was observed by day 7.

Means were as follows:

Scores:	24 h	48 h	72 h	day 7
conjunctival redness	2	2	2	2
conjunctival Chemosis	3	3	3	2
Iris	1	1	1	1
Cornea	2	2	2	3

Conclusion:
It is concluded that Methyl-mercapto-propionaldehyde is considered as severely irritating to the eyes.

Test substance : Purity: 97,3% (Impurities: Methylmercaptan 0.2%, Acrolein 0.1%, water: 1.9%)
Reliability : (2) valid with restrictions
Pre-GLP study, short documentation, purity not stated, short observation period.
Flag : Critical study for SIDS endpoint

(26)

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 168 hour(s)
Comment : other: single application with rinsing (30 sec) or without rinsing
Number of animals : 12
Vehicle : none
Result : irritating
Classification : irritating
Method : other: equivalent to OECD 405
Year : 1975
GLP : no
Test substance : other TS: impurities not specified

Remark : Lesions were not completely reversible by day 7 in unrinsed eyes.
Result : Well-defined erythema were observed in both rinsed and non rinsed eyes. Erythema completely reversed at the end of the observation period. Moderate oedema was observed at the beginning of the observation period completely reversed by day 7 when eyes are rinsed. Slight iris lesion and corneal opacity were observed along the observation period and was completely reversed in rinsed eyes only.

Means were as follows:
Scores:

Without rinsing

	1 h	24 h	48 h	72 h	96h	day 7
Conjunctivae redness	0.2	2	1	1	1.3	0
Conjunctivae chemosis	3	3	3	3	3	1.5
Iris	1	1	1	1	0.5	0.3
Cornea	0.3	1	1	1	1.2	0.6

With rinsing

	24 h	48 h	72 h	day 7
Conjunctivae redness	0	0.6	0.3	0
Conjuctivae chemosis	3.3	2	1	0
Iris	0.3	1	0.6	0
Cornea	0	1	0.6	0

CONCLUSIONS
It is concluded that Methyl-mercapto-propionaldehyde is considered as irritating to the eyes.
Reliability : (2) valid with restrictions
Post observation period to short, puritiy not indicated.
Flag : Critical study for SIDS endpoint

(86)

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 504 hour(s)
Comment : not rinsed
Number of animals : 1
Vehicle : none
Result : corrosive
Classification :
Method : Draize Test
Year : 1986
GLP : no
Test substance : other TS: not specified

Result : Conjunctival irritation (moderate to severe redness, chemosis and discharge) iritis and corneal ulceration was reported for 3 to 7 days. Revesibility of those findings was observed after 7 to 14 days. Corneal opacity persisted through day 21. Pannus and protrusion of the cornea was observed from day 7 to day 21.

Scores:

	24 h	48 h	72 h	7 d	14 d	21 d
Conjunctivae redness	2	3	3	2	0	0
Conjunctivae chemosis	2	2	1	1	1	0
Iris	1	1	1	0	0	0
Cornea opacity	2	3	3	3	4	3

Conclusion:
Based on the corneal findings and the irreversibility the substance was corrosive to eyes in this test.
Test substance : undiluted application
Reliability : (2) valid with restrictions
Purity of test material not indicated.
Flag : Critical study for SIDS endpoint

(76)

Species : rabbit
Concentration : undiluted
Dose : .2 ml
Exposure time : 120 hour(s)
Comment : not rinsed
Number of animals : 3
Vehicle : none
Result : moderately irritating
Classification : irritating
Method : Draize Test
Year : 1956
GLP : no
Test substance : other TS: not speciifed

Remark : 3 animals were tested (2 females/1 male), observation time = 5 days
Result : The following findings were reported: moderate to severe erythema, oedema leading to nearly closing of the lids, lacrimation, corneal opacity.
Cornea and iris began to clear after 48 hours. A slight

redness remained after 5 days.
Average Draize scores (maximum 110):

24 h: 37.3, 48 h: 22.0, 72 h: 10.6, 120 h: 3.3

Test substance : undiluted application, two drops
Reliability : (4) not assignable
No details reported

(77)

Species : rabbit
Concentration : undiluted
Dose :
Exposure time : 504 hour(s)
Comment : not rinsed
Number of animals : 6
Vehicle : none
Result : corrosive
Classification :
Method : Draize Test
Year : 1986
GLP : no data
Test substance : other TS

Method : 6 rabbits (male and female) received 0.1 ml and further 6 rabbits (male and female) 0.01 ml, resp., in one eye. Eyes were scored at 1 h, 4 h, 24 h, 48 h, 72 h, 7 d, 14 d, 21 d.
Result : Two animals developed haemorrhages of the nictitating membrane within 24 h. By 7 days, the cornea of one eye had an irregular shape. In 2 rabbit eyes, there was corneal vascularization after 14 d.

Means were as follows:

0.1 ml

Scores	1h	24h	48h	72h	21d
conjuctival redness	1.8	1.7	1.3	1.2	0.5
conjunctival chemosis	3	2.3	2	1.2	0.3
Iris	0.8	*	*	*	*
Cornea					
opacity	1	1.3	1.5	1.7	1.2
Area	1.8	4	4	4	1.3

*scoring not possible because of corneal opacity.

Irreversible damage possible

Reactions with 0.01 ml were milder and fully reversible after 7 d
Test condition : Dose: 0.1 and 0.01 ml
Test substance : Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).
Reliability : (2) valid with restrictions
Short documentation
Flag : Critical study for SIDS endpoint

(98)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	1st: Induction 5 % active substance intracutaneous 2nd: Induction undiluted occlusive epicutaneous 3rd: Challenge undiluted occlusive epicutaneous
Number of animals	:	20
Vehicle	:	water
Result	:	sensitizing
Classification	:	sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1999
GLP	:	yes
Test substance	:	other TS

Method :

Strain: Dunkin Hartley
Solvent for first induction: propylene glycol.
Re-challenge with 25% MTPA in propylene glycol.

Induction and maximum non irrtiant concentration for challenge was determined in a pre-test:
5% MTPA in propylene glycol administered intradermally produced local necrosis.
25% topical application produced no irritation up to 100% only produced a score of 0.5 in 2 of 6 animals.

