FOREWORD INTRODUCTION

HEXADECANOIC ACID, 2-SULFO, 1-METHYLESTER,SODIUM SALT

CAS N°: 4016-24-4

SIDS Initial Assessment Report

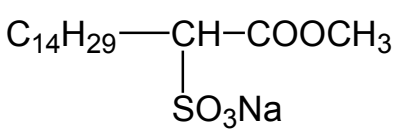
For

SIAM 16

Paris, France; 27-30 May 2003

1. Chemical Name:	Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt
2. CAS Number:	4016-24-4
3. Sponsor Country:	Japan Contact Point: Mr. Yasuhisa Kawamura Director Second International Organizations Division Ministry of Foreign Affairs, Japan
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	
• Process used	
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	The original draft documents were prepared by the Japanese government.
7. Review Process Prior to the SIAM:	
8. Quality check process:	An expert committee performed spot checks on randomly selected endpoints and compared original studies with data in the SIDS dossier.
9. Date of Submission:	21 February, 2003
10. Date of last Update:	
11. Comments:	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	4016-24-4
Chemical Name	Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There is no information on toxicokinetics and metabolism.

In an acute toxicity study [OECD TG 401] with hexadecanoic acid, 2-sulfo, 1-methylester, sodium salt in rats, compound-related changes including death, decrease in the body weight and locomotor activity, ptosis, and piloerection were observed. The oral LD50 values were considered to be 2,142 mg/kg bw in male rats and 1,819 mg/kg bw in female rats. No information on inhalation toxicity is available.

A skin irritation test in guinea pigs showed slightly positive reactions. Dermal exposure to this chemical for 28 days caused primary irritation in rats. There is no available information on eye irritation. This chemical was not sensitizing in a mouse Local Lymph Node Assay.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], Crj:CD (SD) IGS rats (10 animals/sex/dose) were given this compound by gavage at 0, 5, 20, 80, or 300 mg/kg bw/day. Males were dosed for 47 days from day 14 before mating and females were dosed for 42-45 days from day 14 before mating to day 4 of lactation throughout the mating and pregnancy period. An increase in the GPT levels and decrease in the triglyceride levels were found in males at 300 mg/kg bw/day. At necropsy, thickening of the forestomach mucosa was observed in six males and nine females at 80 mg/kg bw/day and in 10 males and females at 300 mg/kg bw/day. In histopathological examinations, squamous hyperplasia, erosion, and edema of lamina propria and/or submucosa and inflammatory cell infiltration were observed in the forestomach of both sexes at 80 and 300 mg/kg bw/day. Based on the pathological findings in the forestomach at 80 mg/kg bw/day, the NOAEL for repeated dose toxicity was considered to be 20 mg/kg bw/day in male and female rats.

In a reverse gene mutation assay [OECD TG 471], this chemical was not mutagenic in *Salmonella typhimurium* TA100, TA1535, TA1537, TA 98 and *Escherichia coli* WP2 *urv*A with and without an exogenous metabolic activation. In a chromosomal aberration test [OECD TG 473], this compound did not cause structural chromosomal aberrations or polyploidy with and without an exogenous metabolic activation in cultured Chinese hamster lung (CHL/IU) cells.

There is no available information on carcinogenicity.

The above-mentioned combined study [OECD TG 422] showed that the reproduction/developmental parameters, i.e. mating, pregnancy, delivery, lactation, and viability and body weight of pups, were not affected by this compound up to 300 mg/kg bw/day. The NOAEL for reproduction/developmental toxicity was considered to be 300 mg/kg bw/day in rats.

Environment

Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt has a melting point of 178.2 – 181.9 degree C and this chemical is estimated to be stable of pH 4, 7 and 9 at 25 degree C for 1 year, and it is readily biodegradable. A critical micelle concentration (CMC) of 0.73 mM (271.9 mg/L) is reported. A vapor pressure of 5.12×10^{-13} Pa at 25

degree C and a Log Pow of 4.06 (for the ionized form) are calculated. This chemical exists primarily in the ionized form under the environmental pHs. Due to the ionizing properties of this chemical and based on data from analogues, it can be assumed that bioaccumulation is not likely to be significant. This chemical on the market contains 20 to 30% (w/w) of tetradecanoic acid, 2-sulfo-, 1-methylester, sodium salt.

In an algal growth inhibition test (OECD TG 201, *Selenastrum capricornutum,* open system), the 72 h ErC50 and the 72 h EbC50 were >9.00 mg/L. For daphnids, a 48 h EC50 of 1.24 mg/L was reported (OECD TG 202, *Daphnia magna*, static). For fish (OECD TG 203, *Oryzias latipes,* semi-static) a 96 h LC50 of 1.50 mg/L was available.

Regarding chronic toxicity to algae, a 72 h NOErC of 9.0 mg/L and a NOEbC of 1.48 mg/L (OECD TG 201, *Selenastrum capricornutum*, open system) were reported. In daphnids, a 21 d EC50 of 0.70 mg and a 21 d NOEC of 0.24 mg/L were reported (OECD TG 211, *Daphnia magna,* semi-static).

There is no available information on toxicity to neither terrestrial nor other organisms.

Exposure

Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt is used as detergent of clothing. In Japan only one company produces this chemical with a production volume of 10,000 to 100,000 tonnes/year (containing up to 30% of tetradecanoic acid, 2-sulfo-, 1-methylester, sodium salt). For 2001, a production volume of 13,400 tonnes is reported.

This chemical is mainly released to the aquatic compartment and it can be expected that the partitioning to other compartments is unlikely but adsorption onto sludge is possible due to the surface active properties.

Occupational exposure to this chemical through inhalation and dermal routes is possible.

Some low level direct exposure to general public is possible during washing cloths by hands via the dermal route and via inhalation of particles.

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 is currently of low priority for further work based on a low hazard potential.

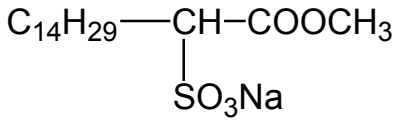
Environment: The chemical possessed properties indicating a hazard for the environment. Although these hazards do not warrant further work as they are related to acute toxicity which may become evident only at very high exposure levels and also this chemical is readily biodegradable, they should nevertheless be noted by chemical safety professionals and users.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 4016-24-4
IUPAC Name: Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt
Molecular Formula: $C_{17}H_{33}NaO_5S$
Structural Formula:



Synonyms: Sodium 1-methoxy-1-oxohexadecane-2-sulfonate
Sodium 1-methoxy-1-oxohexadecane-2-sulphonate
1-Methoxycarbonyl-pentadecane-1-sulfonic acid; sodium-salt

1.2 Purity/Impurities/Additives

Substance type: organic

Physical status: powder

Purity: mixture of tetradecanoic acid, 2-sulfo-, 1-methylester, sodium salt
(Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt is 70 - 80 % w/w,
Tetradecanoic acid, 2-sulfo-, 1-methylester, sodium salt is 30 – 20 % w/w)

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Protocol	Results
Melting Point	OECD TG 102	178.2 – 181.9 °C (CERI 2000)
Boiling Point	OECD TG 103	Decomposition at Ca 260 °C (CERI 2000)
Density	JIS K 7112-1980	1.211 g/cm^3 at 25 °C (CERI 2000)
Vapor Pressure	OECD TG 104 Calculated (MPBPWIN v1.40)	< 0.00017 hPa at 100 °C (CERI 2000) 5.12E-13 Pa at 25 °C
Partition Coefficient (Log P_{ow})	Calculated (KOWWIN)	4.06
Water Solubility (Critical micelle concentration)	Measured. Fujiwara. M. et al. (1993).	271.9 mg/l

Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt is a white powder. Other physical-chemical properties are shown in Table 1. Since the substance has surface active properties, some physical-chemical properties have been difficult to determine by experiments (e.g. log Kow). As the substance forms micelles in water, the water solubility is expressed by critical micelle concentration (CMC).

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The production volume of this chemical is 10,000 – 100,000 tonnes/year and 13,400 tons in 2001 in Japan.

This chemical is used as a detergent for clothing.

2.2 Environmental Exposure and Fate

In water, this chemical exists in an ionized form releasing sodium ions. The pKa value of this chemical is calculated as –1.03 (CompuDrug Pallas v3.0).

This chemical degrades by photochemically induced OH radicals at a half-life of 6.68 hours (AopWin v1.9).

A study on stability in water indicates that this chemical is not hydrolyzed at pHs 4, 7 and 9 for 5 days at 50 °C (CERI 2000).

Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt is readily biodegradable as 91 - 94 % biodegradation based on BOD was observed after 28 days in a test according to OECD TG301C (CERI 2000a).

Due to the ionizing properties of this chemical and based on data from analogues (see Appendix 1), it can be assumed that the bioaccumulation potential is not likely to be significant.

Due to the surface active nature of the substance, the environmental behavior of the substance can probably not be accurately estimated with a fugacity model. Nevertheless, as the substance is mainly released into the aquatic compartment, it can be assumed that the partitioning to other compartment is unlikely.

The maximum concentration of this chemical in the detergent goods is 10.0 % (the usual concentration is 5 – 10 %). The normal (or recommended) concentration of the detergent goods is 15 g in 30 L of water. The concentration of this chemical in washing machine is 50 mg/L when the detergent goods are used normally. The concentration of this chemical in domestic effluent from one family is 1.5 mg/L/family/day as average amount of effluent is 1000 L for one family (four persons). The removal percentage by biodegradation is 98% (the residual amount by HPLC after 3 days was 0 %, and removal percentage by DOC after 14 days was 98% by biodegradation test. The remaining concentration in the effluent is 0.03 mg/L. As the dilution factor is 100 when this chemical releases into a river, a local predicted environmental concentration of this chemical is calculated to be 0.0003 mg/L.

Local Predicted Environmental Concentration

$$= \frac{\text{Content in goods (\%) /100 x Amount of goods (mg) in washing machine x (100 - Removal rate (\%)) / 100}}{\text{Release volume (L) of domestic effluent per family per day x Dillution factor}}$$

$$= \frac{\text{10 (\%) /100 x 15000 (mg) x (100 - 98 (\%)) /100}}{\text{1000 (L) x 100}}$$

= 0.0003 mg/L

2.3 Human Exposure

2.3.1 Occupational Exposure

This chemical is synthesized by sulfonating a mixture of 1-methyl hexadecanoic acid (C16 acid) and 1-methyl tetradecanoic acid (C14 acid) derived from palm oil and coconut oil with sulfur trioxide. The resulting mixture of C14 and C16 sulfo-acids [the ratio of C14/C16 is 20/80 to 30/70(w/w)], bleached by hydrogen peroxide and neutralized by sodium hydroxide, is stored in a tank as a water slurry, and is used to formulate detergents in the same plant. Detergent is formulated by adding several additives to the slurry followed by spray drying, and packaging for commercial use. Synthesis and formulation are continuous processes in remotely controlled closed systems, and fully automated packing machines with enclosure and local exhaust ventilations are used to make commercial packages.

Normally, task of the workers is visual surveillance and direct contact to this chemical is not necessary except sampling of the sulfonated mixture and the final product for quality control. Since this chemical is non-volatile, dermal contact to the slurry and inhalation to dust are possible exposure routes in these sampling operations. The EHE_{der} for sampling and analysis of the water slurry is 0.26 mg/kg/day according to the EASE model, assuming that this work is non-dispersive direct handling with incidental contact to both hands and the duration is 13 minutes. The EHE_{inh} for the sampling and analysis of the detergent is 0.005 mg/kg/day, assuming that this work is direct handling under local exhaust ventilation for a duration of 35 minute, and the detergent is easily aggregated. The estimated exposure concentration according to the EASE model is 0.2-0.5 mg/m^3, and the measured concentration of the total dust at the detergent silo were less than 0.53 mg/m^3.

The workers wear gloves, goggles, and dust mask during sampling operations, and the content of this chemical in detergent is less than 10 %. The actual exposure may therefore be less than these values.

No occupational exposure standard value for this chemical was located.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

There is no information on animals and humans.

3.1.2 Acute Toxicity

Studies in Animals

Two studies on acute toxicity are reported in rats (Table 2). One study was conducted according to an OECD acute oral toxicity test guideline [TG 401] [MHLW, Japan, 2002] under GLP. This study was identified as a key study because it was well conducted. The other was considered insufficient for a key study because of lack of detailed information.

Details of the study by MHLW, Japan (2002) are as follows.

Crj:CD (SD) IGS rats (five animals/sex/dose) were given hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt by gavage at dose of 0, 786, 983, 1,229, 1,536, 1,920, or 2,400 mg/kg bw to males and females. One male and three female deaths occurred at 1,536 mg/kg bw, one male and two female deaths at 1,920 mg/kg bw and four male and four female deaths at 2,400 mg/kg bw. Most deaths were observed during 6-24 hours after administration of this chemical. Decreased locomotor activity, ptosis, diarrhea, soiling of the perianal region, and piloerection were observed in all groups given this chemical. Body weights of male and female rats were decreased in a dose-dependent manner. Distention of the stomach, filled with water, was observed in most of the dead rats. The oral LD50 values were considered to be 2,142 mg/kg bw in male rats and 1,819 mg/kg bw in female rats.

Table 2: Acute toxicity of hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt in rats

Route	Animals	Type	Values	References
Oral	Rat	LD_{50}	= 2,142 mg/kg bw for males = 1,819 mg/kg bw for females	MHLW, Japan: 2002
Oral	Rat	LD_{50}	Between 700 and 1,400 mg/kg bw for males	Lion Corporation: 1990a

Studies in Humans

There is no available information on human toxicity.

Conclusion

The oral LD_{50} values were considered to be 2,142 mg/kg bw in male rats and 1,819 mg/kg bw in female rats.

3.1.3 Irritation and Sentisation

Studies in Animals

Skin Irritation

Skin irritation was measured by the Draize test in guinea pigs (two animals/group) which received a single dermal application of 3.2-32.7% test solution (0.03 ml/animal). The test solution contained hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at 43.7 or 49.0%. Slightly positive reactions were found [Lion Corporation: 1993].

Eye Irritation

There is no available information on eye irritation in animals.

Sensitisation

Sensitizing effects of hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt was determined with the mouse local lymph node assay (four animals/group) according to an OECD guideline [TG 429] [Lion Corporation: 2003c]. This substance was not sensitizing at concentrations of up to 25%.

Studies in Humans

There is no available information on skin and eye irritation and sensitization in humans.

Conclusion

The skin irritation test of this substance in guinea pigs showed slightly positive reactions.

This substance was not sensitizing in a mouse local lymph node assay.

Information on related compound

Sodium methyl α-sulfo-tallowate, sulfated N-(2-hydroxypropyl) tallowamide and sodium N-methyl N-(2-sulfoethyl) tallowamide produced mildly skin irritation and slight eye irritation in rabbits and negative sensitization results in guinea pigs [Maurer et al., 1973].

There is no available information on humans.

3.1.4 Repeated Dose Toxicity

Inhalation

There is no available information on animal and human toxicity.

Dermal

One study is available for repeated dermal application toxicity. This study was conducted according to a guideline of the Chemical Substances Control Law of Japan [Lion Corporation, 2003a].

Crj:CD (SD) rats (five animals/sex/dose) received daily dermal application of 0, 2.1, 7.1, or 21.4% test solution (0.2 ml/animal) for 28 days in males and for 29 days in females. The test solution contained hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at 49.2%. Primary skin irritation was observed at 15% in both sexes. In histopathological examinations, thickening of the epidermis were also found at the highest concentration. No-compound related changes in clinical signs, body weight, food consumption, organ weight, urinalysis, hematological findings, or histopathological findings in the major organs were noted. No other detailed information was available.

Oral

One study is available for repeated dose toxicity. This study was conducted according to an OECD combined repeated dose toxicity study with the reproduction/developmental toxicity screening test guideline [TG 422] [MHLW, Japan, 2002] under GLP. This study was identified as a key study because it was well conducted. Details of the study by MHLW, Japan (2002) are as follows.

Crj:CD (SD) IGS rats (10 animals/sex/dose) were given hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt by gavage at a dose of 0 (vehicle: olive oil), 5, 20, 80, or 300 mg/kg bw/day. Males were dosed for 47 days from day 14 before mating and females were dosed for 42-45 days from day 14 before mating to day 4 of lactation throughout the mating and pregnancy period. Hematological, blood biochemical, and histopathological examinations were performed in both sexes, and urinalysis was conducted in males.

There were no deaths related to administration of this chemical. Transitional soft stool was observed in one male and female at 80 mg/kg bw/day and three males and females 300 mg/kg bw/day. There were no effects of this chemical on the body weight, food consumption, or organ weight of males and females. No compound-related changes in the urinalysis or hematological findings were observed. A significant increase in the GPT levels and decrease in the triglyceride levels were found in males at 300 mg/kg bw/day, but no changes in blood biochemical findings were observed in females. At necropsy, thickening of the forestomach mucosa was observed in six males and nine females at 80 mg/kg bw/day and in 10 males and females at 300 mg/kg bw/day. In histopathological examinations, squamous hyperplasia, erosion, and edema of lamina propria and/or submucos and inflammatory cell infiltration were observed in the forestomach of both sexes at 80 and 300 mg/kg bw/day. No toxic effects were observed at 5 and 20 mg/kg bw/day. Based on a significant increase in the incidence of pathological changes in the forestomach at 80 mg/kg bw/day, the NOAEL for repeated dose toxicity was considered to be 20 mg/kg bw/day in male and female rats.

Conclusion

In an oral repeated dose toxicity study in rats, pathological findings in the forestomach were observed at 80 mg/kg bw/day. The NOAEL for oral repeated dose toxicity was considered to be 20 mg/kg bw/day in male and female rats.

3.1.5 Mutagenicity

In vitro Studies

Table 3: Summary of genotoxicity assays

Type of test	Test system	Highest concentration	Result	Reference
Bacterial test				
Ames test *(reverse mutation)*	*S. typhimurium* (TA100, TA1535, TA1537)	20 µg/plate	Negative (- MA*)	MHLW, Japan: 2002
	S. typhimurium (TA98)	100 µg/plate	Negative (- MA)	
	S. typhimurium (TA100)	2,000 µg/plate	Negative (- MA)	
	S. typhimurium (TA1537)	1,000 µg/plate	Negative (+ MA)	
	S. typhimurium (TA98, TA1535)	200 µg/plate	Negative (+ MA)	
	E. coli (WP2 *uvr* A)	5,000 µg/plate	Negative (+ & - MA)	
Ames test *(reverse mutation)*	*S. typhimurium* (TA98, TA100, TA1535)	35 µg/plate	Negative (- MA)	Lion Corporation : 1990b
	S. typhimurium (TA1537)	7 µg/plate	Negative (- MA)	
	S. typhimurium (TA98, TA100, TA1537)	350 µg/plate	Negative (+ MA)	
	S. typhimurium (TA1535)	700 µg/plate	Negative (+ MA)	
	E. coli (WP2 *uvr* A)	3,500 µg/plate	Negative (+ & - MA)	
Non-bacterial in vitro test				
Chromosomal aberration test	CHL cells	250 µg/mL	Negative (+ & - MA)	MHLW, Japan: 2002
Chromosomal aberration test	CHL cells	104 µg/mL: 24h 88 µg/mL: 48h 200 µg/mL	Negative (- MA) Negative (- MA) Negative (+ MA)	Lion Corporation: 1998

*MA: Metabolic activation

Bacterial test

Two studies were reported (Table 3). In one study, the reverse gene mutation assay was conducted according to a current protocol [OECD TG 471 and Japanese Guideline for Screening Mutagenicity Testing of Chemicals (Chemical Substances Control Law of Japan) [MHLW, Japan: 2002] under GLP. This study was identified as a key study because it was well conducted. The other was considered insufficient for a key study because of lack of detailed information.

Details of the study by MHLW, Japan (2002) are as follows.

Growth inhibition was observed at 20 µg/plate (TA100, TA1535 and TA 1537) and 100 µg/plate (TA98) without S9 mix, and at 2,000 µg/plate (TA100), 1,000 µg/plate (TA1537), and 200 µg/plate (TA1535 and TA98) with S9 mix. This chemical was not mutagenic in *Salmonella typhimurium* TA100, TA1535 and TA1537 at concentrations of up to 20 µg/plate, TA 98 at concentrations of up to 100 µg/plate and *Escherichia coli* WP2 *urv*A at concentrations of up to 5,000 µg/plate without S9 mix, and in *Salmonella typhimurium* TA100 at concentrations of up to 2,000 µg /plate, TA1537 at concentrations of up to 1,000 µg/plate, TA1535 and TA98 at concentrations of 200 µg/plate and *Escherichia coli* WP2 *urv*A at concentrations of up to 5,000 µg/plate with S9 mix.

Non-bacterial test

Two studies were reported (Table 3). In one study, the chromosomal aberration test was conducted according to a current protocol [OECD TG 473] in cultured Chinese hamster lung (CHL/IU) cells [MHLW, Japan: 2002] under GLP. This study was identified as a key study because it was well conducted. The other was considered insufficient for a key study because of lack of detailed information.

Details of the study by MHLW, Japan (2002) are as follows.

A 50% growth inhibition was observed at 125 μg/mL and higher after 6 hr short-term or 24 hr continuous treatment with and without an exogenous metabolic activation. Based on the concentration of the 50% growth inhibition, a maximum concentration was decided at 250 μg/mL. Structural chromosomal aberrations and polyploid were not induced up to 250 μg/mL. Cell toxicity was observed at 187.5 and 250 μg/mL without S9 mix and at 250 μg/mL with S9 mix after short-term treatment and observed at 187.5 and 250 μg/mL after continuous treatment without S9 mix.

In vivo Studies

There is no available *in vivo* information on genotoxicity.

Conclusion

This chemical was not genotoxic with and without an exogenous metabolic activation system in bacterial test and in chromosomal aberration test *in vitro*.

3.1.6 Carcinogenicity

There is no available information on carcinogenicity.

3.1.7 Toxicity for Reproduction

One study is available for reproduction/developmental toxicity. This study was conducted according to an OECD combined repeated dose toxicity study with the reproduction/developmental toxicity screening test guideline [TG 422] [MHLW, Japan, 2002] under GLP. This study was identified as a key study because it was well conducted. Details of the study are as follows.

Crj:CD (SD) IGS rats (10 animals/sex/dose) were given hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt by gavage at dose of 0 (vehicle: olive oil), 5, 20, 80, or 300 mg/kg bw/day. Males were dosed for 47 days from day 14 before mating and females were dosed for 42-45 days from day 14 before mating to day 4 of lactation throughout the mating and pregnancy period.

Three females in the control group did not become pregnant due to abnormality of spermatogenesis in paired males. No decrease in fertility index was observed in the groups given this compound. No compound-related effect on the estrous cyclicity, copulation index, gestation length, numbers of corpora lutea, or number of implantation sites were found in dams. No compound-related effects on the number, sex ratio, body weight, or viability were detected in pups on days 0 and 4 of lactation. No abnormal findings considered to be attributable to administration of this compound were observed in dead pups during lactation and pups at scheduled sacrifice. No external or internal malformations were also noted in pups of any groups. Based on these findings, the NOAEL for reproductive/developmental toxicity was considered to be 300 mg/kg bw/day in rats.

Conclusion

In an OECD combined repeated dose toxicity study with the reproduction/developmental toxicity screening test, there were no evidences of compound-related effects on reproduction/developmental parameters. The NOAEL for reproduction/developmental toxicity was considered to be 300 mg/kg bw/day in rats.

Teratogenicity: dermal application

Results are available from a teratology study by dermal application of this substance. This study was conducted according to a guideline for Toxicity Studies of Drugs [Lion Corporation: 2003b].

Crj:CD (SD) rats (27 females/dose) received daily dermal application of 0, 2.1, 7.1, 21.4% test solution (0.2 ml/rat) on days 7-17 of pregnancy. The test solution contained hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at 49.2%. Female rats were sacrificed at term of pregnancy. Primary skin irritation in maternal rats was observed at 15%. No compound-related changes in clinical signs, body weight, or food consumption of maternal rats, or survival or growth of offspring were found. There was no evidence for teratogenicity of this substance. No other detailed information was available.

3.2 Initial Assessment for Human Health

There is no information on toxicokinetics and metabolism.

In an acute toxicity study [OECDTG 401] with hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt in rats, compound-related changes including death, decrease in the body weight and locomotor activity, ptosis, and piloerection were observed. The oral LD_{50} values were considered to be 2,142 mg/kg bw in male rats and 1,819 mg/kg bw in female rats.