An irritation control group received undiluted MTPA without undergoing the induction procedure.

Alpha-hydroxycinnamaaldehyde served as a positive control group (five animals per sex and an irritation control group of 5 animals per sex).

Result :

Results of pilot study:
Intradermal injections of 5% MTPA only produced local necrosis and the concentration was considered adequate for the main study. Topical application of 25 % produced no local irritation and 50, 70, 100% produced only a score of 0.5 in 2 or 3 of 6 animals. Therefore undiluted MTPA was used for the
main study epicutaneous induction and challenge.

Results of main study:
One female of the MTPA sensitization group died on day 10 of the study.

Positive skin reactions to challenge in the sensitization group:
4/19 score 1 or greater at 24 h, 2 animals score 2 or greater
6/19 score 1 or greater at 48 h, 4 animals score 2 or greater
Rechallenge with 25% MTPA in propyleneglycol:
2/18 score of 1 or greater at 24 h
7/18 score of 1 or greater at 48 h, 4 animals score 2 or greater.

Irritation control 25%:
0/10 had a positive reaction at 24 h
4/10 had a score of 1 at 48 h, 0/10 had a score 2 or greater

at 48 h
The positive control gave the expected reaction.

The irritation reaction was unexpectedly high compared to the pre-study.

In summary, based on the scores of 2 or greater with 25% methylmercaptopropionaldehyde (MTPA) after 48 h, MTPA under the conditions of this study, produced sensitization in 22% of the guinea pigs; therefore, this material was classified as a "mild sensitizer" based on the Magnusson and Kligman allergenicity rating criteria.

Test substance : Purity 97%, impurities: 1.23% water, 0.28% methyl mercaptane, 0.07% acrolein, 0.3% acrolein dimer, 0.26% acetic acid, 0.12% acetone. Densitiy: 1.054 g/ml (20 °C).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
16.04.2004 (5) (107)

Type : Guinea pig maximization test
Species : guinea pig
Concentration : 1st: Induction 1 % intracutaneous
2nd: Induction 5 % occlusive epicutaneous
3rd: Challenge 5 % occlusive epicutaneous
Number of animals : 20
Vehicle :
Result : sensitizing
Classification : sensitizing
Method : other: Magnusson and Kligman
Year : 1979
GLP : no
Test substance : other TS

Remark : No vehicle control. Positive control: Penicilline-G-Na
Result : 20/20 animals showed a positive skin reaction. (not further quantified).
Test condition : Strain: Pirbright White
Test substance : Purity: 97,8%
Impurities: Acrolein, Methanethiol
Reliability : (2) valid with restrictions
Pre-GLP study, short documentation.
Flag : Critical study for SIDS endpoint
(27)

Type : other
Species : guinea pig
Number of animals : 10
Vehicle :
Result : sensitizing
Classification :
Method : other
Year : 1979
GLP : no
Test substance : other TS

Method : Induction period: inhalative (198,3 mg/m3, 6 h/d, 5 days for 2 weeks)
Provocation: intradermal
Test condition : Strain: not indicated
Test substance : Purity: 97,8%
Impurities: Acrolein, Methanethiol
Reliability : (3) invalid

No guideline test

(25)

Type	:	other: Non adjuvant test
Species	:	guinea pig
Number of animals	:	10
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other: Landsteiner-Draize-Test
Year	:	1979
GLP	:	no
Test substance	:	other TS
Method	:	Induction: 0.1 % in water, 0.05 (first injection) or 0.1 ml (further injections), 10 injections (5 per week). 2 weeks. Challenge: 2 weeks later, intradermal injection, 0.05 ml of an 0.1 % aqueous dilution. Inspection of skin after 24 h, diameter, colour, thickness.
Result	:	Slight skin reaction in all control and test animals. One of 10 treated animals showed a more intensive skin reaction.
Test substance	:	Purity: 97,8% Impurities: Acrolein, Methanethiol
Reliability	:	(3) invalid No positive control, all negative controls showed a positive reaction

(25)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	4 weeks
Frequency of treatm.	:	daily /6 days/week
Post exposure period	:	none
Doses	:	21; 104; 521 mg/kg
Control group	:	yes
NOAEL	:	104 mg/kg bw
LOAEL	:	521 mg/kg bw
Method	:	other: similar to OECD Guide-line 407
Year	:	1979
GLP	:	no
Test substance	:	other TS: purity 97.8 %, impurities: acrolein, methanethiol
Method	:	METHOD FOLLOWED: Similar to OECD 407 DEVIATIONS FROM GUIDELINE: No recovery group was included. No weekly off cage observations and no FOB Clinical chemistry was restricted to GOT, GPT, ALP, total protein, total bilirubin, creatinine, glucose, BUN. Organ weights and histopathology was restricted to: liver, kidneys, spleen, heart, lungs, testes. Microscopic evaluation was done for the high dose and control groups with the exception of spleen that was also examined in the

mid and low dose groups.

STATISTICAL METHODS: Student-t-test for organ and body weight data. Wilcocxon test for haematoloigy and clinical chemistry.

The dose levels were reported as 0.02, 0.1 and 0.5 ml/kg bw and converted by using a density of 1.040 g/ml.

Result : No deaths were observed in any of the groups.

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Clinical signs: No substance related clinical signs were observed in all dose groups.
- Body weight gain:
Slightly, but significantly decreased body weight in the high dose group males (7.6%) small, statistically not significant decrease in body weight in females (2.9%) at the end of the exposure period. Body weight gains in the high dose animals were also reduced compared to controls (9.7 and 6.1%), but not analysed statistically.
- Food consumption:
Food intake was comparable in all groups. Food efficiency was decreased in both sexes in the high dose group compared to controls (males: 0.34, contr. 0.37, females, 0.26, contr. 0.27)
- Ophthalmoscopic examination: was not performed
- Clinical chemistry:
Bilirubin levels were significantly increased in both sexes in the 521 mg/kg bw group (males. 3.0 µmol/l, contr.1.9 µmol/l; females 2.8 µmol/l, contr. 2.0 µmol/l). Creatinine levels were slightly, but significantly increased in males of the 104 (68.3 µmol/l) and 521 mg/kg (69.1 µmol/l) bw group compared to controls (63.3 µmol/l), but the changes were not considered biologically significant.
- Haematology: in the 521 mg/kg dose group RBC and Hb levels were relatively low, reaching significance only in the females. (RBC count males: 5.7, contr. 6.1, females: 5.7, contr. 6.5; Hb: males: 8.4 mmol/l, contr. 8.9 mmol/l, females: 8.7 mmol/l, contr. 9.6 mmol/l) White blood cell count was increased in males (16, contr. 11.8) of the high dose group only.
- Urinalysis: not performed
- Organ weights: 521 mg/kg bw. group females had slightly decreased absolute lung weights (0.824, contr. 0.904). Relative organ weights did not differ significantly from controls in all dose groups.
- Gross pathology: No treatment related changes were observed.
- Histopathology: In the spleen of high dose males and females slightly increased extramedullary haematopoesis and deposition of pigment and blood in the red pulp was observed. Incidence of effect in spleen is not given. In the other organs examined no substance related changes were observed.

Test condition : TEST ORGANISMS
- Age: Weanling
- Weight at study initiation: males: 75 +- 1.3 g, females: 65.6+- 1.2 g
- Number of animals: 10 per dose and sex
ADMINISTRATION / EXPOSURE

- Vehicle: Water
- Concentration: 0.4, 2, 10%
- Total volume applied: 5 ml/kg bw
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: daily general condition and behaviour
- Body weight: weekly records
- Food consumption: weekly records
- Water consumption: not recorded
- Ophthalmoscopic examination: not performed
- Haematology: all guideline parameters studied
- Biochemistry:
- Urinalysis: not performed
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Kidney, liver, spleen, lungs, heart, testes
- Microscopic: Kidney, liver, spleen, lungs, heart, testes

Conclusion : The low red blood cell counts and Hb levels and increase in bilirubin together with the finding of increased haematopoesis in the spleen suggest an effect of the substance on the red blood cells in the high dose group. The slight increases in creatinine levels are not considered of toxicological significance by the authors due to the occurrence in males only. The NOAEL was therefore 104 mg/kg bw.

Reliability : (2) valid with restrictions
Restrictions: see method

Flag : Critical study for SIDS endpoint

02.02.2004 (28)

Type : Sub-chronic
Species : rat
Sex : male
Strain :
Route of admin. : oral unspecified
Exposure period : 6 months
Frequency of treatm. :
Post exposure period : no data
Doses : 4,4; 44; 88 mg/kg
Control group : yes
NOAEL : = 4.4 mg/kg
Method : other: no data
Year : 1981
GLP :
Test substance :

Method : Number of animals: 10 males
Result : Effects to redox processes and function of the liver, CNS-effects
Reliability : (4) not assignable
No details reported

(57)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : nine days
Frequency of treatm. : 6 hours/day for 9 days (5 days in first week, 4 days in second week)
Post exposure period :
Doses : 0.5, 5, 50 ppm (2.15, 21.5, 215 mg/m3)
Control group : yes
NOAEL : 50.5 ppm

Method	:	OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year	:	1998
GLP	:	yes
Test substance	:	other TS: purity 97.4 %
Method	:	This study was designed to assess the toxic effects of MTPA when administered by inhalation using whole-body exposure of Sprague Dawley rats (5/sex/group) to the vapor for 6 hours per day, for 9 days (5 days in the first week and 4 days in the second week) at target concentrations of 0.50, 5.0, and 50 ppm. In addition, a control group (5/sex) received air only while in the chamber. Exposure concentrations of MTPA were measured by gas chromatography (GC) four times per chamber per day. In addition, samples for measurements of airborne concentrations of Acrolein were performed once per chamber per day using the GC method. The levels of acrolein were below the detection limit in this study. Physical observations,body weight and food consumption measurements were performed at selected intervals. Hematology, clinical chemistry, and urinalysis were performed on all animals at study termination. After 9 exposures, all animals were sacrificed, selected organs were weighed and organ/body weight and organ/brain weight ratios calculated. Complete macroscopic postmortem examinations and histopathological evaluation of selected tissues were conducted on all animals. The following organs were weighed: Adrenal glands, brain, kidneys, liver, lungs, ovaries, testes. Histology was conducted on the organs that were weighed and additionally on the hearrt, larynx, trachea, nasopharyngeal tissues, spleen and urinary bladder.
Result	:	There were no mortalities during this study. Body weight gains and food consumption were generally unremarkable. Evaluation of hematology parameters showed no statistically or toxicologically significant differences between the control and test material exposed animals. Evaluation of clinical chemistry parameters showed no toxicologically significant differences between the control and test material exposed animals. The few statistically significant differences between values for control and treated groups were slight and occurred in the low exposure group only. They were not attributed to MTPA exposure. In conclusion, under the conditions of this study, the NOAEL was considered greater than 50.5 ppm of MTPA.
Reliability	:	(2) valid with restrictions Test material not fully characterised
Flag	:	Critical study for SIDS endpoint

16.04.2004 (4) (105)

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	9 days
Frequency of treatm.	:	6 hours/day, 4 to 5 days/week for 2 weeks (total 9 exposures)
Post exposure period	:	28 days