A skin irritation test in guinea pigs showed slightly positive reactions. The dermal application of this chemical for 28 days caused primary irritation in rats. This chemical is not sensitizing in mouse local lymph node assay.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], Crj:CD (SD) IGS rats (10 animals/sex/dose) were given hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt by gavage at 0, 5, 20, 80, or 300 mg/kg bw/day. Males were dosed for 47 days from day 14 before mating and females were dosed for 42-45 days from day 14 before mating to day 4 of lactation throughout the mating and pregnancy period. Transitional soft stool was observed in one male and female at 80 mg/kg bw/day and three males and females 300 mg/kg bw/day. There were no effects of this chemical on the body weight or food consumption of males and females. No compound-related changes in the urinalysis or hematological findings were also observed. An increase in the GPT levels and decrease in the triglyceride levels were found in males at 300 mg/kg bw/day, but no changes in blood biochemical findings were observed in females. At necropsy, thickening of the forestomach mucosa was observed in six males and nine females at 80 mg/kg bw/day and in 10 males and females at 300 mg/kg bw/day. In histopathological examinations, squamous hyperplasia, erosion, and edema of lamina propria and/or submucos and inflammatory cell infiltration were observed in the forestomach of both sexes at 80 and 300 mg/kg bw/day. Based on the pathological findings in the forestomach at 80 mg/kg bw/day, the NOAEL for repeated dose toxicity was considered to be 20 mg/kg bw/day in male and female rats.

In a reverse gene mutation assay [OECD TG 471], hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt was not mutagenic in *Salmonella typhimurium* TA100, TA1535, TA1537, TA 98 and *Escherichia coli* WP2 *urv*A with and without an exogenous metabolic activation. In a chromosomal

aberration test [OECD TG 473], sodium 1-methoxycarbonylpentadecane-2-sulfonate did not cause structural chromosomal aberrations or polyploid with and without an exogenous metabolic activation in cultured Chinese hamster lung (CHL/IU) cells.

There is no available information on carcinogenicity.

The above-mentioned combined study [OECD TG 422] showed that the reproduction/developmental parameters, i.e., mating, pregnancy, delivery, lactation, and viability and body weight of pups, were not affected by administration of hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at up to 300 mg/kg bw/day. The NOAEL for reproduction/developmental toxicity was considered to be 300 mg/kg bw/day in rats.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute Toxicity Test Results

The toxicity of hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt on aquatic organisms has been studied in three freshwater species belonging to three trophic levels as shown in Table 4.

Table 4: Summary of effects of hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt on aquatic organisms

Organisms	Test duration	Result (mg/L)	Reference
Aquatic plants, e.g. algae			
Green algae (*Selenastrum capricornutum*)	72 h Open system	Growth rate method ErC_{50} > 9.00 . NOErC = 9.00 Biomass method EbC_{50} > 9.00 . NOEbC = 1.48	MOE, Japan(2001)
Invertebrates			
Daphnids (*Daphnia magna*)	48 h Static	Immobilization EC_0 = 0.63 EC_{50} = 1.24 EC_{100} = 2.21	MOE, Japan(2001)
	21 d Semi-static	Mortality LC_{50} = 1.12 Reproduction EC_{50} = 0.70 LOEC = 0.38 NOEC = 0.24	MOE, Japan(2001)
Fish			
Medaka (*Oryzias latipes*)	96 h Semistatic	LC_0 = 1.13 LC_{50} = 1.50 LC_{100} = 1.99	MOE, Japan(2001)

In an algal growth inhibition test (OECD TG 201, open system), acute toxicity (a 72 h ErC_{50} and a 72 h EbC_{50}) to *Selenastrum capricornutum* were >9.00 mg/L by both the biomass method and the growth rate method. In the experiment, the growth inhibition was 18.1% (biomass) and 2.47 % (growth rate) at the concentration of 9.00 mg/L, the highest concentration.

Regarding acute toxicity to daphnids, a 48 h EC_0 of 0.63 mg/L, a 48 h EC_{50} of 1.24 mg/L and a 48 h EC_{100} of 2.21 mg/L were reported (OECD TG 202, *Daphnia magna*, static).

In a test with fish (OECD TG 203, *Oryzias latipes,* semi-static) a 96 h LC_0 of 1.13 mg/L, a 96 h LC_{50} of 1.50 mg/L and a 96 h LC_{100} of 1.99 mg/L were derived. In this test, all individuals exposed at the highest concentration of 3.76 mg/L died in 24 hours, and at 1.99 mg/L a 100 % mortality was observed until 72 hours, but no mortality and also no symptoms were observed at the concentration

of 1.13 mg/L and the lower concentrations during the test period. Thus this substance has a very steep dose-effect curve. It should be taken into consideration for the assessment.

All acute toxicities were derived from tests conducted in compliance with GLP and the toxicities were estimated based on the mean measured concentration.

Chronic Toxicity Test Results

Regarding chronic toxicity to algae, a 72 h NOErC of 9.00 mg/L and a NOEbC 1.48 mg/L (OECD TG 201, *Selenastrum capricornutum*, open system) were reported. In daphnids, the effect of the substance on reproduction (OECD TG 211, *Daphnia magna* semi-static) was investigated. A 21 d EC_{50} of 0.70 mg/L, a 21 d LOEC of 0.38 mg/L and a NOEC of 0.24 mg/L were reported (MOE Japan, 2001). For the mortality of parent daphnids the 21 d LC_{50} was 1.12 mg/L.

4.2 Terrestrial Effects

There is no available information.

4.3 Other Environmental Effects

There is no available information.

4.4 Initial Assessment for the Environment

Hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt has a melting point of 178.2 – 181.9 degree C and this chemical is estimated to be stable of pH 4, 7 and 9 at 25 degree C for 1 year, and it is readily biodegradable. A critical micelle concentration (CMC) of 0.73 mM (271.9 mg/L) is reported. A vapor pressure of 5.12×10^{-13} Pa at 25 degree C and a Log Pow of 4.06 (for the ionized form) are calculated. This chemical exists primarily in the ionized form under the environmental pHs. Due to the ionizing properties of this chemical and based on data from analogues, it can be assumed that bioaccumulation is not likely to be significant. This chemical on the market contains 20 to 30% (w/w) of tetradecanoic acid, 2-sulfo-, 1-methylester, sodium salt.

In an algal growth inhibition test (OECD TG 201, *Selenastrum capricornutum,* open system), the 72 h ErC50 and the 72 h EbC50 were >9.00 mg/L. For daphnids, a 48 h EC50 of 1.24 mg/L was reported (OECD TG 202, *Daphnia magna*, static). For fish (OECD TG 203, *Oryzias latipes,* semi-static) a 96 h LC50 of 1.50 mg/L was available.

Regarding chronic toxicity to algae, a 72 h NOErC of 9.0 mg/L and a NOEbC of 1.48 mg/L (OECD TG 201, *Selenastrum capricornutum*, open system) were reported. In daphnids, a 21 d EC50 of 0.70 mg and a 21 d NOEC of 0.24 mg/L were reported (OECD TG 211, *Daphnia magna,* semi-static).

There is no available information on toxicity to neither terrestrial nor other organisms.

The predicted no effect concentration (PNEC) for the aquatic compartment was estimated to be 0.0024 mg/L using the lowest NOEC of 0.24 mg/L in daphnids and an assessment factor of 100 because two chronic toxicity values are available.

5 RECOMMENDATIONS

Human Health: The chemical is currently of low priority for further work based on a low hazard potential.

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

The chemical possessed properties indicating a hazard for the environment. Although these hazards do not warrant further work as they are related to acute toxicity which may become evident only at very high exposure levels, they should nevertheless be noted by chemical safety professionals and users.

6 REFERENCES

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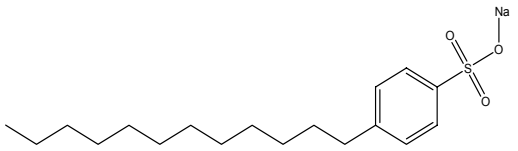
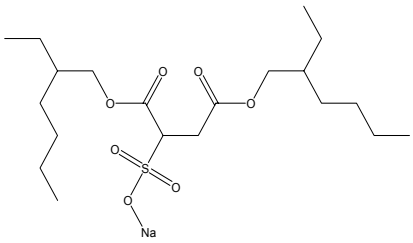
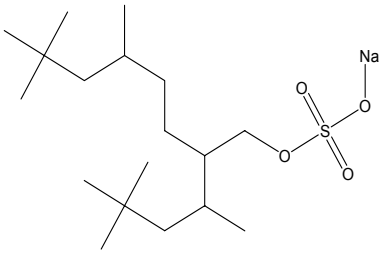
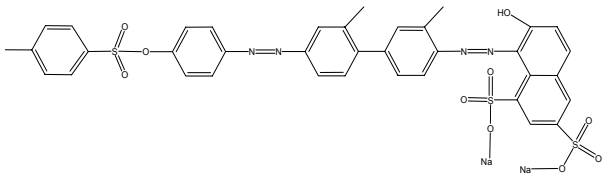
ANNEX

Appendix 1 : log Pow and BCF values for analogues

CAS	logBCF (av)	Calculated log Pow		Chemical name
		non-ionised	ionised	
25155-30-0 7758-29-4	0.51	4.78	3	Sodium_dodecylbenzenesulfonate(branching_form)
58226-28-1	n.d.	2.26	-0.32	Sodium_dinaphthyl_methane_disulfonate
87-02-5	n.d.	-1.39		7-Amino-4-hydroxy-2-naphthalenesulfonic_acid
842-18-2	n.d.	-1.42	-4	7-Hydroxy-1,3-naphthalene_disulfonic_acid_dipotassium_salt
130-13-2	n.d.	-0.91	-2.69	Naphthionic_acid_sodium_salt
5460-09-3	n.d.	-2.33	-6.33	1-Amino-8-naphthol-3,6-disulfonic_acid_monosodium_salt
88-44-8	-0.40	-1.53		2-Amino-5-methylbenzenesulfonic_acid
121-57-3	n.d.	-2.08		4-Aminobenzene-1-sulfonic_acid
6099-57-6	n.d.	-0.47	-2.26	Sodium_1-naphthol-4-sulfonate
135-51-3	n.d.	-1.42	-4	2-Naphthol-3,6-disulfonic_acid_disodium_salt
20324-87-2	n.d.	0.25	-2.32	6,6'-Ureylene-bis(1-naphthol-3-sulfonic_acid_sodium_salt)
127-68-4	n.d.	-1.35	-3.13	Sodium_m-nitrobenzenesulfonate
946-30-5	n.d.	-0.7	-2.49	Sodium_4-nitrochlorobenzenesulfonate
25394-13-2	n.d.	-1.42	-3.99	Sodium_4,4'-diamino-2,2'-stilbene_disulfonate
52789-62-5	n.d.	-2.33	-6.33	Mono_sodium_1-amino-8-hydroxy-2,4-naphthyl_disulfonate
84-57-1	n.d.	0.69		1-(2',5'-Dichloro-4'-sulfophenyl)-3-methyl-5-pyrazolone
9014-90-8	n.d.	1.86	1.13	Sodium=α-sulfonate-ω-nonylphenoxy_polyoxyethylene_(the_polymerization_grade_6)
25638-17-9	n.d.	2.03	0.24	Sodium_monobutylnaphthalene_sulfonate
50925-42-3	n.d.	5.3	1.14	Direct_Yellow-86
1934-21-0	n.d.	-0.01	-10.17	Acid_Yellow-23

3618-60-8	n.d.	2.73	0.95	Mordant_Black-7
6459-94-5	1.83	7.86	0.47	Acid_Red-114
17095-24-8	n.d.	-6.5	-4.13	Reactive_Black-5
16090-02-1	1.14	5.95	3.37	Fluorescent-260
123251-96-7	n.d.	-0.89		3,3'-Dichloro-5,5'-benzidine_disulfonic_acid
24019-05-4	1.84	3.6		N-(3,4-Dichlorophenyl)-N-[2'-(4"-chloro-2"-sulfophenoxy)-5'-chlorophenyl]urea
577-11-7	n.d.	6.1	3.95	di-2-Ethylhexyl_sodium_salt_sulfosuccinate
	n.d.	4.93	4.2	Sodium=2-(3,3-dimethyl-1-methylbutyl)-7,7-dimethyl-5-methyloctylsulfate
2861-02-1	n.d.	-0.5	-3.08	Acid_Blue-45
16470-24-9	n.d.	1.34	-2.83	4-[2-p-Sulfoanilino-4-bis(hydroxyethyl)amino-1,3,5-triazinyl-6-amino]-4'-[2-m-sulfoanilino-4-bis(hydroxyethyl)amino-1,3,5-triazinyl-6-amino]stilbene-2,2'-disulfonic_acid,sodium_salt
81-11-8	n.d.	-1.42		4,4'-Diaminostilbene-2,2'-disulfonic_acid
15046-75-0	n.d.	-0.62	-2.4	Sodium_o-toluenesulfonate
3965-55-7	n.d.	-1.49	-3.28	Dimethyl isophthalate-5-sulfonic acid sodium salt
27457-28-9	n.d.	-0.26	-2.05	Sodium p-vinylbenzenesulfonate
827- 21-4	n.d.	-0.07	-1.86	2,4-Dimethylbenzenesulfonic_acid_sodium_salt
3214-47-9	n.d.	3.39	2.14	Direct_yellow-50
2580-78-1	n.d.	-2.53	-1.85	Reactive_blue-19
121-03-9	n.d.	-0.8		2-Methyl-5-nitrobenzenesulfonic_acid
6258-06-6	-0.13	1.26	-0.53	1-Amino-4-bromoanthraquinone-2-sulfonic acid sodium