Doses	:	25, 100, 250 ppm, acrolein: 1.08-1.72 ppm (107.5, 430, 1075 mg/m3, acrolein: 2.5 - 4 mg/m3)
Control group	:	yes
LOAEL	:	= 25 ppm
Method	:	other
Year	:	1992
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The systemic effect of MTPA were assessed in F344 rats exposed to respirable vapors, 6 hours/day, 4 to 5 days/wee for 2 weeks (a total of 9 exposures). Three groups of 40 F344 rats (20/sex/group) were exposed to MTPA at target concentrations of 25 ppm, 100 ppm, and 250 ppm (107.5, 430, 1075 mg/m3). The mean acrolein vapour concentration during exposure days 3 to 9 for the 250 ppm group was 1.34 ppm (3.12 mg/m3).
A control group of rats (20 males and 20 females) was similarly exposed to filtered conditioned air. Ten rats per sex per group were necropsied on study day 12, the day immediately following the last exposure. Another 10 rats per sex per group were designated as recovery animals and necropsied on study day 40 in order to evaluate the progression or resolution of any tissue changes occurring for signs of moribundity or mortality. Complete physical examinations and body weight measurements were performed on the animals during the exposure period (study days 1, 2, 5, 8, and 9) and then weekly thereafter. Prior to each necropsy,
hematology and clinical chemistry measurements were determined and ophthalmological examinations were performed on the animals. At each necropsy, the liver, lungs, spleen, brain, adrenals and kidneys from all rats and the testes from all males were weighed. Microscopic evaluation of tissues from all major organs systems was performed on the control and 250 ppm exposure groups and the respiratory tract on the 25 ppm and 100 ppm exposure groups at the interim necropsy. Microscopic evaluation of tissues from all recovery groups animals included the respiratory tract.

Result : There were no deaths in this study; however clinical signs of toxicity were observed in the 100 ppm and 250 ppm exposure groups, primarily during the exposure period. These signs included rales, alopecia, rough hair coat, and staining of the hair coat. The incidence of these signs progressively decreased during the recovery period. Additionally, accumulations of red material around the eye were observed during ophthalmological examinations immediately at the end of the exposure period (study day 11). These accumulations
were absent on the following morning (study day 12). No eye changes were observed in the recovery animals. Significant body weight reductions in the 250 ppm rats and reduced body weight gains in the 25 ppm and 100 ppm exposure groups were observed during the exposure period. Body weights in the 250 ppm exposure groups quickly regained and by the end of the recovery period, body weights for all MTPA exposure groups of both sexes were similar to their respective controls.
At the end of the exposure period, decreased alkaline phosphatase, total protein, and globulin levels were observed in the 100 ppm male rats and 250 ppm exposure

groups of both sexes. In the high exposure group male rats, elevated glucose and ALT levels were observed. In the female rats, reduced BUN values in all MTPA groups and reduced triglyceride and LDH levels were observed in the 250 ppm group. At the end of the recovery period, reduced BUN levels were observed in the 100 ppm and 250 ppm males and females. In the 250 ppm exposure groups, elevated alkaline phosphatase and reduced phosphorus and triglyceride levels were observed in the female rats. All MTPA treated males had elevated phosphorus levels.
Terminal body weights at the end of the exposure period were reduced in the 100 ppm males and the 250 ppm groups of both sexes. Reductions in absolute liver and spleen weights in the higher exposure groups and increases in organ-to-body weight ratios in most of the other organs in these exposure groups were considered to be the result of reductions in body weight and not the direct result of MTPA insult to these organs. Treatment related histopathological lesions at the end of the exposure were confined to the respiratory tract and characterized by squamous metaplasia of the epithelium of the nose and respiratory tract, and olfactory lesions consisting of atrophy and erosions. Minimal to mild squamous metaplasia of the larynx, trachea, and major airways of the lungs were observed in the 250 ppm exposure group. Histopathological evaluations of the recovery period indicated a partial to complete resolution of the lesions. In conclusion, evidence of toxicity was observed at all exposure levels; therefore, a NOAEL could not be determined.

The authors conclude, however that it is likely that some or all of the effects observed are attributable and consistent with effects of the co-expsoure to acrolein rather than to MTPA.

Reliability : (3) invalid
mixed exposure with acrolein.

16.04.2004 (4) (99)

Type	:	Sub-chronic
Species	:	rat
Sex	:	
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	100 days
Frequency of treatm.	:	
Post exposure period	:	none
Doses	:	0,006; 0,06;0,6 mg/m3 (0.0014, 0.014, 0.14 mg/m3)
Control group	:	no data specified
NOAEL	:	< .006
Method	:	other: no data
Year	:	1981
GLP	:	no data
Test substance	:	other TS

Method : Number of animals: 10 per group.
Result : Effects to redox processes and functions in the liver (reduced oxygen demand, reduced catalase activity, reduced blood levels of lactic and pyruvic acid); CNS effects.
Reliability : (4) not assignable
No details reported

03.02.2004 (57)

Type	:	Sub-acute
Species	:	rabbit
Sex	:	male/female
Strain	:	New Zealand white
Route of admin.	:	dermal
Exposure period	:	21 days
Frequency of treatm.	:	daily, 5d/w
Post exposure period	:	no
Doses	:	0.2, 0.4, 0.8, 1.6 ml/kg
Control group	:	yes, concurrent no treatment
LOAEL	:	ca. .2 ml/kg bw
Method	:	
Year	:	1975
GLP	:	no
Test substance	:	other TS: purity not mentioned, no indication of stability

Method :

Percutaneous, occlusive application (12 animals per group, 6 males and 6 females of which 50% were skin abraded; 12 scarifications of 3 cm length spaced by 2 cm).
· Statistical method: none
· Test subjects:
· Age at the study initiation: not specified but weight is 3kg
· No of animals per sex per dose: 6 per sex per dose group (12 per group)
· Study design:
· Vehicle: none
· Satellite groups and reasons they were added: none
· Clinical observation performed and frequency:
Body weight; haematology, biochemistry, urine analysis, histopathology
· Organs examined at necropsy:
Heart, liver, spleen, kidney, skin.

Result :

· NOEL (NOAEL)
· Not determined
· LOAEL
· 0.2 ml/kg/d (death of 2 animals / 12)

Mortality and time to death:

Dose ml/kg/d	sex	Death (No/day) Comment (scarified skin)	Comment Death (No/day) (non scarified)
control	m	0	0
	f	0	0
0.2	m	0	0
	f	0	1/10, 1/21
0.4	m	1/5	by accident 1/15
	f	1/18	by accident 0
0.8	m	1/4; 1/9	1/4 sacrificed 1/7 1/13 sacrificed
	f	1/4; 1/9	2/3 1/3 sacrificed
1.6	m	1/2; 1/4	1/2 sacrificed 2/3; 1/4
	f	2/2; 1/4	1/3, 1/4, 1/5

Body weight: decrease due to poor feed uptake. Mortality precluded calculation of most average body weights.
Clinical signs: at the highest dose, paraplegia, loss of movement coordination was interpreted as neurotoxicity.