Examples of measured BCF data on analogue chemicals

	Log Pow	BCF (exp.)
	3.0 (ionized) 4.78 (non-ionized)	3.2
	3.9 (ionized) 6.1 (non-ionized)	< 3.0
	Log Pow 4.2 (ionized) 4.9 (non-ionized)	BCF (exp.) <2.0
	0.47 (ionized) 7.86 (non-ionized)	76

I U C L I D

Data Set

Existing Chemical	:	ID: 4016-24-4
CAS No.	:	4016-24-4
EINECS Name	:	sodium 1-methoxy-1-oxohexadecane-2-sulphonate
EINECS No.	:	223-676-0
Molecular Formula	:	C17H33O5S.Na

Producer Related Part

Company	:	National Institute of Health & Sciences
Creation date	:	29.01.2003

Substance Related Part

Company	:	National Institute of Health & Sciences
Creation date	:	29.01.2003
Memo	:	
Printing date	:	29.07.2003
Revision date	:	
Date of last Update	:	29.07.2003
Number of Pages	:	1
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 7
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 OECD AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

1-Methoxycarbonyl-pentadecane-1-sulfonic acid, sodium-salt
Reliability : (1) valid without restriction
29.07.2003

Hexadecanoic acid, 2-sulfo-, 1-methyl ester, sodium salt
Reliability : (1) valid without restriction
29.07.2003

Sodium 1-methoxy-1-oxohexadecane-2-sulfonate
Reliability : (1) valid without restriction
29.07.2003

Sodium 1-methoxy-1-oxohexadecane-2-sulphonate
Reliability : (1) valid without restriction
29.07.2003

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

Type : use

Category : Surface-active agents
Remark : Detergent for clothing
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
29.07.2003

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value	:	= 178.2 - 181.9 ° C
Sublimation	:	
Method	:	OECD Guide-line 102 "Melting Point/Melting Range"
Year	:	2000
GLP	:	no
Test substance	:	
Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003 (2)

Value	:	= 180.9 - 182.8 ° C
Sublimation	:	
Method	:	
Year	:	1953
GLP	:	no data
Test substance	:	
Reliability	:	(2) valid with restrictions

29.07.2003 (9)

2.2 BOILING POINT

Value	:	ca. 260 ° C at 1013 hPa
Decomposition	:	
Method	:	OECD Guide-line 103 "Boiling Point/boiling Range"
Year	:	2000
GLP	:	no
Test substance	:	
Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003 (3)

2.3 DENSITY

Type	:	density
Value	:	= 1.211 at 25° C
Method	:	other
Year	:	2000
GLP	:	no
Test substance	:	

Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003 (4)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	<= .00017 hPa at 100° C
Decomposition	:	
Method		OECD Guide-line 104 "Vapour Pressure Curve"
Year	:	2000
GLP	:	no
Test substance	:	
Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003 (5)

Value	:	= 0 hPa at 25° C
Decomposition	:	
Method		other (calculated)
Year	:	2003
GLP	:	
Test substance	:	
Remark	:	Modified Grain Method (MPVPWIN v. 1.40)
Conclusion		The vapour pressure is calculated as 5.12E-15 hPa.
Reliability	:	(3) invalid

29.07.2003

2.5 PARTITION COEFFICIENT

Log pow	:	= 4.06 at ° C
Method		other (calculated)
Year	:	2003
GLP	:	
Test substance	:	
Remark	:	A log Kow was of 4.06 was calculated by KOWWIN v1.66.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003

2.6.1 WATER SOLUBILITY

Value	:	= 271.9 mg/l at 20 ° C
Qualitative	:	
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other
Year	:	1993
GLP	:	
Test substance	:	
Remark	:	A critical micelle concentration (CMC) of 271.9 mg/l was reported.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003 (7)

Value	:	= 17 g/l at 25 ° C
Qualitative	:	very soluble (> 10000 mg/L)
Pka	:	-1.03 at 25 ° C
PH	:	= 6.2 - 6.3 at 17 g/l and 25 ° C
Method	:	OECD Guide-line 105 "Water Solubility"
Year	:	2000
GLP	:	no
Test substance	:	
Remark	:	A pKa of acid form was calculated as -1.03 by CompuDrug Pallas v3.0
Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Reliability	:	(2) valid with restrictions

29.07.2003

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Indirect photolysis		
Sensitizer	:	OH
Conc. of sens.	:	1500000 molecule/cm3
Rate constant	:	= .00000000001923 cm3/(molecule*sec)
Degradation	:	= 50 % after 6.9 hour(s)
Deg. Product	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	
Remark	:	AOPWIN v.1.90
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	< 10 - 5 day at 50 degree C
t1/2 pH7	:	< 10 - 5 day at 50 degree C
t1/2 pH9	:	< 10 - 5 day at 50 degree C
Deg. Product	:	
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year	:	2000
GLP	:	no
Test substance	:	
Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Conclusion	:	This chemical is stable at pH 4, 7 and 9 at 50 degree C for 5 days.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.07.2003 (6)

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, non-adapted
Concentration	:	100mg/l related to Test substance related to
Contact time	:	28 day
Degradation	:	= 91 - 94 % after 28 day
Result	:	readily biodegradable
Control substance	:	Aniline
Kinetic	:	**%** **%**
Deg. Product	:	
Method	:	OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year	:	2000
GLP	:	yes
Test substance	:	
Remark	:	The concentration of aniline was 100 mg/l. The concentration of activated sludge was 30 mg/l.
Source	:	Chemicals Evaluation and Research Institute (CERI), Japan
Test substance	:	Lion Corporation Purity: 96.6% Impurity: Disodium alfa-sulfopalmitate 0.5% Sodium methylsulfate 0.3% Methyl palmitate 0.1% Water 2.2%
Conclusion	:	This chemical is readily biodegradable.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

29.07.2003 (1)

Type	:	aerobic
Inoculum	:	activated sludge, non-adapted
Concentration	:	100mg/l related to Test substance related to
Contact time	:	28 day
Degradation	:	ca. 70 % after 28 day
Result	:	
Control substance	:	Aniline
Kinetic	:	**%** **%**
Deg. Product	:	
Method	:	OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year	:	1993
GLP	:	yes
Test substance	:	other TS
Result	:	The biodegradation rates by BOD of 2-Sulfonatofatty acid methyl ester were; 71% using 100 mg/l of test substance with 30 mg/l of activated sludge, 78% using 50 mg/l of test substance with 30 mg/l of activated sludge, 93% using 5 mg/l of test substance with 10 mg/l of activated sludge
Test substance	:	2-Sulfonatofatty acid methyl ester R-CH(SO3Na)COOCH3, R:C12H25-C14H29, Purity 91.0%

Reliability : (1) valid without restriction
29.07.2003 (8)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

BCF : = 70.79
Elimination :
Method :
Year : 2003
GLP :
Test substance :
Remark : A BCF of 70.79 was calculated by BCFWIN v.\2.14.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
29.07.2003

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	Semi static
Species	:	Oryzias latipes (Fish, freshwater)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	Yes
LC0	:	= 1.13
LC50	:	= 1.5
LC100	:	= 1.99
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	2001
GLP	:	Yes
Test substance	:	other TS: Lion Corporation (Japan), Lot. No.: 000203, Purity = 96.6%
Method	:	-Test Organisms: a) Supplier: Test organisms were obtained from Yatomi Chikuyougyojo (Private Fish Farm, Japan). b) Size (length and weight): 2.31 cm (2.18 - 2.46 cm) in length; 0.2105 g (0.1684 - 0.2740 g) in weight c) Age: Not described d) Any pretreatment: Test organisms were acclimated for at least 12 days before testing. During acclimation, test fishes were fed with TETRAMINE. These test organisms were not fed for 24 hours before the test started. The mortality of the test organisms for 7 days before testing was 1%. LC50(96 hr) for a reference substance (copper sulfate pentahydrate) was 0.46 mg/L. -Test substance: 2-Sulfo-hexadecanoic acid 1-methyl ester sodium salt a) Empirical Formula: C17H33NaO5S b) Molecular Weight: 372.49 g/mol c) Purity: =96.6 % -Test Conditions: a) Dilution Water Source: Dilution water was prepared from tap water (Nagoya city, Japan). The tap water was dechlorinated and treated by activated carbon. After that residual chlorine was removed from the water. Before using as the dilution water, aeration was fully carried out. b) Dilution Water Chemistry: pH: = 7.0 Total hardness (as CaCO3): = 25.0 mg/L c) Exposure Vessel Type: 3 L test solution in a 3 L Glass beaker d) Nominal Concentrations: control, 0.26,0.48,0.86,1.54,2.78 and 5.00 mg/L e) Vehicle/Solvent and Concentrations: Any solvent was not used. f) Number of Replicates: 1 g) Fish per Replicates: 10 h) Renewal Rate of Test Water: Every 24 hours i) Water Temperature: 24+/-1ºC j) Light Condition: 16:8 hours, light-darkness cycle k) Feeding: None l) Aeration : Test solution was not aerated during the test period. -Analytical Procedure: The tested concentrations were measured at the start and 24th hour (before exchange of test solution) using LC-MS , with detection limit of 0.02 mg/L.

-Statistical Method:
a) Data Analysis: Binomial method for LC50
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Geometric mean

-

Result : - Measured Concentrations: The test concentrations were measured at 0 h and 24 h (before exchange of test solution). For some of them, the deviations from the nominal were not less than +/- 20%.

Nominal Conc.	Measured Conc., mg/L			Percent of Nominal	
mg/L	0 Hour Fresh	24 Hours Old	Mean* mg/L	0 Hour Fresh	24Hours Old
Control	<0.02	<0.02	---	---	---
0.26	0.22	0.21	0.21	---	---
0.48	0.39	0.36	0.37	81.3	75.0
0.86	0.62	0.60	0.61	72.1	69.8
1.54	1.17	1.09	1.13	76.0	70.8
2.78	2.05	1.94	1.99	73.7	69.8
5.00	3.83	3.70	3.76	76.6	74.0

*: Mean measured concentration (Geometric Mean)
Fresh: Start of renewal period
Old: End of renewal period

- Water chemistry (pH and DO) and temperature in test: Water chemistry and temperature were measured for old and renewal solution with control and each concentration at the start of test and every 24 hours.
pH: 6.8 - 7.3
DO: 5.0 - 8.3 mg/L
Water Temperature: 23.1 - 23.7ºC

-Effect Data(mortality):
LC50 (96hr) = 1.50mg/L (mc)
LC0 (96hr) = 1.13mg/L (mc)
LC100 (96hr) = 1.99mg/L (mc)
mc: based on measured concentration (Geometric mean)

- Cumulative Mortality: None of test organisms were killed during exposure period at control, 0.21, 0.37, 0.61 and 1.13 mg/L, however all test organisms were killed at 1.99mg/L on and after 72 hours and at 3.76mg/L on and after 24 hours.

Measured Conc.	Cumulative Number of Dead (Percent Mortality)			
mg/L	24hr	48hr	72hr	96hr
Control	0 (0)	0 (0)	0 (0)	0 (0)
0.21	0 (0)	0 (0)	0 (0)	0 (0)
0.37	0 (0)	0 (0)	0 (0)	0 (0)
0.61	0 (0)	0 (0)	0 (0)	0 (0)
1.13	0 (0)	0 (0)	0 (0)	0 (0)
1.99	2(20)	8 (80)	10 (100)	--a(--a)
3.76	10 (100)	--a (--a)	--a (--a)	--a(--a)

a: No observation was made because all Medaka were died until this observation time.

-Other Effect: Toxicological symptom was observed at 1.99 mg/L (96 hour) and higher concentration.

Nominal Conc. mg/L	Symptoms 24hr	48hr	72hr	96hr
Control	n	n	n	n
0.21	n	n	n	n
0.37	n	n	n	n
0.61	n	n	n	n
1.13	n	n	n	n
1.99	n	n	n	--a
3.76	--a	--a	--a	--a

n: No abnormalities are detected
a: No observation was made because all Medaka were died before this observation time.

- Calculation of toxicity values: The calculation of toxicity values was the mean measured concentrations.

Source : Ministry of Environment, Japan (2001)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
13.01.2003 (3)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour
Unit : mg/l
Analytical monitoring : yes
EC0 : = .63 (immobility)
EC50 : = 1.24 (immobility)
Method : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilization Test"
Year : 2001
GLP : yes
Test substance : other TS: Lion Corporation (Japan), Lot. No.: 000203, Purity = 96.6%
Method : - Test Organisms:
a) Age: < 24 hours old
b) Supplier/Source: Test organisms were obtained from National Institute for Environmental Studies (JAPAN) and had been reproduced in the testing laboratory.
c) Any pretreatment: Parental daphnids were acclimated for at least 19 days on test condition before testing. During acclimation, test daphnids were fed with Chlorella vulgaris, 0.1 - 0.2 mg carbon/day/individual. Any resting-egg and male daphnia was not observed. EC50(48hr, immobility) for reference substance (potassium dichromate) was 0.90 mg/L.

-Test substance: 2-Sulfo-hexadecanoic acid 1-methyl ester sodium salt
a) Empirical Formula: C17H33NaO5S
b) Molecular Weight: 372.49 g/mol
c) Purity: =96.6 %

-Test Conditions:
a) Dilution Water Source: Elendt M4 described in OECD TG211 was used.
b) Dilution Water Chemistry: pH: = 7.5
Total hardness (as CaCO3): = 252 mg/L
c) Exposure Vessel Type: 100 mL test solution in a 100 mLGlass Beaker
d) Nominal Concentrations: control, 0.48, 0.86, 1.54, 2.78 and 5.00 mg/L
e) Vehicle/Solvent and Concentrations: Any solvent was not used.
f) Number of Replicates: 4
g) Individuals per Replicates: 5
h) Water Temperature: 20+/-1ºC
i) Light Condition: 16:8 hours, light-darkness cycle
j) Feeding: None

- Analytical Procedure: Test concentrations were measured at the start and the end of the test using LC-MS , with detection limit of 0.02 mg/L.

- Statistical Method:
a) Data Analysis: Binominal method for EC50
b) Method of Calculating Mean Measured Concentrations: Geometric Mean

Result **:** - Measured Concentrations: The test concentrations were measured at the start and the end of the test. For some of them, the deviations from the nominal were not less than +/-20%.

Nominal Conc.	Measured Conc., mg/L		Percent of Nominal Mean*		
mg/L	0 Hour Fresh	48 Hour Old	mg/L	0 Hour Fresh	24 Hour Old
Control	<0.02	<0.02	---	---	---
0.48	0.40	0.36	0.38	83.3	75.0
0.86	0.65	0.62	0.63	75.6	72.1
1.54	1.15	1.03	1.09	74.7	66.9
2.78	2.35	2.08	2.21	84.5	74.8
5.00	3.89	3.69	3.79	77.8	73.8

Fresh: freshly prepared test solution
Old: test solution after 48 hours exposure
*: Mean measured concentration (Geometric Mean)

- Water chemistry (pH and DO) and temperature in test: Water chemistry and temperature were measured for control and each concentration at the start and the end of the test.
pH: 7.2 - 7.6
DO: 8.2 - 8.8 mg/L
Water Temperature: 20.2 - 20.7ºC

-Effect Data:
EC0 (48hr) = 0.63 mg/L (mc)
EC50 (48hr) = 1.24 mg/L (mc) (95% C.I.: 0.63 - 2.21 mg/L)
EC100(48hr) = 2.21 mg/L(mc)
mc: based on measured concentration

-Mortality or Immobility: No test organisms were Immobilized at control, 0.38 and 0.63 mg/L. The lowest concentration that the test organisms were affected was 1.09 mg/L after 48 hours. All test organisms were affected at 2.21 and 3.79mg/L on and after 48th hour.

Measured Conc. mg/L	Cumulative Number of Died or Immobilized Daphnids (Percent Mortality or Immobility) 24 Hour	48 Hour
Control	0 (0)	0 (0)
0.38	0 (0)	0 (0)
0.63	0 (0)	0 (0)
1.09	0 (0)	7 (35)
2.21	17 (85)	20 (100)
3.79	17 (85)	20 (100)

- Calculation of toxic values: The calculation of toxicity was made based on the mean measured concentrations..

Source : Ministry of Environment, Japan (2001)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
13.01.2003 (3)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : Growth inhibition (growth rate method and biomass method)
Exposure period : 72 hours
Unit : mg/l
Analytical monitoring : yes
NOEC : = 1.48 (area method), = 9.00 (rate method)
EC50 : > 9.00 (area method), > 9.00 (rate method)
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 2001
GLP : Yes
Test substance : other TS: Lion Corporation (Japan), Lot. No.: 000203, Purity = 96.6%
Method : - Test Organisms:
a) Supplier/Source: Obtained from American Type Culture Collection and reproduced in aseptic culture.
b) Method of Cultivation: Sterile
c) Stain Number: ATCC22662

d) Pre-culture (duration, medium, etc.): Test algae were pre-incubated for 3 days under the same conditions in OECD medium. EbC50 (0-72 hr) for a reference substance (potassium dichromate) was 0.41 mg/L.

-Test substance: 2-Sulfo-hexadecanoic acid 1-methyl ester sodium salt
a) Empirical Formula: C17H33NaO5S
b) Molecular Weight: 372.49 g/mol
c) Purity: =96.6 %

- Test Conditions:
a) Medium: OECD medium
b) Exposure Vessel Type: 100 mL Medium in a 300mL Erlenmeyer Flask with a silicon cap (open system)
c) Nominal Concentrations: control, 0.16, 0.36, 0.82, 1.89, 4.35 and 10 mg/L
d) Vehicle/Solvent and Concentrations: Any solvent was not used.
e) Stock Solutions Preparations and Stability: Test chemical was refrigerated. The stability of the chemical was confirmed by using IR spectrum and NMR spectrum.
f) Number of Replicates: 3
g) Initial Cell Number: 10,000 cells/mL
h) Water Temperature: 23+/-2ºC
i) Light Condition: 4,000 - 5,000 lux, continuously
j) Shaking: 100 rpm

- Analytical Procedure: Test concentrations were measured in all concentrations at the start and the 72nd hour using LC-MS, with detection limit of 0.02 mg/L..

- Statistical Method:
a) Data Analysis: regression analysis for EC50, and Dunnett multiple comparison, Bartlett's test and ANOVA for NOEC.
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Geometric mean

Result : - Measured Concentrations: The tested concentrations were measured at the start and the 72nd hour.

Mean* conc. mg/L	Nominal Conc.	Measured Conc., mg/L 0 Hour	Measured Conc., mg/L 72 Hour	Percent of nominal 0 Hour	Percent of nominal 72 Hour
0.00	Control	<0.02	<0.02	---	---
0.12	0.16	0.14	0.11	87.5	68.8
0.29	0.36	0.31	0.28	86.1	77.8
0.67	0.82	0.72	0.62	87.8	75.6
1.48	1.89	1.69	1.29	89.4	68.3
3.86	4.35	4.23	3.53	97.2	81.1
9.00	10.0	9.75	8.31	97.5	83.1

* Geometric mean

- Water chemistry (pH) and temperature in test: pH and water temperature

were measured for control and each concentration at the start and the end of test period. Each concentration solution was prepared for pH measurement independently of the test solutions. These test solutions were not add Algae.
pH: 7.2 - 7.8
water temperature: 23.0 - 24.9ºC

-Effect Data: biomass
Area Method
EbC50(0-72hr) > 9.0 mg/L (mc) (not available)
NOEC (0-72hr) = 1.48 mg/L (mc)
Rate Method
ErC50(24-48hr) > 9.0 mg/L (mc) (not available)
NOEC (24-48hr) > 9.0 mg/L (mc)
ErC50(0-72hr) > 9.0 mg/L (mc) (not available)
NOEC (0-72hr) > 9.0 mg/L (mc)
mc: measured mean concentration

- Percent Growth Inhibition of Selenastrum capricornutum

Measured Conc. mg/L	Area under the growth curves (Average) Area A (0-72hr)	Inhibition (%)* IA (0-72hr)
Control	15,070,000	---
0.12	14,940,000	0.85
0.29	14,330,000	4.89
0.67	13,950,000	7.43
1.48	14,410,000	4.36
3.86	12,850,000	14.71*
9.00	12,350,000	18.07*

* Significant difference (a=0.05)

Mean Measured Conc. mg/L	Growth rates and percent inhibition (Average) Rate u(24-48hr)	Inhibition (%) Im(24-48hr)	Rate u(0-72hr)	Inhibition (%) Im(0-72hr)
Control	0.0717	---	0.0798	---
0.12	0.0756	-5.51	0.0792	0.65
0.29	0.0708	1.27	0.0775	2.89
0.67	0.0721	-0.65	0.0775	2.81
1.48	0.0744	-3.75	0.0791	0.89
3.86	0.0719	-0.26	0.0789	1.11
9.00	0.0732	-2.13	0.0778	2.47

- Growth Curves: During the test period alga grew almost linearly in each concentration.

-Remarks
The Maximum Inhibition rate of 18.07 %, was observed at the highest concentration, 9.00mg/L by biomass method, however EC50s could not taken in this test by both biomass method and growth rate method.
And, at all concentrations the inhibition rates were not significant difference

to the control, so LOECs was not available.

Source : Ministry of Environment, Japan (2001)
Reliability : (12) valid with restrictions

Flag : Critical study for SIDS endpoint
13.01.2003 (3)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Endpoint : Reproduction rate
Exposure period : 21 day
Unit : mg/l
Analytical monitoring : yes
NOEC : = 0.24
LCEC : = 0.38
EC50 : = 0.7
Method : OECD Guide-line 211 "Daphnia sp., Reproduction Test"
Year : 2001
GLP : yes
Test substance : other TS: Lion Corporation (Japan), Lot. No.: 000203, Purity = 96.6%
Method : -Test Organisms:
a) Age: < 24 hours old
b) Supplier/Source: Test organisms were obtained from National Institute for Environmental Studies (JAPAN) and had been reproduced in the testing laboratory for 5 years and 9 months.
c) Any pretreatment: Parental daphnids were acclimated for at least 21 days on test conditions before testing, any groups showing high mortality were not used for testing. EC50(48 hr, immobility) for a reference substance (potassium dichromate) was 0.90mg/L.

-Test substance: 2-Sulfo-hexadecanoic acid 1-methyl ester sodium salt
a) Empirical Formula: C17H33NaO5S
b) Molecular Weight: 372.49 g/mol
c) Purity: =96.6 %

- Test Conditions:
a) Dilution Water Source: Elendt M4 described in OECD TG211 was used.
b) Dilution Water Chemistry:
pH: = 6.7
Total hardness (as CaCO3): = 244 mg/L
c) Exposure Vessel Type: 80 mL test solution in a heat-resistance glass jar
d) Nominal Concentrations: control, solvent control, 0.08, 0.14, 0.26, 0.46, 0.83 and 1.50 mg/L
e) Vehicle/Solvent and Concentrations: Any solvent was not used.
f) Stock Solutions Preparations and Stability: Test chemical was refrigerated. The stability of the chemical was confirmed by IR spectrum

and NMR spectrum.
g) Number of Replicates: 10
h) Individuals per Replicates: 10
i) Renewal Rate of Test Water: three times per week
j) Water Temperature: 20+/-1ºC
k) Light Condition: 16:8 hours, light-darkness
l) Feeding: 0.1 - 0.2 mg carbon/day/individual (Chlorella vulgaris: Green Algae)

- Analytical Procedure: The test concentrations were measured for both renewal and old test solution at the start of test and 2nd, 6th 8th, 13th and 15th day by a LC-MS method with a detection limit of 0.06 mg/L..

- Statistical Method:
a) Data Analysis: Bartlett's test and one-way analysis of variance for NOEC and LOEC logit method for EC50
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Time-weighted Mean

Remark : NOEC was determined based on the cumulative number of living juveniles produced per adult alive for 21 days.

Result : - Effect: reproduction- Measured Concentrations: The test concentrations were measured for both renewal and old test solution at the start of test and 2nd, 6th 8th, 13th and 15th day.