Unfortunately the description is quite poor.
Haematology: no significant variations in survivors compared to controls.
Biochemistry: no significant variations in survivors compared to controls.
Urinary analysis: no significant variations in survivors compared to controls.
Histopathology: the thickness of the skin (described as oedema) increased immediately after exposure in all animals; it was proportional to the applied dose. At high doses slight erythema was observed as well. Acanthosis, hyperkeratosis and dryness was observed up to the end of the treatment. The observed alterations in organs other than skin are not considered as toxicologically significant.

Conclusions:
3-(Methylthio)propionaldehyde repeatedly applied by cutaneous administration induced skin necrosis at all tested dose levels. At the highest dose death occurred between day 2 and day 4. Clinical signs at this dose level included paralysis and motion disorders. No clinical signs were seen at the lower dose levels. A death occurred also in the lowest dose group, a NOAEL could not be determined.

Reliability : (2) valid with restrictions
The study was not performed according to modern standards. The dose levels were to high and caused severe local effects. Furthermore the skin was abraded in half of the animals. Purity not stated, to few animals, no statistical evaluation.

(86)

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	dermal
Exposure period	:	9 days
Frequency of treatm.	:	5 days per week (week 1), 4 days per week (week 2)
Post exposure period	:	4 weeks recovery period
Doses	:	52.7, 210.8 and 527 mg/kg/day (0.05, 0.2 and 0.5 ml/kg/day)
Control group	:	yes
NOAEL	:	= 208 mg/kg bw
LOAEL	:	= 520 mg/kg bw
Method	:	other:
Year	:	1999
GLP	:	yes
Test substance	:	other TS: purity: 97.1 %

Method : This study was designed to assess the potential toxicity of MTPA when administered to the skin of 70 Sprague-Dawley rats (10/sex/group II and III; 15/sex/group IV) at doses of 0.05, 0.2, and 0.5 ml/kg/day (groups II, III, IV) for a period of 9 days. The doses corresponded to 52.7, 210.8, 527 mg/kg bw/day. Control animals (15/sex; group I) were administered water at the same dose volume as administered to the treated animals. Five animals/sex from group I and IV were held for an additional 4 week recovery period. Physical observations, neurological examinations, cutaneous evaluations, body weight, food consumption and water consumption measurements were performed on all animals pretest and at selected intervals during the treatment

period. Hematology, clinical chemistry, and urinalyses were performed on all surviving animals at termination and recovery. After 9 days of treatment, 10 animals/sex/group were sacrificed, selected organs (adrenals, brain, liver, kidneys, ovaries and testes) were weighed and organ/body weight and organ/brain weight ratios calculated. Recovery animals (5/sex/groups Iand IV) were sacrificed four weeks after the last treatment.
Complete macroscopic postmortem examinations were conducted on all animals. Histopathological evaluation of selected tissues of brain, kidneys, nerves, skin, spinal cord testes were performed on controls and high dose animals. conducted on all animals.

Result : All animals survived until their scheduled sacrifice and were
free of significant abnormal clinical signs throughout the dosing and recovery periods. Most mid- and high-dose animals
had very slight to slight erythema; several animals also had desquamation. A few high dose animals had moderate erythema. A few low dose animals also had very slight erythema.
By Day 18, the high dose recovery animals were free of erythema, and by day 25, were also free of desquamation.
Mean cumulative bodyweight gains of high-dose males and females were statistically significantly lower than control gains throughtout most or all the treatment period. Mean body weights at termination were 7% (males) and 5% (females) lower than control means. Gains during the recovery period were comparable for control and high-dose animals. The mean body weight values of the mid- and low-dose males and females were comparable to the controls throughout most of the study. The mean food consumption per bw. in all treated groups of males was 10 to 15% ($p<0.01$) higher than in controls from day 5 until day 10 but not dose-related. No effects were seen in the water consumption.
Mean hematology, urinalysis and urine chemistry values of the treated males and females were comparable to the values of the control males and females, or were within normal range. In high dose male and females creatine kinase was significantly reduced and Glucose significantly elevated. Lactate dehydrogenase activity was significantly reduced in high dose males and reduced, but not significantly, in high dose females. Mean organ weight values of the treated males and females were comparable to the mean
values of the control males and females, or were within normal ranges. There were no significant treatment related lesions in the nervous system tissues and kidneys examined histologically. Treatment related histopathologic findings in the skin of the high-dose animals consisted of an occasional trace to mild inflammatory cell infiltrates in the dermis. Histologic changes in other organs were considered incidental or spontaneous in nature and were not associated with test material administration. In conclusion, MTPA when administered to the skin of Sprague-Dawley rats for a period of 9 days produced only mild local skin effects at doses up to 0.2 ml/kg/day or 210.8 mg/kg/day, but produced body weight and mild to moderate skin effects at a dose of 0.5 ml/kg/day or 527 mg/kg/day. Therefore, under the conditions of this study, the NOAEL for systemic toxicity is 0.2 ml/kg per day or

210.8 mg/kg bw per day.

Reliability : (2) valid with restrictions
GLP study, but test material not fully characterised, limited study duration.