Nominal Conc.	Measured Conc., mg/L							
mg/L Date	0	2	6	8	13	15	TWM*	% of
	Fresh	Old	Fresh	Old	Fresh	Old	mg/L	Nominal
Control	<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	---	---
0.08	0.08	0.06	0.09	0.09	0.09	0.06	0.08	100.0
0.14	0.13	0.12	0.15	0.11	0.17	0.12	0.13	92.9
0.26	0.27	0.20	0.24	0.26	0.28	0.20	0.24	92.3
0.46	0.39	0.36	0.42	0.36	0.41	0.34	0.38	82.6
0.83	0.68	0.65	0.68	0.64	0.71	0.63	0.67	80.7
1.50	1.69	1.15	1.18	1.18	1.23	1.09	1.25	83.3

Fresh: Start of renewal period
Old: End of renewal period
*: Time-weighted mean of measured concentration during 21 days

- Measured Concentration as a Percentage of Nominal

Nominal Conc.	Measured Concentration as a Percentage of Nominal					
mg/L Date	0	2	6	8	13	15
	Fresh	Old	Fresh	Old	Fresh	Old
0.08	100	75.0	112.5	112.5	112.5	75.0
0.14	92.9	85.7	107.1	107.1	121.4	85.7
0.26	103.8	76.9	92.3	92.3	107.7	76.9
0.46	84.8	78.3	91.3	91.3	89.1	73.9
0.83	81.9	78.3	81.9	81.9	85.5	75.9
1.0	112.7	76.7	78.7	78.7	82.0	72.7

Fresh: Start of renewal period
Old: End of renewal period

- Water chemistry (pH and DO) and temperature in test: Water chemistry and temperature were measured for control and each concentration at the start of test and before and after renewal of the test solutions.
pH: 6.7 - 7.7
DO: 7.4 - 9.1 mg/L
Water Temperature: 20.0 - 20.8ºC

- Total hardness: 241 - 258 mg/L

-Effect Data:
Mortality of parents daphnids
LC50 (21day) = 1.12 mg/L (mc) (95% c.l.: 0.85 - 4.07 mg/L)
Inhibition of reproduction
EC50 (21day) = 0.70 mg/L (mc) (95% c.l.: 0.63 - 0.79 mg/L)
NOEC (21day) = 0.24 mg/L (mc)
LOEC (21day) = 0.38 mg/L (mc)
mc: based on measured concentration (Time weighted mean)

- Cumulative Number of Died Parental Daphnids: No test organism was killed at control solvent control, 0.13, 0.24 and 0.38 mg/L. The lowest concentration that test organisms were dead was at 0.08 mg/L after 5days.

Measured Conc. (mg/L)	Cumulative Number of Dead Parental Daphnids (Days) 1	2	3	4	5	6	7	8	9	10
Control	0	0	0	0	0	0	0	0	0	0
0.08	0	0	0	0	1	1	1	1	1	1
0.13	0	0	0	0	0	0	0	0	0	0
0.24	0	0	0	0	0	0	0	0	0	0
0.38	0	0	0	0	0	0	0	0	0	0
0.67	0	0	0	0	0	1	1	1	1	1
1.25	0	1	1	1	1	1	1	1	1	1

Measured Conc. (mg/L)	Cumulative Number of Dead Parental Daphnids (Days) 11	12	13	14	15	16	17	18	19	20	21
Control	0	0	0	0	0	0	0	0	0	0	0
0.08	1	1	1	1	1	1	1	1	1	1	2
0.13	0	0	0	0	0	0	0	0	0	0	0
0.24	0	0	0	0	0	0	0	0	0	0	0
0.38	0	0	0	0	0	0	0	0	0	0	0
0.67	1	1	1	1	1	1	1	1	1	1	1
1.25	1	4	5	5	5	5	5	5	5	5	6

-Effect Data(reproduction):Juveniles were first produced on the 8th day control and 0.24mg/L.

Measured Conc. mg/L	Mean Cumulative Numbers of Juveniles Produced per Adult (days) 0 --- 7	8	9	10	11	12	13	14
Control	0 --- 0	0.4	12.6	14.5	17.5	53.7	59.0	64.5
0.08	0 --- 0	0.0	11.8	17.1	17.1	48.4	60.1	60.1
0.13	0 --- 0	0.0	11.5	17.2	17.2	39.6	59.8	59.8
0.24	0 --- 0	1.2	15.4	15.4	19.0	57.1	57.1	63.0
0.38	0 --- 0	0.0	4.0	6.4	6.4	23.8	33.1	33.1
0.67	0 --- 0	0.0	0.2	0.4	1.2	11.1	17.3	18.7
1.25	0 --- 0	0.0	0.0	0.0	0.0	9.3	17.3	20.5

Measured Conc. mg/L	Mean Cumulative Numbers of Juveniles Produced per Adult (days) 15	16	17	18	19	20	21
Control	104.4	108.7	113.2	151.1	155.3	159.4	185.4
0.08	90.4	100.6	100.6	136.9	148.1	148.1	174.4
0.13	88.1	104.7	104.7	132.7	150.3	150.4	176.5
0.24	103.0	103.0	107.1	149.2	149.2	153.4	186.1
0.38	56.5	63.9	64.0	92.4	99.2	99.2	121.8
0.67	34.9	39.4	39.4	47.3	49.8	49.8	66.9
1.25	34.0	40.8	42.5	54.5	55.8	55.8	71.5

-Cumulative numbers of juveniles produced per adult alive for 21days

Vessel No.	Nominal Conc., mg/L (Measured Conc.1), mg/L) Cont.	0.08 (0.08)	0.14 (0.13)	0.26 (0.24)	0.46 (0.38)	0.83 (0.67)	1.50 (1.25)
1	188	158	179	185	152	47	---
2	209	---	158	161	129	53	---
3	211	207	140	194	113	19	44
4	165	---	211	172	127	47	---
5	175	202	191	182	102	---	40
6	185	172	138	180	123	78	---
7	162	123	199	211	132	99	105
8	195	149	208	190	140	107	97
9	157	216	147	202	100	72	---
10	207	168	194	184	100	80	---
Mean	185.4	174.4	176.5	186.1	121.8	66.9	71.5
S. D.	20.16	31.98	28.36	14.29	17.79	27.93	34.26
Inhibition rate(%)	5.9	4.8	-0.4	34.3**	63.9**	61.4**	

1): Time-weighted mean measured concentration.
*: Significant (alpha = 0.05)
**: significant at alpha = 0.01 level

- Calculation of toxicity values: The calculation of toxicity values was the mean measured concentrations. The reason is that some of the deviations

from the nominal concentration were not less than +/-20%.

Source : Ministry of Environment, Japan (2001)
Reliability : (1) Valid without restriction

Flag : Critical study for SIDS endpoint
13.01.2003 (3)

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	other: Crj:CD(SD)IGS
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: olive oil
Method	:	OECD Guideline 401 "Acute Oral Toxicity"
Year	:	
GLP	:	yes
Test substance	:	other TS: Lion Corporation, Lot No.000203, Purity:97.0%(impurities; disodium alpha-sulfopalmitate, sodium methylsulfate, palmitin acid)
Remark	:	Doses were 0, 786, 983, 1229, 1536, 1920 and 2400mg/kg bw for both sexes.
Result	:	LD50 values were 2142mg/kg bw for males and 1819mg/kg bw for females. One male and three female deaths at 1536 mg/kg bw, one male and two female deaths at 1920 mg/kg bw and four male and female deaths at 2400 mg/kg bw were observed. Most mortality was observed 6 to 24 hours after administration. Clinical signs such as decreased locomotor activity, ptosis, diarrhea, soiling of the perianal region and piloerection were observed in treated groups. Body weights in the treated groups were dose-dependently decreased. On necropsy, distention of the stomach with water content was observed in most of the animals that died.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

01.07.2003 (10)

Type	:	LD50
Species	:	rat
Strain	:	Crj: CD(SD)
Sex	:	male
Number of animals	:	5
Vehicle	:	no data
Method	:	other
Year	:	1990
GLP	:	no data
Test substance	:	other TS: Lion Corporation, A mixture (fatty acid, 2-sulfo-, 1-methylester, sodium salt) contained hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at 70%
Remark	:	Study design Ages of animals: 6 weeks Dosage : 350, 700, or 1400 mg/kg bw
Result	:	Deaths occurred on day 1 after treatment in 4 of 5 animals at 1400 mg/kg bw. Diarrhea at 350 and 700 mg/kg bw, and diarrhea, decreased locomotor activity and piloerection at 1400 mg/kg bw were observed on the day of treatment. The clinical signs in the survivor disappeared after the next day of treatment. No effects were detected on the body weight gain of the survivors. At necropsy, redness in the forestomach in 2 survivors at 350 and 700 mg/kg bw, and thickening of the forestomach mucosa in each one survivor at 700 and 1400 mg/kg bw, and erosin and retention of viscous liquid in the stomach and ileum in all dead animals were detected.
Reliability	:	(2) valid with restrictions

06.07.2003 (11)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : guinea pig
Concentration :
Exposure :
Exposure time :
Number of animals : 2
PDII :
Result : slightly irritating
EC classification :
Method : Draize test
Year : 1993
GLP : no data
Test substance : other TS:Lion Corporation; A mixture (tetradecanoic acid, 2-sulfo-,1-methylester, sodium salt : hexadecanoic acid, 2-sulfo-1-methylester, sodium salt = 20 : 80), Purity, 61.2%
Remark : Animal :Female Hartley guinea pig
Study design: A dose of 0.03 mL of 3.3, 8.2, 16.3, or 32.7% of test solution was applied to the test site (2 x 2 cm).
Animals were examined for signs of erythemes and edema at 24, 48, 72, 96, 120, 144 and 168 hours after treatment.
Dermal irritation was scored and recorded according to the grades in the Table 1, below.
Table 1
Erythema and eschar formation
No erythema ----------0
Very slight erythema (barelyperceptible)----------1
Well-defined erythema ----------2
Moderate to severe erythema ----------3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)----------4
Edema formation
No edema ----------0
Very slight edema (barely perceptible)----------1
Slight edema (edges of area well defined by definite raising)----------2
Moderate edema (raising approximately 1 millimeters)----------3
Severe edema (raising more than 1 millimeters and extending beyond area of exposure)----------4

Result : Results of skin response scored

Concentration(%)	24	48	72	96	120	144	168 (hrs)
32.7	0.5	0.5	0.5	0.5	0	0	0
16.3	0.5	0.5	0.5	0.5	0	0	0
8.2	1.0	0.5	0.5	5	0.5	0	0
3.3	0	0	0	0	0	0	0

Note: Each value expresses mean (scores of erythema + scores of edema/number of animals)

Reliability : (2) valid with restrictions
06.07.2003 (12)

Species : guinea pig
Concentration :
Exposure :
Exposure time :
Number of animals : 2
PDII :
Result : slightly irritating
EC classification :
Method : Draize test
Year : 1993
GLP : no data
Test substance : other TS: Lion Corporation, A mixture (tetradecanoic acid, 2-sulfo-,1-methylester, sodium salt : hexadecanoic acid, 2-sulfo-1-methylester, sodium salt = 30 : 70); Purity, 62.4%
Remark : Animal :Female Hartley guinea pig
Study design: A dose of 0.03 mL of 3.2, 8.0, 16.0, or 32.5% of test solution was applied to the test site (2 x 2 cm).
Animals were examined for signs of erythemes and edema at 24, 48, 72, 96, 120, 144 and 168 hours after treatment.
Dermal irritation was scored and recorded according to the grades in the Table 1, below.
Table 1
Erythema and eschar formation
No erythema ----------0
Very slight erythema (barelyperceptible)----------1
Well-defined erythema ----------2
Moderate to severe erythema ----------3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)---------- ----------4
Edema formation
No edema ----------0
Very slight edema (barely perceptible) ----------1
Slight edema (edges of area well defined by definite raising)----------2
Moderate edema (raising approximately 1 millimeters)----------3
Severe edema(raising more than 1 millimeters and extending beyond area of exposure)----------4

Result : Results of skin response scored

Concentration(%)	24	48	72	96	120	144	168 (hrs)
32.5	1.0	1.0	1.0	1.0	1.0	0.5	0
16.0	0.5	0.5	0.5	0.5	0	0	0
8.0	0.5	0	0	0	0	0	0
3.2	0	0	0	0	0	0	0

Note: Each value expresses mean (scores of erythema + scores of oedema/number of animals)

Reliability : (2) valid with restrictions
06.07.2003 (12)

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

Type : other: Local Lymph Node Assay
Species : Mouse
Number of animals :
Vehicle : other: dimethylformamide
Result : not sensitizing
Classification :
Method : other: OECD TG 429
Year : 2003
GLP : no data
Test substance : other TS: Purity 97.0%
Remark : Animal: Female CBA/J mice, ages of 9-10 weeks
No. of animals: four animals/group
Method: Local Lymph Node Assay
Result : Animal number vehicle group

		5%	10%	25%
1	432.9	393.4	515.0	721.6
2	248.3	506.4	461.8	267.9
3	318.3	238.3	331.9	220.9
4	198.1	214.4	1375.4	411.6
Mean	299.4	338.1	671.0	405.5
SD	101.7	137.4	475.8	225.8
SI		1.1	2.2	1.4

note
SD: Standard deviation
SI: Stimulation Index

Results: SL < 3 in any concentrations of the test substance
Reliability : (2) valid with restrictions
01.07.2003 (13)

5.4 REPEATED DOSE TOXICITY

Species : Rat
Sex : male/female
Strain : other: Crj:CD(SD)IGS
Route of admin. : Gavage
Exposure period : Males: 47 days.
Females: 42-45 days from 14 days before mating to day 4 of lactation.
Frequency of treatment : Once a day
Post obs. period : None
Doses : 5, 20, 80, 300 mg/kg bw/day
Control group : yes, concurrent vehicle
Method : OECD combined study TG422
Year : 2002
GLP : Yes
Test substance : other TS: Lion Corporation, Lot No.000203, Purity:97.0%(impurities; disodium alpha-sulfopalmitate, sodium methylsulfate, palmitin acid)
Remark : This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an

OECD screening combined study (Test guideline: 422).
Study design:
Vehicle: Olive oil
Clinical observation performed and frequency: General condition was observed once a day, body weights were determined on days 1 (before dosing), 8, 15, 22, 29, 36, 43 and 49 of treatment for males and on days 1, 8 and 15 of treatment and on days 0, 7, 14, and 20 of gestation and on days 0 and 4 of lactation and on day of autopsy for females, food consumption was determined on days 1, 8, 15, 22, 29, 36, 43 and 48 of treatment for males and on days 1, 8 and 15 of treatment and on days 0, 7, 14 and 20 of gestation and on days 0 and 4 of lactation for females, but food consumption was not determined during the mating period for males and females.
For all males, urinalysis was carried out on day 41 or 42 of the administration period. For all males and all females after childbirbirth, hematology and biochemistry were carried out at time of necropsy after 48 days for males and at 5 days after delivery for females. Organs were examined at necropsy.

Organ weights measured: Brain, heart, liver, kidney, spleen, adrenal, thymus, testis and epididymis in males, and brain, heart, liver, kidney, spleen, adrenal, thymus in females.
Organ weight was determined in 9 males at 20 mg/kg bw/day, in 10 males at 0 (control), 5, 80, and 300 mg/kg bw/day, in 7 females at 0 (control), 8 females at 5 mg/kg bw/day, in 9 females at 20 and 300 mg/kg bw/day, in 10 females at 80 mg/kg bw/day.

Microscopic examination: Brain, spinal code, stomach, intestine, liver, kidney, adrenal, spleen, heart, thymus, thyroid, parathyroid, trachea, lung, uterus, ovary, urinary bladder, ischiadic nerve, bone marrow, mesentery lymph node, mandibular lymph node, submandibular gland, sublingual gland for 5 males and 5 females in 0 and 300 mg/kg bw:/day groups, and stomach for 5 males and 5 females in 5, 20, 80 mg/kg bw/day groups.

Statistical methods: Dunnett's or Scheffe's test for continuous data and Chi square test for quantal data.

Result : NOAEL:20 mg/kg bw/day
Mortality: There was no mortality related to the test substance treatment.
Clinical signs: Transitional softening stools in a few males and females were observed in the 80 and 300 mg/kg bw/day groups.
Body weight: No statistically significant changes for males and females.
Food consumption: No statistically significant changes for males and females.
Urinalysis: No statistically significant changes.
Hematology: No statistically significant changes for males and females.
Blood biochemistry: Males: An increase in GPT levels and a decrease in triglyceride levels in 300 mg/kg bw/day groups.

Dose (mg/kg bw/day)		0	5	20	80	300
No. of animals		10	10	9	10	10
GPT(IU/L)	Mean	41	40	38	44	53**
	SD	4	6	3	6	7

Triglyceride (mg/dL)	Mean	63	43	50	49	29*
	SD	28	18	22	18	13

Note:**,P<0.01; *,P<0.05
Females: No statistically significant changes.

Necropsy: Thickening of the forestomach mucosa was observed in 6 of 10 males and 10 of 10 females at 80 mg/kg bw/day and 10 of 10 males and 9 of 9 females at 300 mg/kg bw/day.

Organ weights: No statistically significant changes for males and females.

Histopathology: Squamous hyperplasia, erosion, and lamina propria and/or submucosa edema and inflammatory infiltration were observed in the forestomach in both sexes of 80 and 300 mg/kg bw:/day groups.

Males:

Dose(mg/kg bw/day)	0	5	20	80	300
No. of animals examined	5	5	5	5	5
Forestomach					
Hyperplasia, squamous -	5	5	5	1	0
+,++,+++	0	0	0	4*	5**
Erosion -	5	5	5	5	2
+,++	0	0	0	0	3
Edema, lamina propria/submucosa					
-	5	5	5	2	1
+,++	0	0	0	3	4*
Cellular infiltration, inflammatory cell, lamina propria/ submucosa -	5	5	5	5	1
+,++	0	0	0	0	4*

Females:

Dose(mg/kg bw/day)	0	5	20	80	300
No. of animals examined	5	5	5	5	5
Forestomach					
Hyperplasia squamous -	5	5	5	1	0
+,++	0	0	0	4*	5**
Erosion -	5	5	5	5	4
++	0	0	0	0	1
Edema, lamina propria/submucosa					
-	5	5	5	3	0
+,++	0	0	0	2	5**
Cellular infiltration, inflammatory cell, lamina propria/ submucosa -	5	5	5	4	3
+	0	0	0	1	2

Note:-, Not detected; +,slight; ++,moderate;***,severer ;**,P<0.01; *,P<0.05

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
11.07.2003 (10)

Species : Rat
Sex : male/female
Strain : Crj: CD(SD)
Route of admin. : Dermal
Exposure period : Males:28 days, Females: 29 days

Frequency of treatment	:	Once a day
Post obs. period	:	None
Doses	:	2.1, 7.1, or 21.4%
Control group	:	yes, concurrent vehicle
Method	:	other: Chemical Substances Control Law of Japan
Year	:	2003
GLP	:	no data
Test substance	:	other TS: Lion Corporation, A mixture (dodecanoic acid, 2-sulfo-, 1-methylester,sodium salt : tetradecanoic acid, 2-sulfo-,1-methylester, sodium salt : hexadecanoic acid, 2-sulfo-1-methylester, sodium salt = 10 : 20 : 70), Purity, 70.3%
Remark	:	Crj:CD(SD) rats (five animals/sex/dose) were received daily dermal application of 0.2 mL per rat of test solution at concentration of 0, 2.1, 7.1, or 21.4%. Males were applied for 28 days and females were applied for 29 days. Observation and examination items: Clinical sign, reaction of skin, body weight, food consumption, urinalysis, hematological examination, blood chemical examination, necropsy, organ weight and histopathological examination.
Result	:	A primary skin irritation was observed at 21.4% in both sexes. In histopathlogical examination, thickening of the epidermis were also found at the highest concentration. No-compound related changes in clinical signs, body weight, food consumption, organ weight, urinalysis, hematological findings, blood chemical findings or histopathological findings in the major organs were noted. No other detailed information was available.
Reliability	:	(2) valid with restrictions

06.07.2003 (14)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Test species/strain: Salmonella typhimurium TA100, TA1535, TA98, TA1537, Escherichia coli WP2 urvA
Concentration	:	0, 0.625, 1.25, 2.5, 3.13, 5, 6.25, 10, 12.5, 20, 25, 31.3, 50, 62.5, 100, 125, 156, 200, 250, 313, 500, 625, 1000, 1250, 2000, 2500, 5000 µg/plate
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	Negative
Method	:	other: Chemical Substances Control Law of Japan and OECD Test Guideline 471
Year	:	2002
GLP	:	Yes
Test substance	:	other TS: Lion Corporation; Lot No.000203, Purity:97.0%(impurities; disodium alpha-sulfopalmitate, sodium methylsulfate, palmitin acid)
Remark	:	Solvent: Dimethyl sulfoxide Dosage of each strain with or without S9 -S9 mix:0, 0.625, 1.25, 2.5, 5, 10, 20 µg/plate(TA100, TA1535, TA1537) -S9 mix:0, 156, 313, 625, 1250, 2500, 5000 µg/plate(WP2 uvrA) -S9 mix:0, 3.13, 6.25, 12.5, 25, 50, 100 µg/plate(TA98) +S9 mix:0, 62.5, 125, 250, 500, 1000, 2000 µg/plate(TA100) +S9 mix:0, 31.3, 62.5, 125, 250, 500, 1000 µg/plate(TA1537) +S9 mix:0, 6.25, 12.5, 25, 50, 100, 200 µg/plate(TA1535, TA98) +S9 mix:0, 156, 313, 625, 1250, 2500, 5000 µg/plate(WP2 uvrA) S9:Rat liver, induced with phenobarbital and 5,6-benzoflavone Positive control: -S9 mix; 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, TA98, WP2

uvrA), sodium azide (TA1535) and 9-Aminoacridine (TA1537)
+S9 mix; 2-Amonoanthracene (all strains)
Plates/test:3
Number of replicates:2

Result : Cytotoxic concentration: Toxicity was not observed up to the highest dose in any strain with or without S9. Growth inhibition was observed at 20 µg/plate (TA100, TA1535 and TA1537) and at 100 µg/plate (TA98) without S9 mix, and at 2000 µg/plate (TA100), at 1000 µg/plate (TA1537), and at 200 µg/plate (TA1535 and TA98) with S9 mix.
Genotoxic effects:
Positive control
Without metabolic activation: positive
With metabolic activation: positive

Salmonella typhimurium TA100, TA1535, TA98, TA1537
Without metabolic activation: negative
With metabolic activation: negative

Escherichia coli WP2 uvrA
Without metabolic activation: negative
With metabolic activation: negative

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
06.07.2003 (10)

Type : Ames test
System of testing : Test species/strain: Salmonella typhimurium TA100, TA1535, TA98, TA1537, Escherichia coli WP2 urvA
Concentration : From1 to 3500 µg/plate (8 steps)
Cycotoxic conc. : -S9 mix: more than 17.5 µg/plate for TA98, TA100, TA1535; more than 0.9 µg/plate for TA1537; +S9 mix: more than 175 µg/plate for TA98, TA1537; at 350 µg/plat for TA100; more than 350 µg/plate for TA1535
Metabolic activation : with and without
Result : Negative
Method : other: Guideline for toxicity studies of drugs in Japan, OECD TG 471 and 472
Year : 1990
GLP : no data
Test substance : other TS: Lion Corporation, A mixture (fatty acid, 2-sulfo-, 1-methylester, sodium salt) contained hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at 70%, Purity: 86.1%
Remark : Solvent: Distilled water
Result : Cytotoxic concentration:
-S9 mix: More than 17.5 µg/plate for TA98, TA100, TA1535
More than 0.9 µg/plate for TA1537
Cytotoxicity was not observed up to 3500 µg/ plate for WP2uvrA.
+S9 mix: More than 175 µg/plate for TA98, TA1537
At 350 µg/plate for TA100
More than 350 µg/plate for TA1535
Cytotoxicity was not observed up to 3500 µg/ plate for WP2uvrA.