Flag : Critical study for SIDS endpoint

16.04.2004 (5) (106)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Salmonella typhimurium reverse mutation assay
System of testing : strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100
Test concentration : up to 0.316 µl/plate
Cycotoxic concentr. : 0316 µl/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1994
GLP : yes
Test substance : other TS

Method : Using the preincubation approach, four log dilutions of MTPA, to a maximum concentration of 10 ul/plate, were tested in strain TA100 in a preliminary concentration range-finding test, with and without activation, and concentration-related toxicity was observed. MTPA was then tested over a range of four half-log dilutions to 0.316 ul/plate in a mutagenesis assay using strains TA1535, TA1537, TA1538, TA90, and TA100.
Positive controls:
In the absence of metabolic activation:
For strains TA1535 and TA100: sodium azide
For strain TA1537: 9-aminoacridine
For strains TA98 and TA1538: 4-nitro-o-phenylenediamine
In the presence of metabolic activation: 2-Anthramine for all stains.
Negative control: solvent DMSO

Result : In the mutagenesis assay, toxicity as evidenced by a significant reduction in colonies was observed at 0.316 ul/plate for strain TA1537 in the absence of activation, for all concentrations of MTPA tested in strain TA1537 in the presence of activation, and for all concentrations of MTPA tested in strain TA100 in the absence of metabolic activation. However, no concentration related increase in mean histidine revertant colonies/plate was observed for any strain in the absence or presence of metabolic activation.
In summary, MTPA failed to induce a significant increase in mutation frequency in any of the five strains of Salmonella, in the absence and presence of metabolic activation.
Thus it is concluded that MTPA was negative in the Salmonella typhimurium histidine reversion mutagenesis test in the presence and absence of metabolic activation.

All positive and negative controls gave the expected results that were within the ranges of the laboratory and consitent with those reported in the literature.

Test substance : 97% MTPA with Acetaldehyde 0.15%, methyl mercaptan 0.3%, Acetone 0.6%, Acrolein 0.05%, Acetic acid 0.25%, Pyridine 0.3%, Hydroquinone 0.1%, Benzene 0.0002%.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

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Type	:	Mouse lymphoma assay
System of testing	:	L5178Y/tk+/- mouse lymphoma cells
Test concentration	:	0.0001 to 0.1 µl/ml
Cycotoxic concentr.	:	0.02 µl/ml, 0.15 µl/ml
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1994
GLP	:	no data
Test substance	:	other TS

Method : Solvent: DMSO, S9: from Aroclor 1254-induced male Sprague Dawley rat livers.
Because the first mutagenesis assay did not yield concentrations for analysis in the 10 to 20% RTG range and because of suspected toxicity of the metabolic activation mixture that was used, the mutagenesis assay was repeated, with and without metabolic activation, with the cells exposed
to 23 concentrations of MTP, over a range of 0.0001 to 0.1 ul
MTP/ml in the absence of activation, to 23 concentrations of MTP, over a range of 0.001 to 1.0 ul MTP/ml in the presence of activation, and to the positive and solvent controls. In this assay, each culture contained approximately 5 x 10^6 cells in 5 ml of F10HP, for cultures tested without exogenous metabolic activation. Aliquots from 8 cultures tested without metabolic activation and 6 cultures tested with activation and the solvent and the positive control cultures were cloned. Colonies in the mutant count and cloning efficiency dishes were counted, and the colonies in the solvent and positive control mutant count plates were sized by hand using a dissecting microscope to enumerate mutant colonies.

Remark : In a first assay with concentrations of 0.0001 to 0.0562 µl/ml without metabolic activation and 0.0562 to 0.562 µl/ml with metabolic activation no concentration tested yielded survival in the range of 10 to 20%. Therefore a second assay used MPTA concentrations of 0.001 to 0.04 µl/ml without S9 and 0.01 to 0.25 µl/ml with S9.

Result : The average absolute cloning efficiencies of the solvent controls were 67.4% in the absence of activation and 94.6% in the presence of metabolic activation, and the average spontaneous (solvent control) mutant frequencies were 64 x 10exp-6 without activation and 45 x 10exp-6 with activation. Concentration related depressions in RTG and concentration related increases in mutation frequencies were obtained in the absence and presence of metabolic activation in the assay. In the absence of activation, an induced mutation frequency of 80 x 10exp-6 with 35.2% RTG was obtained at 0.025 ul MTPA/ml, which is evaluated as a positive (+) response,
and at 0.030 ul MTPA/ml the induced mutation frequency was 110 x 10exp-6, with 17.4% RTG, which is evaluated as strong positive (++) response. Mutation frequencies continued to increase at higher concentrations in the absence of activation, but, for these concentrations, RTG values were <= 10%. The presence of activation, an induced mutation frequency of 184 x 10exp-6 with 11.5% RTG was obtained at 0.2 ul MTPA/ml, which is evaluated as a strong positive (++)

response. A higher mutation frequency was obtained at 0.25 ul MTO/ml, but the RTG value was 2.4%.
MTPA appeared to be toxic and mutagenic at approximately 10-fold lower concentrations in the absence of metabolic activation than in it presence. Therefore, the toxicity and mutagenicity of MTPA, or of an impurity present in the sample
was reduced in the presence of metabolic activation. In summary, in the absence and presence of metabolic activation, 97.1% MTPA, or an impurity present in the sample, induced a strongly positive (++) mutagenic responses and primarily chromosomal mutations at the thymidine kinase (tk) locus in L5178Y mouse lymphoma cells.

Concentration related increases in mutation frequency were seen with and without S9. With S9 the mutation frequency only reached significance at concentrations which yielded <=10% survival. The increase was mainly due to sigma-colonies (indicating chromosomal aberrations). Lambda colonies (indicating point mutations) were only significantly increased at the
highest concentrations tested (survival rate below 3 %). This indicates that the test substance primarily induced chromosomal aberrations in this test system.

According to the authors an impurity in the sample might have caused the positive result. However, no further evidence was provided for this statement.

Test condition : SYSTEM OF TESTING
- Metabolic activation system: S9 mix from Arochlor 1254 induced male Spraque Dawley rat livers.

- Number of replicates: 2
- Positive and negative control groups and treatment: negative: solvent DMSO, positive Hycanthone, Cyclophosphamide

Test substance : 97% MTPA with Acetaldehyde 0.15%, methyl mercaptan 0.3%, Acetone 0.6%, Acrolein 0.05%, Acetic acid 0.25%, Pyridine 0.3%, Hydroquinone 0.1%, Benzene 0.0002%.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

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5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : i.p.
Exposure period : 2 single administrations, once daily on 2 consecutive days
Doses : 50, 100, 200 mg/kg bw
Result : negative
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 2000
GLP : yes
Test substance : other TS: purity 99.8%

Method : Dose levels were chosen based on an initial range finding study with groups of 3 male and female mice at a dose range

of 50 to 400 mg/kg bw, once daily for two consecutive days. Death of all animals occured at dose levels of 300 and 400 mg/kg bw. Clinical symptoms were observed from 100 mg/kg. Consequently doses of 50, 100 and 200 mg/kg were chosen for the main study.
Vehicle: corn oil
Negative controls: vehicle
positive control: cyclophosphamide, i.p., 40 mg/kg bw
Sampling time: 24 h after the last administration (48 h after the first administration).
A minimum of 1000 cells per animal and 2000 PCE per animal was counted.

Result : MORTALITY:
Several animals (6/6 males and 2/6 females) of the high dose group died prior to the sampling time.
CLINICAL SIGNS:
Clinical symptoms
were observed in all high dose animals: Abnormal breathing, lethargy, eye closure, prostration, abnormal gait. In the mid dose group lethargy and eye closure were observed.

EFFECT ON MITOTIC INDEX OR PCE/NCE RATIO:
PCE/NCE ratios of the treated animals were similar to those of the vehicle controls. Group mean frequencies of micronucleated PCE were also similar to that seen in the vehicle controls and not significantly different by chi-square test.The number of micrunucleated PCe of the control animals fell within the historical control rate. The positve control substance induced a statisitcally significant increase in the frequency of micronucleated PCEs.

GENOTOXIC EFFECTS:
Methylmercaptopropionaldehyde did not induce micronuclei in the PCEs of the bone marrow of male and female mouse treated up to 200 mg/kg day, a dose at which clinical signs and limited mortality was observed.

Test condition : TEST ORGANISMS:
- Age: 5 wk
- Weight at study initiation:
  males: 22-31 g, females: 21-27 g
- No. of animals per dose: 6
ADMINISTRATION: i.p.
- Vehicle: corn oil
- Duration of test: 2 days
- Frequency of treatment: twice on 2 consecutive days
- Sampling times and number of samples: 24 h after last adminstration (=48 h after first administration)
- Control groups and treatment:
Negative controls: vehicle
positive control: cyclophosphamide, i.p., 40 mg/kg bw

EXAMINATIONS:
A minimum of 1000 cells per animal and 2000 PCE per animal was counted.
- Clinical observations: Immediately after, 1/4 and 1.5 hours after first dose. prior to dosing, immediately after dosing, 1/4, 1,5 hours after dosing day 2. day 3.

- Criteria for evaluating results:
- Statisitcally significant increase in the frequency of

micronucleated PCE at least at one dose.
- Frequency of micronucleated PCE at such a point exceeds the historical vehicle control range.
- Criteria for selection of M.T.D.:
Toxic symptoms and deaths at the next higher dose level in the range finding study.

Vehicle: corn oil

Sampling time: 24 h after the last administration (48 h after the first administration).

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Material Safety Dataset, Critical study for SIDS endpoint

(54)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : C57BL
Route of admin. : inhalation
Exposure period : 1 h on 2 consecutive days
Doses : 0, 37.4, 88.5, 155.6 ppm (approx. 161.6, 382, 672 mg/m3)
Result : positive
Method : other: TSCA test guidelines Fed. Reg. 50, #188, part 798, 1985
Year : 1994
GLP : yes
Test substance : other TS

Method : Groups of 5 animals of each sex were exposed nose only, 1 h on two consecutive days to atmospheres containing 37.4, 88.5, 155.6 ppm. Analytical determination of the test compound by GC was mentioned, but the records were not included in the report. The negative control inhaled filtered air. The positive control recieved 0.4 mg triethylenemelamin i.p.. Sampling time: 24 h after last exposure.
Peripheral blood cells were obtained from the mice which were sacrificed 24 hours after the second exposure such that newly formed erythrocytes were in the bone marrow during exposure. Cells from mice exposed to the three highest concentrations of the test material, and to the vehicle and positive controls, were evaluated for toxicity and the presence of micronuclei. The positive control, 0.4 mg triethylenemelamine (TEM)/kg significantly elevated the number of micronuclei in newly formed erythrocytes (PCE's, polychromatic erythrocytes) from male and female mice Peripheral erythrocytes were analysed for micronuclei. The percentage PCe was recorded per 1000 erythrocytes, but the number of cells counted per animal is not clear from the report.

Remark : According to the authors it remains unclear if the response could be due to an impurity (which was possibly enriched in the test atmosphere e.g. acetaldehyde).
Some pecularities in the protocol and the results cause some doubts on the relevance and validity of the findings reported:
The number of erythrocytes counted per animal is not clearly stated.

There are big differences in the amount of micronuclei/1000 PCE between the animals of the same dose group. In males of all 3 dose groups 1 to 3 animals had no micronucleated PCEs, while in others of the same groups the ratio was 2.5 to 15 independent of the dose. The numbers obtained for the MN/PCE ratios are all multiples of 5.

Result : No toxic symptoms were noted in the treated animals. A dose related depression in PCE/NCE ratios was seen in female mice, however they were higher than the untreated controls. In male mice no clear dose related depression in PCE/NCE ratios was observed. Significant elevation of micrunucleated PCEs was observed in males of the low and high dose group, but initially not of the middle dose group. When 1000 additional PCEs were evaluated in the mid dose male mice and the negative control an increase was also observed at this dose level. In female mice the number of micronuclated PCEs was not elevated significantly compared to the negative controls. The result in females was considered equivocal by the authors.

Test substance : purity: 97.1% MTPA, acetaldehyde 0.15 %, methylmercaptan 0.3 %, acetone 0.06 %, acrolein 0.05 %, acetic acid 0.25 %, pyridine 0.3%, hydroquinone 0.1%, benzene 0.0002%

Reliability : (2) valid with restrictions
Some information (generation of the test atmosphere, analytical determination of impurities in the atmosphere etc.), number of scored cells pe ranimal is lacking.