Positive control
Without metabolic activation: positive
With metabolic activation: positive

Salmonella typhimurium TA100, TA1535, TA98, TA1537
Without metabolic activation: negative
With metabolic activation: negative

Escherichia coli WP2 uvrA
Without metabolic activation: negative

With metabolic activation: negative

Reliability : (2) valid with restrictions
01.07.2003 (15)

Type : Chromosomal aberration test
System of testing : Type of cell used: Chinese hamster lung(CHL) cell
Concentration : 0, 15.6, 31.3, 62.5, 125, 187.5, 250 µg/mL
Cycotoxic conc. : 187.5 and 250 µg/mL
Metabolic activation : with and without
Result : Negative
Method : other: Chemical Substances Control Law of Japan and OECD Test Guideline 473
Year : 2002
GLP : Yes
Test substance : other TS: Lion Corporation; Lot No.000203, Purity:97.0%(impurities; disodium alpha-sulfopalmitate, sodium methylsulfate, palmitin acid)
Remark : Solvent:Physiological saline
Dosage:
-S9 mix(6 hr short-term treatment):0, 31.3, 62.5, 125, 187.5, 250 µg/mL
+S9 mix(6 hr short-term treatment):0, 31.3, 62.5, 125, 187.5, 250 µg/mL
-S9 mix(24 hr continuous treatment):0, 15.6, 31.3, 62.5, 125, 187.5, 250 µg/mL
S9 mix: Rat liver, induced with phenobarbital and 5,6-benzoflavone
Positive control:
-S9 mix;1-Methyl-3-nitro-1-niterosoguanidine
+S9 mix;3,4-Benzo[a]pyrene
Plates/test:2
50% growth inhibition was observed between 125 and 250 µg/mL for short-term treatment and continuous treatment with or without S9 mix.
Result : No increase in chromosomal aberrations was observed after short-term or continuous treatment with or without S9 mix.
Cytotoxicity was observed at 187.5 and 250 µg/mL without S9 mix and at 250 µg/mL with S9 mix after 6 hr short-term treatment, and observed at 187.5 and 250 µg/mL after 24 hr continuous treatment without S9 mix.
Genotoxic effects:

	clastogenicity			polyploid		
	+	?	-	+	?	-
Without metabolic activation:	[ ]	[ ]	[*]	[ ]	[ ]	[*]
With metabolic activation:	[ ]	[ ]	[*]	[ ]	[ ]	[*]

Positive control	clastogenicity			polyploid		
	+	?	-	+	?	-
Without metabolic activation:	[*]	[ ]	[ ]	[ ]	[ ]	[*]
With metabolic activation:	[*]	[ ]	[ ]	[ ]	[ ]	[*]

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
06.07.2003 (10)

Type : Chromosomal aberration test
System of testing : Type of cell used: Chinese hamster lung(CHL) cell
Concentration : 0.02 to 0.20 mg/mL
Cycotoxic conc. :
Metabolic activation : with and without
Result : Negative
Method : other: Guideline for toxicity studies of drugs in Japan and OECD TG 473
Year : 1998
GLP : no data

Test substance	:	other TS: Lion Corporation, A mixture (fatty acid, 2-sulfo-, 1-methylester, sodium salt) contained hexadecanoic acid, 2-sulfo-, 1-methylester, sodium salt at 80%, Purity: 64.5%
Remark	:	Solvent: Physiological saline Dosage: -S9 mix(24 hr continuous treatment):Five concentrations from 0.04 to 0.12 mg/mL by factor 0.025 -S9 mix(48 hr continuous treatment):Five concentrations from 0.02 to 0.10 mg/mL by factor 0.025 +S9 mix:Five concentrations from 0.04 to 0.20 mg/mL by factor 0.05 Each highest dose was more than the concentration of 50% growth inhibition for 24 hr and 48 hr continuous treatment without S9mix and for with S9 mix. Positive control: -S9 mix; MMC +S9 mix; BP
Result	:	50% growth inhibition was observed at concentrations of 0.104 mg/mL for 24 hr continuous treatment, 0.088 mg/mL for 48 hr continuous treatment and 0.20 mg/mL for with S9mix. No increase in chromosomal aberrations was observed.
Reliability	:	(2) valid with restrictions

01.07.2003 (16)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

Type	:	Other
Species	:	Rat
Sex	:	male/female
Strain	:	other: Crj:CD(SD)IGS
Route of admin.	:	Gavage
Exposure period	:	Males:47 days. Females:42-45 days from 14 days before mating to day 4 of lactation.
Frequency of treatment	:	Once a day
Premating exposure period		
Male	:	14 days
Female	:	14 days
Duration of test	:	Males: 48 days. Females: from 14 days before mating to day 5 of lactation
Doses	:	5, 20, 80, 300 mg/kg bw/day
Control group	:	yes, concurrent vehicle
Method	:	other: OECD Test guideline 422
Year	:	2002
GLP	:	Yes
Test substance	:	other TS: Lion Corporation; Lot No.000203, Purity:97.0% (impurities; disodium alpha-sulfopalmitate, sodium methylsulfate, palmitin acid)
Remark	:	This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study (Test guideline: 422).

Study design:
Vehicle: Olive oil
Clinical observation performed and frequency: General condition was observed once a day, body weights were determined on days 1 (before dosing), 8, 15, 22, 29, 36, 43 and 49 of treatment for males and at days 1, 8 and 15 of treatment and on days 0, 7, 14,and 20 of gestation and on days 0 and 4 of lactation and on day of autopsy for females, food consumption was determined on days 1, 8, 15, 22, 29, 36, 43 and 48 of treatment for males and on days 1, 8 and 15 of treatment and on days 0, 7, 14 and 20 of gestation and on days 0 and 4 of lactation for females, but food consumption was not determined during the mating period for males and females.
For all males, urinalysis was carried out on day 41 or 42 of the administration period. For all males and all females after childbirth, hematology and biochemistry were carried out at time of necropsy after 48 days for males and at 5 days after delivery for females. Organs were examined at necropsy.

Organ weights measured: Brain, heart, liver, kidney, spleen, adrenal, thymus, testis and epididymis in males, and brain, heart, liver, kidney, spleen, adrenal, thymus in females.
Organ weight was determined in 9 males at 20 mg/kg bw/day, in 10 males at 0(control), 5, 80, and 300 mg/kg bw/day, in 7 females at 0(control), 8 females at 5 mg/kg bw:/day, in 9 females at 20 and 300 mg/kg bw/day, in 10 females at 80 mg/kg bw/day.

Microscopic examination: Brain, spinal code, stomach, intestine, liver, kidney, adrenal, spleen, heart, thymus, thyroid, parathyroid, trachea, lung, uterus, ovary, urinary bladder, ischiadic nerve, bone marrow, mesentery lymph node, mandibular lymph node, submandibular gland, sublingual gland for 5 males and 5 females in 0 and 300 mg/kg bw/day groups, and stomach for 5 males and 5 females in 5, 20, 80 mg/kg bw/day groups.

Reproductive and developmental parameters: No. of pairs with successful copulation, No. of pregnant females, copulation index (No. of pairs with successful copulation/No. of pairs mated x 100), fertility index (No. of pregnant animals/No. of animals with successful copulation x 100), estrous cycle, No. of pregnant females with live pups, gestation length, No. of corpora lutea, No. of implantation sites, No. of pups born, No. of pups alive on day 0 of lactation, sex ratio, No. of dead pups, gestation index (No. of females with live pups/No. of pregnant females x 100), implantation index (No. of implants/No. of corpora lutea x100), delivery index (No. of pups born/No. of implants x100), live birth index (No. of live pups born/No. of pups born x 100), and viability index on day 4 (No. of live pups on day 4 after birth/No. of live pups born x 100).

Statistical methods: Dunnett's or Scheffe's test for continuous data and Chi square test for quantal data.

Result : NOAEL: 300mg/kg bw/day for reproductive performance of parental animals and for offspring development.
Mortality: There was no death related to the test substance treatment.
Clinical signs: Transitional softening stools in a few males and females were observed in the 80 and 300 mg/kg bw/day groups.
Body weight: No statistically significant changes for males and females.
Food consumption: No statistically significant changes for males and females.
Urinalysis: No statistically significant changes.
Hematology: No statistically significant changes for males and females

Blood biochemistry: Males: An increase in GPT levels and a decrease in triglyceride levels in the 300 mg/kg bw/day group.

Necropsy: Thickening of the forestomach mucosa was observed in both sexes of the 80 and 300 mg/kg bw/day groups.

Organ weights: No statistically significant changes for males and females.

Histopathology: Squamous hyperplasia, erosion, and lamina propria and/or submucosa edema and inflammatory infiltration were observed in the forestomach in both sexes of the 80 and 300 mg/kg bw/day groups.

Reproductive and developmental parameters: No effects of this substance were observed on reproductive performance in males and females or on viability and body weight of offspring. No malformations were found in offspring in any groups.

Dose (mg/kg bw/day)		0	5	20	80	300
Estrous cycle (days)	Mean	4.2	4.0	4.0	4.0	4.0
	SD	0.6	0.0	0.0	0.1	0.1
No. of pairs mated		10	10	10	10	10
No. of pairs copulated		10	10	9	10	10
Copulation index (%)		100	100	90	100	100
No. of pregnant females		7	10	9	10	10
Fertility index (%)		70	100	100	100	100
No. of pregnant females with parturition		7	8	9	10	10
No. of pregnant females with live pups		7	8	9	10	10
Gestation length(days)	Mean	22.4	22.5	22.4	22.6	22.5
	SD	0.5	0.5	0.5	0.5	0.5
No. of corpora lutea	Mean	19.7	18.4	19.3	17.5	18.2
	SD	2.8	4.1	3.3	1.9	2.6
No. of implantation sites	Mean	15.6	13.2	14.9	15.9	15.3
	SD	1.6	6.3	2.4	1.5	2.4
No. of pups born	Mean	15.0	11.9	13.1	14.8	13.9
	SD	1.7	6.4	4.0	2.0	1.7
Delivery index(%)	Mean	96.3	73.8	85.4	93.3	91.4
	SD	4.8	39.4	20.0	10.1	6.1
Sex ratio(Male/female)		0.78	0.98	0.97	0.85	0.88
No. of pups alive on day 0 of lactation	Mean	15.0	14.9	13.0	14.4	12.3
	SD	1.7	1.6	3.9	2.0	4.2
Live birth index(%)	Mean	100	100	99.3	97.4	88.3
	SD	0	0	2.1	4.6	27.2
No. of pups alive on day 4 of lactation	Mean	14.7	14.9	12.9	14.2	12.0
	SD	1.4	1.6	3.8	1.8	4.7
Viability index	Mean	98.3	100	99.3	98.7	89.3
	SD	2.9	0	2.2	2.7	31.5

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
11.07.2003 (10)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	Rat
Sex	:	Female
Strain	:	Crj: CD(SD)
Route of admin.	:	Dermal
Exposure period	:	Days of 7-17 of pregnancy
Frequency of treatment	:	Once a day
Duration of test	:	no data
Doses	:	2.1, 7.1, 21.4%
Control group	:	yes, concurrent vehicle
Method	:	other: Guideline for toxicity studies of drugs, 1988(Japan)
Year	:	2003
GLP	:	no data
Test substance	:	other TS: Lion Corporation, A mixture (dodecanoic acid, 2-sulfo-, 1-methylester,sodium salt, tetradecanoic acid : 2-sulfo-,1-methylester, sodium salt : hexadecanoic acid, 2-sulfo-1-methylester, sodium salt = 10 : 20 : 70), Purity, 70.3%
Remark	:	Study design: Vehicle: Distilled water The test solution was applied uniformly over an area (3 x 4 cm) of the skin on the back of the test animal once a day for 11 days from 7 to 17 days of gestation. The volume of dose was 0.2 mL/head. Dose levels: 0(distilled water), 2.1, 7.1, 21.4% Number of animals examined: 27(control group), 27(2.1% group), 28(7.1% group), or 28(21.4% group) Observation and examination: The observations of clinical signs and reaction of the skin at the treated area, body weight, and food consumption and morphological fetal examination were carried out.
Result	:	No effects were detected in the maternal examination such as clinical signs, body weight gain, food consumption, and necropsy of dams, and in the fetal examination.
Reliability	:	(2) valid with restrictions

05.07.2003 (17)

5.10 OTHER RELEVANT INFORMATION

Type	:	other: Information on irritation and sensitization of related compound
Remark	:	Three soap-based detergent formulations contain sodium methyl alfa-sulfo-tallowate, sulfated N-(2-sulfoethyl)tallowamide, and sodium N-methyl N-(2-sulfoethyl)tallowamide. The test compound was carried out to examine the skin and eye irritation using rabbits and sensitization using guinea pigs.
Reliability	:	(4) not assignable

06.07.2003 (18)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) Chemicals Evaluation and Research Institute (CERI), Japan. (2000). Unpublished data. Report number 21515.

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(3) Chemicals Evaluation and Research Institute (CERI), Japan. (2000b). Unpublished data. Report number K-1515.

(4) Chemicals Evaluation and Research Institute (CERI), Japan. (2000c). Unpublished data. Report number K-1515.

(5) Chemicals Evaluation and Research Institute (CERI), Japan (2000d). Unpublished data. Report number K-1515.

(6) Chemicals Evaluation and Research Institute (CERI), Japan (2000e). Unpublished data. Report number K-1515.

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(8) Masuda, M. et al., J. Jpn. Oil Chem. Soc. (YAKUGAKU), 42, 643 (1993).

(9) Weil et al., J. Amer. Chem. Soc.

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(11) a Lion Corporation (1990), Acute toxicity study of MES in rats. Unpublished

(12) Lion Corporation (1993), Skin irritation study of C146-MES in guinea pigs. Unpublished data

(13) Lion Corporation (2003), Skin sensitization study of hexadecanoic acid, 2-sulfo-, 1-methyleater, sodium salt by mouse local lymph node assay. Unpublished data

(14) Lion Corporation (2003), Twenty-eight days dermal application toxicity study of C1246-MES in rats. Unpublished data

(15) Lion Corporation (1990), Bacterial reverse gene mutation assay of MES. Unpublished data

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