Flag : Material Safety Dataset, Critical study for SIDS endpoint

16.04.2004 (100)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : Day 6 to 15 of gestation
Frequency of treatm. : 6 h/day
Duration of test : 20 days
Doses : 0, 10, 58, 128 ppm (0, 43, 249, 550 mg/m3)
Control group : yes
NOAEL maternal tox. : < 10 ppm
NOAEL teratogen. : = 128 - ppm
Method : OECD Guide-line 414 "Teratogenicity"
Year : 1999
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : whole body exposure. Controls: sham air exposed in exposure chamber, 24 animals per group. Observation cage site: Twice per day, detailed physical examination (during treatment interval pre- and postexposure) on days 4,6,16 and 20 of gestation.

Result : Tables on Body weight development.

Mean Body weight dams:

Day	control	10 ppm	58 ppm	128 ppm
0				
mean	211	212	209	210
S.D	12.5	11.5	12.2	15.9
4				
mean	235	235	234	234
S.D.	13.5	14.5	12.5	15.9
6				
mean	254	254	253	250
S.D.	16.2	14.9	14.1	17.3
9				
mean	268	266	264	250**
S.D	17.6	18.1	13.9	16.4
12				
mean	289	281	279	265**
S.D.	20.1	21.3	13.6	17.1
16				
mean	319	311	308	290**
S.D.	22.9	23.1	15.3	19.2
18				
mean	349	338	334	319**
S.D.	28.7	25.8	20.8	23.0
20				
mean	381	373	367	349**
S.D.	31.0	27.0	25.1	28.6

** = $p < 0.01$

Body weight gains:

Days	control	10 ppm	58 ppm	128 ppm
0-4				
mean	24	23	24	23
S.D	4.4	8.0	5.3	6.3
4-6				
mean	19	19	19	17
S.D.	5.6	6.7	5.9	4.9
6-9				
mean	14	13	11	0**
S.D.	4.5	4.9	4.1	6.3
9-12				
mean	20	14	15	15
S.D.	6.0	8.8	6.8	5.5
12-16				
mean	30	30	29	25
S.D.	10.2	10.4	9.1	8.3

6-16				
mean	64	57	55*	40**
S.D.	12.6	10.4	7.0	11.6
16-18				
mean	30	27	26	29
S.D.	9.8	7.9	8.2	8.2
18-20				
mean	32	35	34	30
S.D.	7.2	5.5	8.5	7.5

* = p< 0.05, ** = p< 0.01

Net body weight change minus gravide uterine weight at termination (terminal body weight minus day 6 body weight minus uterine weight):

	control	10 ppm	58 ppm	128 ppm
mean	52	40*	41*	28**
S.D.	12.7	11.4	13.6	9.7

* = p< 0.05, ** = p< 0.01

Fetal body weights

	control	10 ppm	58 ppm	128 ppm
males				
mean	4.1	4.2	4.4	4.1
S.D	0.22	0.25	0.77	0.40
females				
mean	4.0	4.1	4.2	3.9
S.D.	0.25	0.20	0.75	0.43
litter				
mean	4.0	4.2	4.3	4.0
S.D.	0.21	0.23	0.74	0.40

The concentrations of acrolein in the inhalation chambers for the 4 dose groups were 0, below detection limit, 1.19 ppm and 2.34 ppm (2.8 and 5.5 mg/m3). Actual concentration of test substance was only between 30 and 50% of nominal, no explanation given by the authors.

Maternal effects: No mortality
Maternal toxicity was restricted to reduced body weight gains and food consumption in all dose groups and some clinical signs in the mid and high dose group and a single low dose animal consisting of yellow and brown staining of the angogenital area and ventral surface (dose related). Theeffects were observed between day 8 and day 20 of gestation.
Animals of the high dose group had additional red/brown stains on the snout and the nose. The high dose group animals showed lacrimation, labored breathing and closed eyes, less frequently mucoid nasal discharge, salivation, chromodacryorrhea in the in chamber observations.
Dose related decreases in body weight were observed during the treatment period, not statistically significant in the

low dose group. Mean body weights of the low dose group at termination were only slightly lower than controls. Mean weight gain in the 10 ppm group over day 6 to 20 with the corrected Day 20 gestation weight was slightly, but significantly lower than controls. This was in part attributed to the higher mean gravid uterine weight in this group. At 65 ppm statistically significant body weight gain differences occurred only in the day 6-16 treatment period and in the day 6 to 20 period when using the corrected 20 day gestation weights. The mean body weights at termination were only slightly and not significantly lower than controls. In the high dose group all body weight gain and body weight data were significantly lower than controls. Statistically significant differences in food intake from the controls were observed in the low dose group at a single interval (day 12-16), at day 9-12 and 12-16 for the mid dose group and at all intervals for the high dose group.

Pregnancy rates were comparable to controls.
The number of corpora lutea, uterine implants, live fetuses and resorption sites per female were all comparable to control data in all treatment groups. Pre- and postimplantation loss data were also not different from controls.
Macroscopic post-mortem examination of the foeti did not reveal any treatment related effect. Mean fetal weights were all not different from controls (single sex and sexes combined). No treatment related effects were seen on the fetal sex distribution.
Examination of external skeletal and visceral effects did not reveal any treatment related effects.
The NOAEL for maternal toxicity was close to 10 ppm and the NOAEL for developmental toxicity was 128 ppm, representing the highest dose tested which showed clear maternal effects.

Test substance : purity: 97.54%, contained 0.08 % acrolein.
Reliability : (1) valid without restriction
Guideline study, GLP
Flag : Material Safety Dataset, Critical study for SIDS endpoint
03.02.2004 (55)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : In the workplace air of a russian MTPA and Acrolein production plant air concentrations for MTPA (0.1 - 6.0 mg/m3 (0.023 - 1.38 ppm))
formaldehyde (0.05 - 8.1 mg/m3), acetaldehyde (0.48 - 22.0 mg/m3) and acrolein (0.1 - 8.2 mg/m3 (0.043-3.5 ppm)) were measured.
During the years 1971 - 1973 occured an increase of diseases in dependency of the period of employment and in female workers the incidence was higher than in males. But the

incidence of disease was lower in comparison with the rate of disease of all workers at this production area.

The qualitative and quantitative contribution of MTPA for the observed human disease can not be assessed from this paper, because a lot of other harmful compounds in the same concentration range were identified in the working area. Occupational Exposure

16.04.2004 (64)

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